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The Intersection of Robotic Surgery and AI: Revolutionizing Healthcare

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Integrating robotic technology and advanced intelligence systems in surgery into a suite of precision, efficiency and improvement in patient outcomes represents a new era in surgery. Surgical procedures are undergoing these developments that are changing the procedures and have great potential for innovation in techniques and protocol streamlining.

In particular, modern robotic surgical platforms help surgeons during complex procedures including minimally invasive surgery. Because of how precise, dexterous and minimally invasive these systems are, they not only shorten patient recovery time, but there is reduced blood loss and smaller incisions. The da Vinci system is certainly one of the Halls of Movers. Computational intelligence takes these systems to the next level by broadening their capabilities and conceiving new space in the field of surgical practice.

Real time assistance for robotic surgery is gained by intelligence based systems which led to increase in robotic surgery efficacies. Extensive data is processed by advanced algorithms, patterns are found, and suggestions are provided to guide surgeons around operating table.

For instance, these systems can use medical imaging to generate three-dimensional visualizations of organs and tissues with great detail and thus help surgeons plan surgery more accurately. When the surgery is on, the technology follows the surgical field to suggest the best instrument position and to minimize risks. These algorithms also can find potential complication earlier, so surgeons can perform remedial procedures.

Advanced computing and robotic surgery promises tremendous advance in patient care. Together these technologies minimize invasive approaches and decrease the risk of infection, scarring, and protracted recovery periods. Less pain, shorter hospital stays and faster recoveries for daily activities are typical for patients. Beyond that, the systems learn and get better, getting increasingly more precise and personal with each procedure.

Whilst robotic surgical systems currently have a high cost, this does so far prevent wider spread adoption in resource constrained settings. However, as more and more computational help becomes a fundamental piece of the surgery puzzle, it is necessary to think about data privacy, algorithmic bias and etc that can ensure ethical activity.

However, the future of robotics and intelligent endo surgery seems bright. While these technologies are not just helping to refine surgical capabilities, they are revolutionizing patient care making procedures safer, more precise and less invasive. This integration will certainly have an impact on our modern era of medicine.

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Original Article

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Patterns of Asthma Control among Asthmatic Patients Presenting at Tertiary Care Hospital, Larkana

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ABSTRACT

Asthma is the most prevalent pediatric chronic condition and the leading cause of preventable pediatric hospitalization. Despite its prevalence, asthma is a poorly managed condition. Effective therapies to enhance and sustain asthma control are required. **Objective:** To determine the frequency of patterns of asthma control among asthmatic patients presenting at a tertiary care hospital, Larkana. **Methods:** Cross-sectional research was conducted at the Children's Hospital in Larkana between January 21 and June 23. Quantitative and qualitative data were gathered, presented, and evaluated. Effect modifiers were controlled via stratification to determine their impact on the result variable. The chi-square test was used after post-stratification, with a p-value of ≤0.05 considered significant. **Results:** The study involved 143 patients, with an average age of 7.14 ± 3.49 years and a duration of 25.72 ± 10.24 months, with 72 (50.3%) men and 71 (49.7%) women. Of the 143 patients, 45.5%, 30.1%, and 24.5% had well, partially, and poorly controlled asthma, respectively. **Conclusions:** It was concluded that 45.5% achieved well-controlled asthma, 30.1% exhibited partial control, and 24.5% had poorly controlled asthma. These findings highlight the need for personalized interventions, emphasizing the importance of exploring factors influencing suboptimal control.

INTRODUCTION

Asthma, a common chronic non-communicable illness, affects 280 million people worldwide and is estimated to kill half a million people by 2022, including children and adults [1]. Childhood asthma is defined as children with medically diagnosed asthma based on clinical history by a physician for more than six months (at least two previous episodes of wheezing), physical examination (musical, high-pitched, whistling sound), and the improvement of symptoms on treatment with B2 agonist. In Pakistan, the world's fifth-most populated country, 4.3% of its 221 million people are suspected of having asthma. Seasonal asthma is more common in specific areas, impacted by indoor and outdoor allergens, occupational asthma, environmental pollutants, and lifestyle changes [2]. Asthma, a common chronic non-communicable illness, affects over 260 million people and claims over 450,000 lives each year. According to the Global Initiative for Asthma (GINA) study, the prevalence in adult's ranges between 1% and 21%, with potentially greater rates in children [2, 3]. Countries with prevalence rates in this range include Pakistan (13.07%), Kuwait (13.66%), and Libya (12.55%), with certain populations having prevalence rates ranging from 8 to 11% [4]. Research conducted in Karachi in 2006 indicated that asthma incidence was 18% among teenagers aged 13 to 14, while Pakistan's GINA report indicates a prevalence of 4-5% [3, 4]. Rising urbanization, air pollution, tobacco smoke exposure, and antibiotic usage, genetics, and other modern lifestyle variables continue to contribute to the expanding asthma

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pandemic [5, 6]. It is generally documented that effective asthma control depends on the patient's commitment to daily medication regimens. Taboos and misunderstandings about asthma in our culture are additional risk factors that impede good asthma care [7]. Adherence to asthma drug regimens varies widely, with studies reporting adherence rates ranging from 30% to 70%. Bad adherence to treatment regimens reduces the effectiveness of prescription drugs and hence raises the chance of bad outcomes [8]. The literature identifies many measures that are now in use to explicitly assess asthma control in adults and children based on patient symptoms, rescue medicine usage, and daily activity limitations. The Asthma control questionnaire (ACQ), Asthma control test (ACT), and Asthma therapy assessment questionnaire (ATAQ) are commonly used clinical instruments in assessing asthma control, therapy, and control [9]. Asthma is diagnosed based on clinical presentation, history, physical assessment, and diagnostic tests, including spirometry and PEFR. Similar tests are required to monitor sickness progression, severity, and changes in duration and intensity. Reliable and accurate results require adequate abilities and high-quality spirometry [10]. In study conducted by Mansoor et al., 33 (25.58%) of patients had asthma control category A on ACT, indicating that their asthma was well managed; 65 (50.38%) had asthma control category B on ACT, indicating that their asthma was somewhat controlled; and 31 (24.01%) had asthma control category C on ACT, indicating that their asthma was badly controlled [11]. Previously, the Global Initiative for Asthma (GINA) guidelines divided asthma severity into categories based on the number of symptoms, airway limitation, and variability. However, it is vital to note that asthma severity comprises both the severity of the underlying illness and the response to treatment. As a result, the amended GINA recommendations propose that asthma control be assessed regularly rather than just based on severity. The Asthma Control Test (ACT) questionnaire can assist us in assessing the pattern of asthma control in resource-limited settings. Furthermore, the majority of patients are uneducated, and even those who are read lack awareness. Simple questionnaires like the Asthma Control Test (ACT) are essential for timely intervention, quantifying asthma control, preventing emergency admissions, and educating patients about asthma management, making them cost-effective, understandable, and accessible to illiterate patients. Asthma is a prevalent chronic respiratory condition worldwide, affecting patients' quality of life and burdening healthcare systems. Effective asthma control is crucial to prevent exacerbations, reduce hospital admissions, and improve patient outcomes. However, asthma control patterns can vary due to factors like treatment adherence, environmental triggers, and comorbidities. Tertiary care hospitals often have diverse patients with varying asthma severity, making understanding the frequency and patterns of asthma control essential for identifying management strategies and optimizing care delivery. Limited data exists on specific trends and factors influencing asthma control among patients.

This study aimed to investigate the frequency of patterns of asthma control amongst asthmatic patients admitted to children's hospitals. The study seeks to evaluate the proportion of patients achieving controlled, partially controlled, and uncontrolled asthma and also to analyze factors contributing to variations in asthma control.

METHODS

A descriptive cross-sectional study was carried out during the period from January 2021 to June 2023 at the Department of Pediatrics, Children's Hospital, Larkana. This study was approved by the hospital's ethical review committee and the College of Physicians and Surgeons of Pakistan with Ref No: CPSP/REU/PED-2020-221-5990. The required sample size was calculated to be 143 patients; by assuming the frequency of 24.01% poorly controlled asthma [11], the margin of error is 7%, and the confidence level 'C.I.' is 95%. This sample size was determined using WHO software. Consecutive (non-probability) sampling was used during the sampling process. Patients between 4-12 years of age, either gender, having had childhood asthma for more than six months were selected. The study included patients with a history of allergic rhinitis, pneumonia, or tuberculosis; those who have a history of cleft lip & palate, congenital heart disease, or drug allergy were excluded. Patients known to have childhood asthma, meeting inclusion criteria, were documented in the study from the Outpatient Department (OPD) of Pediatrics, Children's Hospital, Larkana. Parents were informed about the risks, benefits, and purpose of the study. Before being included, written informed permission was obtained. All data obtained during the study was kept confidential in a computer that was password protected. A brief demographic history was obtained. The parents filled out the questionnaire in the presence of the researcher. Patients were categorized into the category of asthma control and were assessed by applying the Asthma Control Test (ACT) questionnaire. All patients were classified as A, B, or C based on their asthma control test. Asthma scores of ≥20 were classified as well-controlled (category A), 16-19 as partially controlled (category B), and ≤15 as poorly controlled (category C). The results of quantitative variables (age and childhood asthma duration) and qualitative variables (gender, residential status, family history of asthma, family monthly income status, maternal educational status, and pattern of asthma control) were

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noted in the performance. The data were processed using SPSS Version 22.

RESULTS

The study involved 143 patients aged 4-12 years at Children's Hospital Larkana. In the study, the mean age and duration of asthma were 7.14 ± 3.49 years and 25.72 ± 10.24 months, respectively. In the study, different demographic frequencies were observed; for example, in gender distribution, out of 143 patients, 72 (50.3%) and 71 (49.7%) were male and female, while in age distribution, 47 (32.9%) in 4-8 years and 96 (67.1%) in 9-12 years' patients, respectively. Out of 143 patients, 116 (81.1%) and 27 (18.9%) had urban and rural residences, respectively. Additionally, 50 (35%) and 93 (65%) had asthma durations of ≤24 months and >24 months, respectively. Frequency distribution of family history of asthma showed that out of 143 patients, 14 (9.8%) and 129 (90.2%) had and did not have a family history of asthma, and other variables such as frequency distribution of family monthly income status and frequency distribution of educational status (Table 1).

Table 1: Frequency Distribution of Demographic and Other Variables (n=143)

Baseline Characteristics	Categories	n (%)
Mean Age	7.14 ± 3.49 Years	
Duration of Asthma	25.72 ± 10.24 Months	
Gender Distribution	Male	71 (49.65%)
	Female	72 (50.35%)
Age Distribution	4-8 Years	47 (32.87%)
	9-12 Years	96 (67.13%)
Residence Status	Urban	116 (81.12%)
	Rural	27 (17.88%)
Asthma Duration	<2 Months	50 (34.97%)
	>2 Months	93 (65.03%)
Family History of Asthma	Yes	14 (09.79%)
	No	129 (90.21%)
Family Monthly Income Status	<50000	71 (49.65%)
	>50000	72 (50.35%)
Educational Status	Illiterate	07 (04.90%)
	Primary	15 (10.49%)
	Secondary	52 (36.36%)
	Higher	69 (48.25%)

Out of 143 patients, 65 (45.5%) and 78 (54.5%) had and did not have well-controlled asthma, and 43 (30.1%) and 100 (69.9%) patients had and did not have partially controlled asthma, while 35 (24.5%) and 108 (75.5%) patients had and did not have poorly controlled asthma (Figure 1).

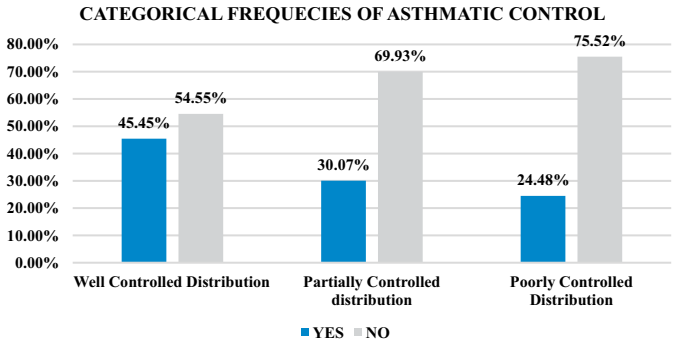

Figure 1: Frequencies of Asthmatic Control Categories in Study Population

The study found that 55.3% of patients aged 4-8 years had well-controlled asthma, while only 40.6% of patients aged 9-12 years had well-controlled asthma. In contrast, 44.7% and 59.4% of patients aged 4-8 years and 9-12 years, respectively, had poorly controlled asthma, with no significant relation. (p-0.09). Within the well-control stratum for men, females and males are almost evenly split at 33 (45.8%) and 39 (54.2%), respectively. In the female group, 32 (45.1%) and 39 (54.9%) had and did not have well-controlled asthma, respectively; the p-value was not significant (0.92). Stratification by residence status in relation to well-controlled asthma revealed that among urban residents, 54 (46.6%) had well-controlled asthma, while 62 (53.4%) did not. In contrast, among rural residents, 11 (40.7%) had well-controlled asthma, while 16 (59.3%) did not. The difference between the two groups was not statistically significant (p=0.58). In stratification of asthmatic duration, it was revealed that 40% of patients with asthma for ≤24 months had well-controlled asthma, while 48.4% of those with asthma for >24 months had well-controlled asthma. No significant difference was observed in well-controlled asthma based on duration with a p-value. The study found that 50% of subjects with an asthmatic family history had and did not have well-controlled asthma, while 45% and 55% of those without a family history had and did not have well-controlled asthma. 43.7% and 56.3% of patients with monthly incomes of ≤50000 and >50000 had well-controlled asthma, while 47.2% and 52.8% did not have well-controlled asthma in patients with monthly incomes of ≤50000 and >50000, respectively, with p-value (0.66). Stratification by education level about well-controlled asthma showed that among the patients belonging to illiterate, primary, and secondary categories, 05 (71.4%), 07 (46.7%), 22 (42.3%), and 31 (44.9%) had well-controlled asthma in the illiterate, primary, secondary, and higher education groups. On the other hand, among the patients belonging to the illiterate, primary, and secondary groups and above, 02 (28.6%), 08 (53.3%), 30 (57.7%), and 38 (55.1%) had well-controlled asthma. p-value (0.54) (Table 02).

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Table 2: Stratification Distribution of Different Variables with Well-Controlled Asthma Patients

Baseline Characteristics	Categories	Well Controlled Distribution		p-value
		Yes	No	
Gender Distribution	Male	33 (45.8%)	39 (54.2%)	0.92
	Female	32 (45.1%)	39 (54.9%)	
Age Distribution	4-8 Years	26 (55.3%)	21 (44.7%)	0.09
	9-12 Years	39 (40.6%)	57 (59.4%)	
Residence Status	Urban	54 (46.6%)	62 (53.4%)	0.58
	Rural	11 (40.7%)	16 (59.3%)	
Asthma Duration	< 02 Months	20 (40.0%)	30 (60.0%)	0.33
	> 02 Months	45 (48.4%)	48 (51.6%)	
Family History of Asthma	Yes	07 (50.0%)	07 (50,0%)	0.66
	No	58 (45.0%)	71 (55,0%)	
Family Monthly Income Status	< 50000	31 (43.7%)	40 (56.3%)	0.66
	>50000	34 (47.2%)	38 (52.8%)	
Educational Status	Illiterate	05 (71.4%)	02 (28.6%)	0.54
	Primary	07 (46.7%)	08 (53.3%)	
	Secondary	22 (42.3%)	30 (57.7%)	
	Higher	31 (44.9%)	38 (55.1%)	

Statistical analysis of the relationship not seen in age stratification of partially managed asthma indicated that 15 (31.9%) and 28 (29.2%) people in the age groups (4-8 years and 9-12 years) had partially controlled asthma. In comparison, 32 (68.1%) and 68 (70.8%) patients aged 4-8 and 9-12 years old did not have partially controlled asthma. (p=0.09). Statistical analysis revealed that 25 (34.7%) of males had some control over their asthma, but 47 (65.3%) did not. In the female group, 18 (25.4%) had partially controlled asthma, whereas 53 (74.6%) did not. (p=0.22). In comparison, among rural residents, 10 (37.0%) had moderately managed asthma, whereas 17 (63.0%) did not. The difference between the two groups was statistically insignificant (p=0.38). Stratification for the duration of asthma concerning partially controlled asthma observed that patients who had asthma for ≤24 months, 14 (28%) and 36 (72%), had and did not have partially controlled asthma, respectively. Whereas patients who had asthma for >24 months, 29 (31.2%) and 64 (68.8%) had and did not have partially controlled asthma. The p-value was 0.69, indicating no statistically significant difference in the prevalence of partially controlled asthma between the two groups. The stratification analysis not reveal that among patients with a family history of asthma, 7 (50%) had partially controlled asthma, while 7 (50%) did not. In contrast, among patients without a family history of asthma, 36 (27.9%) had partially controlled asthma, and 93 (72.1%) did not. These results suggest no statistically significant relationship between family history of asthma and partially controlled asthma, as indicated by a p-value of 0.080. Stratification by family monthly income showed that among patients with a monthly income of ≤50,000, 23 (32.4%) had partially controlled asthma, whereas 48 (67.6%) did not. Similarly, among patients with a monthly income of > 50,000, 20 (27.8%) had partially controlled asthma, and 52 (72.2%) did not. The analysis did not reveal a statistically significant relationship between family monthly income and partially controlled asthma, with a p-value of 0.54. The stratification analysis revealed that stratification based on educational status for partially controlled asthma revealed that 00 (00%), 02 (13.3%), 28 (53.8%), and 13 (18.8%) of patients from illiterate, primary, secondary, and higher educational groups, respectively, had partially controlled asthma. In comparison, 07 (100%), 13 (86.7%), 24 (46.2%), and 56 (81.2%) patients with illiteracy, elementary, secondary, and higher education levels had partially managed asthma (p-0.01), respectively (Table 03).

Table 3: Stratification Distribution of Different Variables with Partially Controlled Asthma Patients

Baseline Characteristics	Categories	Partially Controlled Distribution		p-value
		Yes	No	
Gender Distribution	Male	25 (34.7%)	47 (65.3%)	0.22
	Female	18 (25.4%)	53 (74.6%)	
Age Distribution	4-8 Years	15 (31.9%)	32 (68.1%)	0.73
	9-12 Years	28 (29.2%)	68 (70.8%)	
Residence Status	Urban	33 (28.4%)	83 (71.6%)	0.38
	Rural	10 (37.0%)	17 (63.0%)	
Asthma Duration	< 02 Months	14 (28.0%)	36 (72.0%)	0.69
	> 02 Months	29 (31.2%)	64 (68.8%)	
Family History of Asthma	Yes	07 (50.0%)	07 (50.0%)	0.08
	No	36 (27.9%)	93 (72.1%)	
Family Monthly Income Status	< 50000	23 (32.4%)	48 (67.6%)	0.66
	>50000	20 (27.8%)	52 (72.2%)	
Educational Status	Illiterate	00 (00.0%)	07 (100.0%)	0.01
	Primary	02 (01.3%)	13 (86.7%)	
	Secondary	28 (53.8%)	24 (46.2%)	
	Higher	13 (18.8%)	56 (81.2%)	

Age stratification of poorly managed asthma revealed that 16 (34%) and 19 (19.8%) individuals in the age groups (4-8 years and 9-12 years) had poorly controlled asthma, respectively. In contrast, 31 (66%) and 77 (80.2%) patients aged 4-8 and 9-12 years did not have poorly managed asthma, respectively. The p-value (0.06). In terms of poorly managed asthma, gender stratification revealed that 20 (27.8%) and 52 (72.2%) males had and did not have it, respectively. In the female group, 15 (21.1%) had poorly managed asthma, whereas 56 (78.9%) did not. The p-value was 0.35. Significant association not observed between residence status and poorly controlled asthma revealed that 25 (21.6%) and 91 (78.4%) who lived in cities had and did not have poorly controlled asthma, respectively, whereas 10 (37%) and 17 (63%) who lived in rural areas and did not have poorly controlled asthma. p-value (0.09). Asthmatic

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duration about poorly controlled asthma seemed that patients who had asthma for ≤ 24 months, 15 (30%) and 35 (70%), had and did not have poorly controlled asthma, respectively. Of patients who had asthma for >24 months, 20 (21.5%) and 73 (78.5%) had and did not have poorly controlled asthma, respectively. p-value (0.26). Family history of asthma with regards to poorly controlled asthma showed that patients who had a family history of asthma, 00 (00%) and 14 (100%), had and did not have poorly controlled asthma, respectively. Of the patients who did not have a family history of asthma, 35 (27.1%) and 94 (72.9%), had and did not have poorly controlled asthma, respectively (p=0.02). Family monthly income status concerning poorly controlled asthma showed 14 (19.7%) and 57 (80.3%) had poorly controlled asthma in patients who belonged to a monthly income of ≤50000 and >50000, respectively. Whereas 21 (29.2%) and 51 (70.8%) did not have poorly controlled asthma in patients who belonged to monthly incomes of ≤50000 and >50000 (p=0.18). For poorly controlled asthma, stratifying for educational status, 00 (00%), 02 (13.3%), 06 (11.5%), and 27 (39.1%) had poorly controlled asthma in patients belonging to illiterate, primary, secondary, and higher educational categories. While 07 (100%), 13 (86.7%), 46 (88.5%), and 42 (60.9%) have poorly controlled asthma in patients of illiterate, primary, secondary, and higher educational groups, therefore it is a statistically significant association between educational status and poorly controlled asthma (p-0.01) (Table 4).

Table 4: Stratification Distribution of Different Variables with Poorly Controlled Asthma Patients

Baseline Characteristics	Categories	Poorly Controlled Distribution		p-value
		Yes	No	
Gender Distribution	Male	20 (27.8%)	52 (72.2%)	0.35
	Female	15 (21.1%)	56 (78.9%)	
Age Distribution	4-8 Years	16 (34.0%)	31 (66.0%)	0.06
	9-12 Years	19 (19.8%)	77 (80.2%)	
Residence Status	Urban	25 (21.6%)	91 (78.4%)	0.09
	Rural	10 (37.0%)	17 (63.0%)	
Asthma Duration	<2 Months	15 (30.0%)	35 (70.0%)	0.36
	>2 Months	20 (21.5%)	73 (78.5%)	
Family History of Asthma	Yes	00 (00.0%)	14 (100%)	0.08
	No	35 (27.1%)	94 (72.9%)	
Family Monthly Income Status	<50000	14 (19.7%)	57 (80.3%)	0.18
	>50000	21 (29.2%)	51 (70.8%)	
Educational Status	Illiterate	00 (00.0%)	07 (100%)	0.01
	Primary	02 (13.3%)	13 (86.7%)	
	Secondary	06 (11.5%)	46 (88.5%)	
	Higher	27 (39.1%)	42 (60.9%)	

DISCUSSION

Asthma, a prevalent chronic inflammatory respiratory disorder affecting 8-9% of the global population, presents significant challenges in diagnosis and treatment [12, 13]. The National Health Insurance Scheme (NHIS) estimates have experienced a significant decrease in recent years, dropping from 8.4% in 2017 [14] to 7.5% in 2018 [15], 7.0% in 2019 [16], and 5.8% in 2020 [17]. The study aims to evaluate the frequency of different patterns of asthma control among a cohort of asthmatic patients, shedding light on the variability in control levels within the population. By understanding these patterns, healthcare providers can enhance individualized treatment strategies, contributing to improved overall asthma management and patient outcomes. The study involved 143 patients with asthma, with a mean age of 7.14 ± 3.49 years and a duration of 25.72 ± 10.24 months, with a majority of male 72 (50.3%) and female 71 (49.7%). Out of 143 patients, 45.5%, 30.1%, and 24.5% had well-controlled, partially controlled, and poorly controlled asthma, respectively. The survey was completed by 2429 children diagnosed with asthma (or their caretakers). The frequency of uncontrolled asthma was 46 percent. Patients examined for a non-respiratory ailment had a 35% frequency of uncontrolled asthma, compared to 54% for respiratory complaints. Children with uncontrolled asthma who were examined for a non-respiratory-related complaint had a higher likelihood of missing one or more school days in the preceding four weeks than children with managed asthma (53% vs 24%) [18]. Urban vs. rural healthcare disparities reveal barriers like socioeconomic disparities, overcrowding, and lack of education. Rural areas have limited access, fewer specialists, and longer travel distances, impacting disease management and outcomes. Understanding these differences can inform care delivery strategies [19]. The study found that 67.9% of patients had uncontrolled asthma, with a clear link between asthma management and quality of life. The cut-off for quality of life was 4.97. Most patients were using two or three anti-asthmatic medications, with oral pills and Short-acting beta 2-agonists (SABA) inhalers being the most popular combination. Uncontrolled asthma is associated with several characteristics, including male gender, marital status, comorbidities, and oral SABA usage. In middle-aged individuals, male gender, intermittent asthma, oral corticosteroid usage, and SABA use are all linked to poor asthma-related quality of life. Male gender, intermittent asthma, and usage of oral corticosteroids are all associated with poor asthma-related quality of life. These findings emphasize the need to control asthma in persons to enhance their quality of life [20].

CONCLUSIONS

Notably, the findings demonstrated that 45.5% of the participants had well-controlled asthma, indicating successful management strategies for a substantial proportion of the study population. However, 30.1%

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exhibited partially controlled asthma, suggesting a need for further intervention and optimization of treatment plans. Importantly, 24.5% of patients experienced poorly controlled asthma, signalling a subset that may require more intensive monitoring and tailored therapeutic approaches. These results underscore the heterogeneity of asthma control within the studied population and emphasize the importance of individualized management strategies. While a considerable number of patients achieved optimal control, a significant proportion still faces challenges in attaining the desired asthma control levels. The findings from this study contribute valuable insights to the understanding of asthma control patterns in the specific patient population.

Authors Contribution

Conceptualization: MAJ
Methodology: MAJ, N, M, VKG
Formal analysis: N
Writing review and editing: NFS, SLB

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Demographic Analysis of Ophthalmic Surgeries in a Tertiary Care Center in Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

Different age groups and genders have unique needs when it comes to eye surgeries. Understanding these trends can help improve eye care services in resource-limited areas. **Objectives:** To study the types of eye surgeries performed in a tertiary care center in Khyber Pakhtunkhwa, Pakistan, and examine their link to age and gender. **Methods:** This retrospective observational study reviewed records of 3,016 patients. Data on age, gender, and procedures were analyzed using Chi-square tests, with $p<0.05$ considered significant. **Results:** The most common surgeries were intraocular lens (IOL) implantation (18.0%), primary repair surgeries (12.0%), phacoemulsification (11.6%), and extracapsular cataract extraction (10.4%). Older patients mostly underwent cataract-related surgeries, while younger patients had intraocular lens implantation and squint correction. Male patients had more cataract surgeries, while females had more primary repair surgeries. **Conclusions:** It was concluded that significant associations between age, gender, and surgical procedures were found, underscoring the need for more focused resource allocation and easier access to ophthalmic care, especially for women and older adults.

INTRODUCTION

Ophthalmic diseases pose a significant global health burden, affecting people of all ages and socioeconomic backgrounds. The World Health Organization (WHO) estimates that over 2.2 billion individuals suffer from some visual impairment, however, 1 billion of these instances may be avoidable or cured with the right care, such as medication and surgery [1, 2]. The frequency of blindness and impaired vision is quite high; according to research, the prevalence among Pakistanis aged 30 and over is about 2.5%, which corresponds to over 1.25 million blind people nationwide [3, 4]. The burden of vision loss has steadily increased over the past 20 years, beginning in 1990, and is predicted to continue to rise until at least 2025 [5]. Pakistan is among the countries with the highest burden of blindness and visual impairment in South Asia, with significant public health implications [4]. The demand for ophthalmic care is increasing in Khyber Pakhtunkhwa (KP) due to improved awareness, better access to healthcare facilities, and an ageing population vulnerable to age-related eye diseases [6, 7]. The most common causes of

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blindness and visual impairment in Pakistan are age-related macular degeneration, diabetic retinopathy, cataracts, and glaucoma. 15 million of the 33.6 million instances of blindness globally are caused by cataracts alone, making cataract surgery one of the most common operations done anywhere in the globe, including Pakistan [11-13]. The need for ophthalmic care is anticipated to rise with the increasing prevalence of diabetes and other systemic disorders that impact ocular health [8]. Timely diagnosis and appropriate treatment can help prevent loss of vision and improve the quality of life [8]. Early diagnosis and prompt treatment are essential to avoid vision loss and enhance quality of life. But getting access to specialist eye care is still difficult, especially in Pakistan's rural areas. To close this gap, tertiary care facilities offer crucial treatments, such as intricate surgical operations [8].

This study aims to determine the frequency and distribution of ophthalmic surgeries performed at a tertiary care center in Khyber Pakhtunkhwa, Pakistan.

METHODS

This retrospective, observational study was carried out at the Ophthalmology Department of the Hayatabad Medical Complex in Peshawar, Khyber Pakhtunkhwa, Pakistan, from September 2022 to October 2024. A standardized data collection protocol was implemented to ensure reliability. Open-Epi software was used to determine the necessary sample size, which had a 1% margin of error and a 95% confidence level. Based on previous epidemiological studies and local hospital records, the projected prevalence of cataracts among Peshawar's 2,480,550 population was 8.6%, resulting in a target sample size of 3,016 individuals [9]. Data were separately retrieved from medical records by two trained researchers, and reliability was evaluated by an interobserver agreement analysis using Cohen's kappa coefficient. Disagreements were settled after consulting with a senior ophthalmologist. Age, gender, and information on ocular treatments received during the research period were among the demographics that were retrieved. Included were all patients with complete medical records who had ophthalmic operations performed in the indicated departments. Patients treated outside of the hospital or with insufficient medical data were not included. Because medical records were inconsistent, socioeconomic status, comorbidities, and other patient-specific characteristics that could affect the kind of operation or its result were not evaluated. In the discussion section, this shortcoming is recognized and discussed. Data analysis was conducted using SPSS version 26.0. Using means and standard deviations for continuous data and frequencies and percentages for categorical variables, descriptive statistics provided an overview of the distribution and frequency of ophthalmic operations. Associations between categorical variables, including age group, gender, and procedure type, were evaluated using the chi-square test. Cohen's kappa coefficient was used to further assess interobserver reliability. Associations between categorical variables were evaluated using the Chi-square test; a p-value of less than 0.05 was considered statistically significant. The Hayatabad Medical Complex's Institutional Review Board granted ethical approval (Ref. No: HMC-QAD-F-1155), guaranteeing rigorous commitment to patient confidentiality and privacy throughout the investigation.

RESULTS

A total of 3,016 patients were included in the study, with a mean age was 35.16 years (SD ± 26.52), with a median age of 33 years, indicating a wide distribution of ages among patients. The majority of the participants were aged ≤18 years (40.5%), followed by those ≥61 years (25.0%). Other age groups included 51–60 years (13.0%), 19–30 years (8.1%), 41–50 years (7.1%), and 31–40 years (6.3%). Detailed distributions are presented in Table 1.

Table 1: Age-Wise Distribution of the Participants

Variable		Frequency (%)
Age Groups	≤18 Years	1221 (40.5%)
	19 to 30 Years	243 (8.1%)
	31 to 40 Years	189 (6.3%)
	41 to 50 Years	215 (7.1%)
	51 to 60 Years	392 (13.0%)
	≥ 61 Years	756 (25.0%)
	Total	3016 (100.0%)

In terms of gender, male represented a larger portion of the sample, with 57.3% (n=1,727) of the patients, while female made up 42.7% (n=1,289), as illustrated in Figure 1.

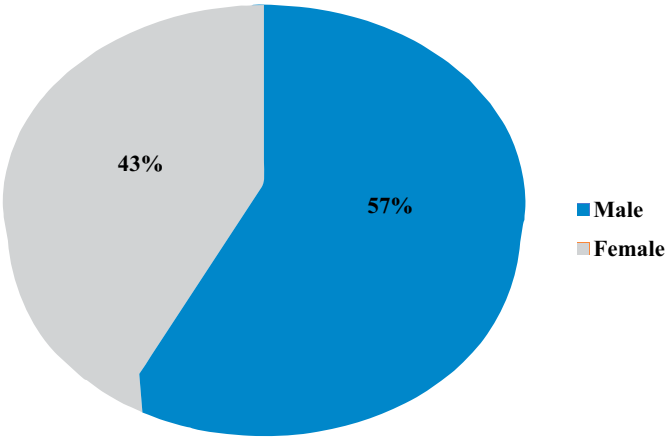

Figure 1: Gender-Wise Distribution of the Participants

The study analyzed 3,016 patients who underwent various ophthalmic procedures. The most commonly performed procedures were cataract-related, including intraocular lens (IOL) implantation (18.0%, n=543), phacoemulsification (11.6%, n=349), and extracapsular cataract extraction

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(ECCE) (10.4%, n=314). Other notable procedures included primary repair surgeries (12.0%, n=361), scleral tunnel manual small incision cataract surgery (MSICS) with IOL insertion (4.7%, n=143), keratoplasty and keratectomy (4.7%, n=141), and dacryocystorhinostomy (DCR) for tear duct obstruction (4.6%, n=139). Less frequent procedures included pars plana vitrectomy (PPV) at 3.7% (n=113), squint horizontal muscle surgery (2.8%, n=85), anterior chamber wash with diagnostics (2.9%, n=87), and conjunctivoplasty (2.1%, n=63). Rarely performed surgeries such as enucleation (0.1%, n=2), pterygium excision (0.6%, n=18), levator resection (0.5%, n=14), and the Weiss procedure (0.2%, n=6) were also noted. Additional recorded procedures included evisceration (1.7%, n=50), benign eyelid lesion removal (1.6%, n=47), orbital implants (1.9%, n=57), and Fasanella-Servat & sling for ptosis (1.9%, n=57). Excision of conjunctival lesions (1.8%, n=55), tectonic graft (0.9%, n=27), cryopexy (1.3%, n=39), and foreign body removal (0.7%, n=22) were also documented as shown in Figure 2.

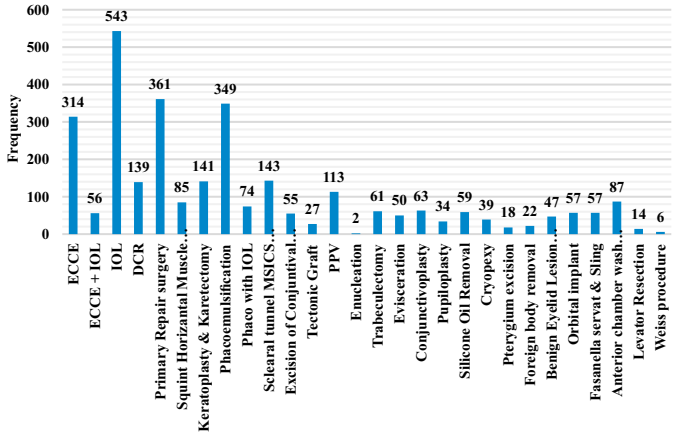

Figure 2: Different Types of Procedures Performed at the Facility

A significant association was observed between age group and the type of procedure performed (Pearson Chi-Square =1543.656, df=135, p<0.001). Among the ≤18 years' age group (n=1,221), IOL implantation (n=439) and ECCE (n=48) were the most common procedures, while squint horizontal muscle surgery (n=52) was also performed frequently. In the ≥61 years' age group (n=756), ECCE (n=143) and phacoemulsification (n=154) were the most frequently performed procedures, reflecting the prevalence of cataract-related surgeries in older patients. Younger age groups, such as 19–30 years (n=243) and 31–40 years (n=189), underwent primary repair surgeries (n=206) and squint horizontal muscle surgeries (n=20 and n=17, respectively), focusing on conditions like strabismus and refractive errors. The analysis between gender and type of procedure also showed a significant association (Pearson Chi-Square=151.052, df=27, p<0.001). Male patients (n=1,727) were more likely to undergo cataract-related procedures, including ECCE (n=159) and IOL implantation (n=350), while female patients (n=1,289) had higher frequencies of primary repair surgeries (n=127). The distribution of ophthalmic procedures across different age groups and genders was analyzed using crosstabs and Chi-square tests, as presented in Table 2.

Table 2: The Demographic Factors Influencing Procedure Selection

Variable		Ophthalmic Procedure							
		ECCE	IOL	Primary Repair	Squint	Keratoplasty	Orbital implant	Cryopexy	p-value
Age Groups	≤18 Years	48	439	206	52	64	25	12	<0.001
	19 to 30 Years	12	26	42	20	26	7	7	
	31 to 40 Years	13	23	30	1	21	0	2	
	41 to 50 Years	26	16	17	3	7	3	2	
	51 to 60 Years	72	13	23	3	11	4	4	
	> 61 Years	143	26	43	6	12	18	12	
	Total	314	543	361	85	141	57	39	
Gender	Male	159	350	234	49	95	31	27	0.049
	Female	155	193	127	36	46	26	12	
	Total	314	543	361	85	141	57	39	

DISCUSSION

This study analyzed ophthalmic procedures performed in a tertiary care center. The findings show that the kind of therapies administered depending on these demographic factors varied significantly.The data provided by these patterns might potentially guide operations and the allocation of medical resources in the region. This study examined the kinds of eye care treatments carried out in Khyber Pakhtunkhwa's tertiary care facilities, paying particular attention to demographic differences. Significant disparities in procedure distribution between

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age groups and genders are highlighted by the data, which are important for informing regional healthcare policy and allocating resources.Male made up 57.3% and female 42.7% of the 3,016 patients that were examined [10]. IOL implantation accounted for 18% of procedures, with primary repair operations (12%), phacoemulsification (11.6%), and extracapsular cataract extraction (ECCE) (10.4%) following closely behind.These patterns highlight the strong demand for cataract-related operations, especially among patients who are older than 61. According to a gender-specific analysis, women had a greater rate of primary repair procedures while men had more surgeries associated with cataracts [10].This emphasizes the necessity of removing any possible obstacles to women's access to healthcare in the area. The differences observed between this study and Jeon *et al.*, could be attributed to variations in regional healthcare accessibility, patient demographics, and surgical preferences. The higher incidence of IOL implantation (51.2%) reported by Jeon *et al.*,compared to our findings (18.0%), may be due to differences in population demographics or variations in access to cataract treatment services [11]. Jeon *et al.*, reported a significantly higher rate, with intraocular lens (IOL) implantation accounting for 51.2% of each patient in their research,compared to our analysis where IOL implantation was the most popular operation at 18% [11]. Hashemi *et al.*, and Mees *et al.*, studied that elevated IOL operation frequency could be a sign of a higher percentage of older patients or a greater focus on cataract therapy [12, 13]. The higher frequency of pars plana vitrectomy (PPV) (49.6%) reported by Riaz *et al.*, suggests differences in the availability of specialized retinal care services, which may not be as widely accessible in our study setting. Similarly, the disparity in primary repair surgeries (31.6%) reported by Al-Khersan *et al.*, compared to 12.0% in our findings, could be influenced by variations in trauma-related cases or differing healthcare priorities across study populations [14, 15]. This variation may result from regional deviations in the prevalence of cataracts and other eye disorders that call for lens implantation,changes in patient demographics,or discrepancies in healthcare accessibility. In contrast to Riaz's findings, our analysis reveals a distinct trend for pars plana vitrectomy (PPV) and PPV together with IOL therapies [14]. PPV alone accounted for 49.6% of the activities in their analysis, whereas PPV with IOL accounted for 27.1%. On another hand, PPV was only used in 3.7% of the cases in our analysis, and it was strange to see PPV and IOL coupled [14]. Unlike our findings, Al-Khersan *et al.* claimed that primary repair operations were the most common, making up 31.6% of patients [15]. However, primary repair only made up 12.0% of all surgeries in our analysis. Variations in patient demographics, injury rates, or the focus of the healthcare settings in each research might be the cause of this discrepancy. Furthermore, the average age of patients obtaining primary repair operation was 50 years old, according to Al-Khersan *et al.*, which is considerably older than the average age of almost 35 years (SD ± 26.52) in our study. These age differences may reflect variances in the sorts of eye illnesses or injuries that lead to primary repair, as well as injustices in the age distribution of the patient groups. In line with our results of age-related trends in optical operations, the statistical significance of age in the Al-Khersan *et al.*, study ($p<0.0001$) indicates the need to modify treatment methods to age demographics [15]. Our study aligns partially with the findings of those who reported that older age, female gender, and lower socioeconomic status are associated with a higher cataract burden [16]. Similar to their findings, our data show that cataract-related procedures, including IOL implantation, are indeed more common among older age groups. However, unlike Fang et al., observations, we found a slightly higher representation of male patients undergoing these procedures, which could reflect gender-specific health-seeking behaviours or accessibility differences in our study setting [16]. The impact of socioeconomic status, which we didn't directly assess in our study, is an important factor that should be explored in future research. Socioeconomic challenges may affect access to eye care services in the region, possibly causing delays in cataract treatment or leading to a higher demand for procedures when patients eventually seek care [17, 20]. Moreover, due to the nature of the available data used for this study, patient factors that might influence the types and frequency of procedures, such as comorbidities or socioeconomic status, were not reviewed.This study acknowledges the potential for selection bias, as the data is derived from a single tertiary care center, which may not fully represent the broader population of the region. Furthermore, adding assessments of socioeconomic factors and access to care could point out potential barriers and thus enable health authorities and hospitals to improve accessibility and distribute resources more properly among the at-risk groups.

CONCLUSIONS

It was concluded that this retrospective observational study demonstrated important patterns in ophthalmic surgical interventions across different age groups and genders. Cataract-related procedures, such as phacoemulsification and extracapsular cataract extraction (ECCE), were predominantly performed on older patients aged 61 years and above, emphasizing the need to allocate resources for this demographic. Interestingly, intraocular lens (IOL) implantation was the most common procedure among children and adolescents under 18 years,

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likely due to the prevalence of congenital or traumatic cataracts in this group, which require timely intervention to prevent long-term vision issues. Gender differences were also observed, with men undergoing more cataract-related surgeries, while women had a higher frequency of primary repair procedures. These findings suggest the importance of targeted outreach to address potential barriers women may face in accessing timely eye care.

Authors Contribution

Conceptualization: SS, AZ
Methodology: SA, SS
Formal analysis: HT, AUR, YIM
Writing review and editing: AUR, AZ, YJM

All authors have read and agreed to the published version of the manuscript

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Original Article

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Prevalence and Correlates of Hyperuricemia in Patients with Hypertension: A Cross-Sectional Study from a Tertiary Care Hospital in Pakistan

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ABSTRACT

The link between Serum Uric Acid (SUA) and hypertension debated among researchers. **Objective:** To determine the prevalence and correlates of hyperuricemia in patients with hypertension. **Methods:** This cross-sectional study was conducted at the General Medicine Department, Saidu Teaching Hospital, Swat (October 2023–April 2024), analyzing hypertensive patients aged 30–60 years. SUA was measured via an automated micro lab, with hyperuricemia defined as SUA >7.0 mg/dl (men) and >6.0 mg/dl (women). Chi-square tested categorical data, while Pearson correlation assessed SUA relationships with SBP, DBP, and BMI ($p<0.05$ significant). **Results:** In a total 266 patients, 136 (51.1%) were male. The mean age, BMI were 45.41 ± 25.92 years, and 27.28 ± 3.25 kg/m2, respectively. The obesity was noted in 72 (27.1%) patients. Dyslipidemia was found in 42 (15.8%) patients. There were 54 (20.3%) patients who were newly diagnosed cases of hypertension. The mean systolic blood pressure (SBP), diastolic blood pressure (DBP) were 141.76 ± 8.24 mm Hg, and 91.36 ± 8.45 mm Hg, respectively. The mean SUA level was 6.03 ± 1.13 mg/dl, and the frequency of hyperuricemia was noted in 61 (22.9%) patients. Obesity ($p=0.033$), and known diagnosis of hypertension ($p<0.001$) were significantly linked with hyperuricemia, Scatter plot revealed positively linear and significant correlation of SBP ($r=0.261$, $p<0.001$), and DBP ($r=0.319$, $p<0.001$) with SUA levels. The BMI was also found to have positively linear and significant relationship with SUA levels ($r=0.122$, $p=0.047$). **Conclusion:** Hyperuricemia (22.9%) in hypertensive patients correlated with blood pressure and BMI, indicating its role in complications.

INTRODUCTION

Hypertension (HTN) is a major global health issue. Data from the developed world depicts that one out of four adults are estimated to be affected by HTN [1]. Predicting the underlying causes of HTN is a challenging task due to the intricate interaction between genetic predispositions and environmental influences. Numerous factors contribute to the development of HTN, making it a multifaceted condition to analyze and understand [2]. Among these potential contributors, the association between elevated serum uric acid (SUA) levels and HTN has been a subject of ongoing debate and extensive research within the medical community [3-5]. While some studies suggested a possible link between hyperuricemia (HU) and HTN, it is crucial to account for various confounding factors that may influence this relationship. Metabolic syndrome, diabetes mellitus, chronic kidney disease (CKD), along with lifestyle factors and high salt intake, are all significant contributors to the development of both hyperuricemia (HU) and HTN. Therefore, it is essential to account for these overlapping factors when studying the link between the two conditions. [6, 7]. Any attempt to establish a clear connection between HU and HTN must carefully consider these confounders to avoid oversimplification and to provide a more accurate understanding of the underlying mechanisms at play. In developing countries, very limited data exists about the burden of HU and its possible linkage with HTN. One study done in Nepal concluded a positive connection among HU and HTN, showed that almost 29% of HTN patients had HU [8]. The impact of SUA on arterial stiffness was studied in China, and it was concluded that a

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higher baseline SUA is an independent risk factor for developing arterial stiffness butt the predictive value of SUA on arterial stiffness is still unanswered in long-term longitudinal studies [9]. The ROVIGO study took into account the role of HU in resistant HTN in the general population, and concluded that in older females, SUA above 6.8 mg/dl increased the risk of resistant HTN as 3 folds [10]. Due to the increasing incidence of asymptomatic HU in HU patients [11], there is a need to conduct trials on the interrelationship of HU and HTN It is hypothesized that the burden of HU might be high in HTN. In developing countries, limited data exists regarding the burden of HU and its relationship with HTN, particularly among different ethnic and regional populations. Studies conducted in other parts of the world have shown varying frequencies of HU among hypertensive patients, influenced by genetic, dietary, and environmental factors [8-10]. Not such studies have been conducted in Khyber Pakhtunkhwa Province, Pakistan, where cultural and lifestyle variations may influence this relationship. Given the lack of region-specific data, this study aims to determine the prevalence of HU and its clinical correlates in hypertensive patients presenting to a tertiary care hospital in Swat, Pakistan.

Understanding the burden of HU in this specific population may contribute to improved hypertension management strategies and help identify high-risk groups requiring early intervention.

METHODS

This cross-sectional study was carried out at the Outpatient Department of the Department of Medicine, Saidu Teaching Hospital, Swat, Pakistan, from October 2023 to April 2024. Approval from Ethical Review Committee was obtained (letter number: 489/MMWA/023). A sample size of 266 was calculated, with a 95% confidence interval, 7% margin of error, and keeping the anticipated frequency of HU as 29% in HTN patients [8]. The inclusion criteria were patients of either gender, aged 30-60 years, and presenting with HTN. The exclusion criteria were patients with suspected secondary HU (e.g., drugs, malignancies, uremia, and other conditions with repaid cell turnovers like psoriasis (confirmed through SUA>7.2 mg/dl). Sample selection was made using a non-probability consecutive sampling technique. Informed and written consents were obtained from all study participants. Necessary demographics like age, gender, and residential status were recorded. The HTN was defined as systolic blood pressure (SBP) ≥ 130 mm Hg and/or diastolic blood pressure (DBP) ≥ 80 mm Hg [12]. Standard protocols were followed for the diagnosis of newly diagnosed cases (high BP on two or more occasions at least one week apart). The blood pressure measurement was taken in the right arm with the help of a mercury sphygmomanometer with an adequate sized cuff, with an individual seated quietly in a chair for 5 minutes with feet on the floor. A detailed physical examination was conducted for all patients. A blood sample was taken from the peripheral vein to measure SUA in the institutional laboratory through an automated micro lab. HU was labeled as a SUA level of > 7.0 mg/dl in men and > 6.0 mg/dl in women [13]. Patients with a BMI >30.0 kg/m2 were labeled obese. Dyslipidemia was defined as any one of these; total cholesterol ≥ 200 mg/dl, high-density lipoprotein ≤ 40 mg/dl for men or ≤ 50 in women, low-density lipoprotein ≥ 100 mg/dl, or triglycerides ≥ 150 mg/dl [14]. All the concerned data were recorded on a specifically pre-designed proforma. The statistical analysis was performed employing IBM-SPSS Statistics version 26.0. Mean and standard deviation were calculated for age, BMI, SBP, DBP, and SUA level. Frequency and percentages were calculated for gender, smoking status, obesity, dyslipidemia, and HU. HU was stratified by age, gender, obesity, smoking status, and dyslipidemia to see the effect modification. A post-stratification chi-square test was applied. Pearson correlation test was applied to explore the correlation of SUA levels with SBP, DBP, and BMI. For all statistical inferences, $p<0.05$ was taken as statistically significant.

RESULTS

In a total 266 patients, 136 (51.1%) were male. The mean age was 45.41 ± 25.92 years, ranging between 30-60 years. There were 106 (40.8%) patients who had age between 51-60 years. The mean BMI was 27.28 ± 3.25 kg/m2 while obesity was noted in 72 (27.1%) patients. Dyslipidemia was found in 42 (15.8%) patients. There were 54 (20.3%) patients who were newly diagnosed cases of HTN. The mean SBP, DBP were 141.76 ± 8.24 mm Hg, and 91.36 ± 8.45 mm Hg, respectively. Family history of hyperuricemia was documented in 39 (14.7%) patients. Table 1 shows demographic and clinical characteristics of hypertensive patients studied (Table 1).

Table 1: Frequency Distribution of the Study Characteristics of Patients with Hypertension (n=266)

Characteristics	Category	Frequency (%)
Age (Years)	30-40	51 (19.2%)
	41-50	109 (41.0%)
	51-60	106 (39.8%)
Gender	Male	136 (51.1%)
	Female	130 (48.9%)
Residence	Urban	103 (38.7%)
	Rural	163 (61.3%)
Smoking status	Yes	88 (33.1%)
	No	178 (66.9%)
Obesity	Yes	106 (39.8%)
	No	160 (60.2%)
Dyslipidemia	Yes	59 (22.2%)

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	No	207 (77.8%)
Newly diagnosed hypertension	Yes	54 (20.3%)
	No	212 (79.7%)
Family history of hyperuricemia	Yes	39 (14.7%)
	No	227 (85.3%)

The mean SUA level was 6.03 ± 1.13 mg/dl, and the frequency of HU was noted in 61 (22.9%) patients. Stratification of HU showed that no statistically significant associations were found with respect to gender (p=0.956), age groups (p=0.992), smoking status (p=0.955), dyslipidemia (p=0.178), or family history of hyperuricemia (p=0.094). Obesity (p=0.033), and known diagnosis of HTN (p<0.001) were significantly linked with HU, and the details are shown in table 2.

Table 2: Stratification of Hyperuricemia with Respect to Study Characteristics of the Patients with Hypertension (N=266)

Characteristics	Category	Hyperuricemia Frequency (%)		p-Value
		Present (n=61)	Absent (n=205)	
Gender	30-40	31 (51.7%)	105 (51.2%)	0.956
	41-50	30 (48.3%)	100 (48.8%)	
Age (Years)	51-60	12 (19.7%)	39 (19.0%)	0.992
	Male	25 (41.0%)	84 (41.0%)	
	Female	24 (39.3%)	82 (40.0%)	
Smoking Status	Urban	20 (32.8%)	68 (33.2%)	0.955
	Rural	41 (67.2%)	137 (66.8%)	
Obesity	Yes	23 (37.7%)	49 (23.9%)	0.033
	No	38 (62.3%)	156 (76.1%)	
Dyslipidemia	Yes	13 (21.3%)	29 (14.1%)	0.178
	No	48 (78.7%)	176 (85.9%)	
Newly Diagnosed Hypertension	Yes	6 (9.8%)	48 (23.4%)	<0.001
	No	55 (90.2%)	157 (76.6%)	
Family History of Hyperuricemia	Yes	13 (21.3%)	26 (12.7%)	0.094
	No	48 (78.7%)	179 (87.3%)	

Scatter plot revealed positively linear and significant correlation of SBP (r=0.261, p<0.001), and DBP (r=0.319, p<0.001) with SUA levels as exhibited in figure 1.

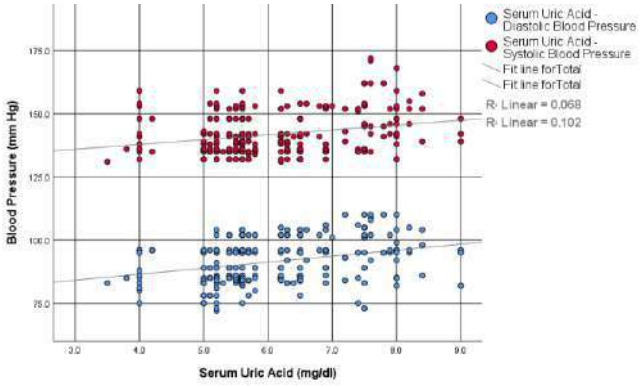

Figure 1: Relationship of Blood Pressure with SUA Levels

Figure 2 illustrated the correlation between Body Mass Index (BMI) and Serum Uric Acid (SUA) levels among hypertensive patients. The scatter plot demonstrated BMI was also found to have positively linear and significant relationship with SUA levels (r=0.122, p=0.047).

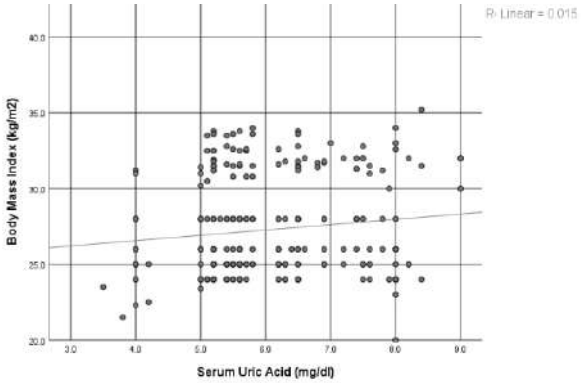

Figure 2: Relationship of BMI with SUA Levels

DISCUSSION

The literature proposes linkage between elevated SUA and an increased risk for HTN and cardiovascular diseases, but these associations have been uncertain [15, 16]. In this study, the frequency of HU was found to be 22.9% among patients with HTN. Local data described the frequency of HU in adult patients with HTN to be 41.0% which is much more than what we documented [17]. Another study by Raja et al., analyzing risk factors for HU in adult population showed that mean SUA levels were 6.64 ± 1.63 mg/dl versus 5.35 ± 1.60 mg/dl in hypertensive and non-hypertensive patients (p<0.001), respectively [18]. Long ago, Breckenridge demonstrated that 58% of patients receiving anti-hypertensive medication had elevated SUA levels, while 27% of patients presenting to the clinic at that time had HU [19]. Messerli et al., analyzed established hypertensive cases showed that 72% of them had a raised SUA [20]. The hypothesis argued that the burden of HU in HTN may be explained to either diminished renal perfusion or underlying renal dysfunction. A study by Khaliq et al analyzing patients of HU described that 84% patients with HU had HTN versus 41% controls (odds ratio: 7.55; p<0.001) [21]. It was found that among hypertensive patients, presence of HU had significant association with obesity. Some researchers have shown that the correlation between raised SUA and HTN decreased after adjusting for BMI, which implies that the association may be linked to obesity [22]. This association linked to obesity is also demonstrated by Qiu et al, in which attenuation was observed after adjustment of waist circumference [23]. Obesity is associated with hyperinsulinemia, which in turn causes decreased excretion of SUA. This implies increased chances of progression to HTN in metabolic syndromes (central obesity, insulin resistance, and HTN) [24]. These insights can further emphasize the linkage between HU, with hypertriglyceridemia which should be considered confounders while studying the linkage between HU and

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HTN. Some researchers have proposed that toxins in the blood cause damage to the kidney and heart's vasculature, leading to HTN, while a potential agent could be uric acid as a key HTN mediator [25]. Experts also connect high blood pressure to uric acid and recommend dietary modifications to reduce uric acid and regulate blood pressure in the general public [26]. Apart from being a distinct risk factor for incident HTN in the general population, HU could have significant differences in consequences depending on age, sex, and race. With appropriate intervention in the early phases of HTN, this model implies that there can be a period of reversible HTN. Although no significant association was found between hyperuricemia and gender or age groups, prior studies have suggested that hormonal factors in premenopausal women may contribute to lower SUA levels [27], while aging-related metabolic changes may influence uric acid metabolism [28]. The non-significance in this study could be due to a relatively uniform age range (30-60 years) and a lack of differentiation between premenopausal and postmenopausal women. Present findings suggested that HU is highly prevalent in patients with HTN has significant clinical implications. HU in its coexistence with HTN can further elevate the likelihood of adverse cardiovascular events, necessitating careful monitoring and management of uric acid levels in these patients. HU can further contribute to the development and worsening of HTN, potentially complicating blood pressure control. This underscores the importance of integrating strategies to lower uric acid levels, such as lifestyle modifications and appropriate pharmacotherapy, into the management plan for hypertensive patients. The combination of HTN and HU may also heighten the risk of CKD, as both conditions independently contribute to renal damage. Therefore, regular assessment of renal function is crucial in hypertensive patients with elevated uric acid levels to prevent the progression of CKD and ensure comprehensive care. Being a single center study, conducted on a relatively modest sample were some of the inherent limitations of this study. We were unable to record the impact of various anti-hypertensive treatments and its relationship to existing uric acid levels. Cross-sectional design of this research may not explore causal inferences, so a longitudinal design could provide better insights in the future.

CONCLUSIONS

The frequency of hyperuricemia was high (22.9%) in patients with hypertension. Further prospective studies should be planned to record the clinical impact of hyperuricemia among hypertensive patients.

Authors Contribution

Conceptualization: AA, SQ, TK, SK
Methodology: AA, SQ,
Formal analysis: SK
Writing, review and editing: AA, SQ, SK, TK, SK, FK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Clinical and Pathological Spectrum of Wilson Disease in Children at a Tertiary Care Hospital of Faisalabad, Pakistan

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ABSTRACT

Wilson disease is a genetic disorder related to copper metabolism that follows an autosomal recessive pattern. **Objectives:** To document the clinical and pathological spectrum of Wilson disease at a tertiary setting in Punjab, Pakistan. **Methods:** This cross-sectional study was conducted at the Department of Pediatric Gastroenterology, Children's Hospital, Faisalabad, Pakistan, from December 2019 to October 2024. A total of 60 children of both genders aged below 18 years, and presenting with Wilson disease were analyzed. Physical and clinical examinations were performed and medical history was taken in all Wilson disease cases. Demographic and clinical characteristics were noted, and relevant laboratory investigations were done. **Results:** In a total of 60 children with Wilson disease, 42 (70.0%) were boys. The mean age was 10.25 ± 3.10 years. The most frequent signs and symptoms were Jaundice, hepatomegaly, ascites, and coagulopathy, noted in 53 (88.3%), 41 (68.3%), 36 (60.0%), and 24 (45.0%) children respectively. Kaiser Fischer ring was noted in 16 (26.7%) children. The mean Wilsons index score was 9.77 ± 2.98 while 31 (51.7%) children had scores ≥10. The mean ceruloplasmin and 24-hour urinary copper levels were 7.03 ± 7.51 mg/dl and 746.03 ± 451.06 µg. **Conclusions:** It was concluded that hepatic manifestations are the most common among children with Wilson disease. The most frequent signs and symptoms among children were Jaundice, hepatomegaly, and ascites. There is a need to identify factors that contribute to early diagnosis and prompt treatment, thereby preventing severe brain damage and liver failures in affected patients.

INTRODUCTION

Wilsons disease (WD) is a genetic disorder related to copper metabolism that follows an autosomal recessive pattern. Its prevalence globally ranges from 1 in 10,000 to 1 in 30,000 individuals [1]. The condition arises due to mutations in a gene responsible for copper transport, leading to reduced or absent copper transportation into bile. This leads to the accumulation of toxic copper in the liver, causing damage to hepatocytes [2]. As the disease advances, copper deposition occurs in other organs such as the brain, cornea, kidneys, and heart. The clinical manifestation of the disease directly corresponds to the location of copper accumulation and the extent of tissue harm [3]. WD presents with various clinical forms, with hepatic involvement being the most common in individuals under 11 years old [4]. Hepatic presentations range from asymptomatic cases with elevated liver enzyme levels to severe conditions like fulminant hepatic failure, chronic liver disease, spleen enlargement, and liver cirrhosis. While

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neuropsychiatric symptoms are more frequently observed in individuals in their second or third decade of life, they can also manifest in pediatric patients [5]. Isolated neurological symptoms are present in about 8-22% of pediatric patients [6]. Neurological signs can be diverse and include behavioural irregularities, decline in school performance, handwriting deterioration, dysarthria, and excessive saliva production [7, 8]. Psychiatric issues such as depression, anxiety, and even psychosis can coexist [9]. Neurological symptoms in Wilson's disease may or may not be accompanied by symptomatic liver disease. Atypical presentations of Wilson's disease may encompass conditions such as renal stones, early-onset osteoporosis, cardiomyopathy, pancreatitis, and hypoparathyroidism [10, 11]. The primary goal of pharmacological treatment for WD is to prevent further copper accumulation by decreasing absorption or enhancing its elimination through urine bile, or both. Liver transplantation is indicated in cases of progressive liver failure, worsening neurological symptoms, portal hypertension complications (even with medical and dietary intervention), and acute liver failure [12]. The available literature has limited detailed studies on pediatric WD cases. In Pakistan, there is scarce data on the disease burden and its various presentations.

We aimed this research to shed light on the diverse manifestations of WD in children. This study might help add to what little is already known about the various sociodemographic and clinical aspects of WD among children in Pakistan. This study was conducted to document the clinical and pathological spectrum of WD at a tertiary setting in Punjab, Pakistan.

METHODS

This cross-sectional study was conducted at the Department of Pediatric Gastroenterology, Children's Hospital, Faisalabad, Pakistan from December 2019 to October 2024. Considering the proportion of isolated neurological symptoms in WD as 8% [6], with a 95% confidence level and 7% margin of error, the required sample size was calculated to be 58. For this study, 60 children who fulfilled the eligibility criteria were considered. Inclusion criteria were children of both genders, aged below 18 years, and newly diagnosed cases of WD. Children with incomplete medical records or unclear diagnoses were excluded. Approval from the "Institutional Ethical Committee" was taken (letter number: 05/2019). Informed consents were obtained from parents/guardians. Demographic characteristics like gender, age, residence, clinical information like presenting signs and complaints, children's score, Wilson index, and relevant laboratory parameters like liver function tests, ceruloplasmin and urine copper were noted. A comprehensive physical examination was performed, focusing on the identification of jaundice, hepatosplenomegaly, ascites, and indicators of liver dysfunction. Neurological and psychiatric evaluations were also conducted. All cases underwent a slit-lamp eye examination by an ophthalmologist to detect the presence of Kayser-Fleischer (KF) rings and/or sunflower cataracts. The diagnosis of WD was established based on 24-hour urinary copper excretion and serum ceruloplasmin levels. Urinary copper excretion >100 µg/24 hours was used to diagnose WD, and this test was performed using atomic absorption spectrophotometry (PerkinElmer Analyst 400 [USA]) after ensuring proper sample collection and excluding other liver diseases [13]. Serum ceruloplasmin levels <20 mg/dL were considered diagnostic for WD, measured using nephelometry. Family history was considered positive if there was a history of WD in a sibling or 1st degree relative. Consanguinity was considered "yes" if the parents of the affected children were 1st cousins. Penicillamine, zinc acetate, and liver-supportive fat-soluble vitamin supplements were advised to all patients. All the study data were entered and analyzed utilizing "Statistical Package for Social Sciences (SPSS)", version 26.0. Descriptive representations of the qualitative data were made as frequency and percentages. Quantitative data were shown as calculating mean along with standard deviation.

RESULTS

In a total of 60 children with WD, 42 (70.0%) were boys representing a boy-to-girl ratio of 2.3:1. The mean age was 10.13±3.08 years ranging between 5 to 16 years while 47 (78.3%) children were aged between 5-12 years. The residential status of 35 (58.3%) children was rural. Family history of WD was present in 15 (25.0%) children whereas consanguinity of marriage among parents was noted in 27 (45.0%) cases. Details about the demographical and clinical characteristics of children are shown in table 1.

Table 1: Demographic and Clinical Characteristics at the Time of Diagnosis of Wilson's Disease (n=60)

Demographic and Clinical Characteristics		N (%)
Gender	Boys	42 (70.0%)
	Girls	18 (30.0%)
Age	5-12	47 (78.3%)
	13-18	13 (21.7%)
Residence	Urban	25 (41.7%)
	Rural	35 (58.3%)
Child Score	A	29 (48.3%)
	B	12 (20.0%)
	C	19 (31.7%)
Family History		15 (25.0%)
Consanguinity		27 (45.0%)

The most frequent signs and symptoms were Jaundice,

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hepatomegaly, ascites, and coagulopathy, noted in 53 (88.3%), 41 (68.3%), 36 (60.0%), and 24 (45.0%) children respectively. The details about the most frequent signs and symptoms among children with WD are shown in figure 1.

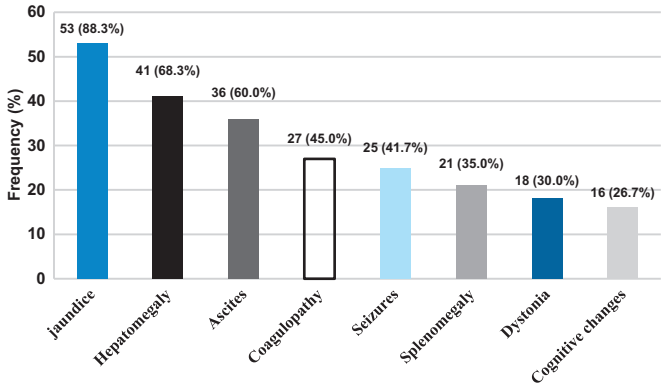

Figure 1: Frequency of Signs and Symptoms in Children at the Time of Diagnosis of Wilson's Disease (n=60)

Kaiser Fischer ring was noted in 16 (26.7%) children. The mean Wilsons index score was 9.77±2.98 while 31 (51.7%) children had scores ≥10 shown in figure 2.

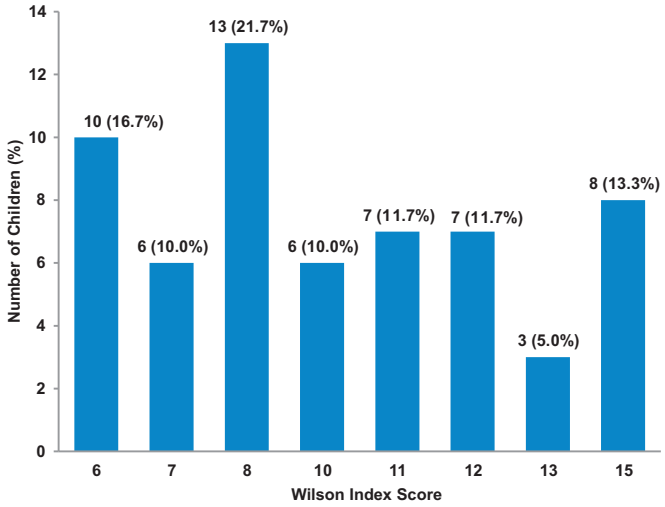

Figure 2: Distribution of Wilson Index Scores at the Time of Diagnosis of Wilson's Disease (n=60)

The mean ceruloplasmin and 24 hours' urinary copper levels were 7.03 ± 7.51 mg/dl and 746.03 ± 451.06 µg. Details about the biochemical parameters are shown in table 2.

Table 2: Biochemical Parameters at the Time of Diagnosis of Wilson's Disease (n=60)

Parameters	Mean ± SD	Normal range
Ceruloplasmin (mg/dl)	7.03 ± 7.51	20-40
Serum Alanine Aminotransferase (U/L)	102.82 ± 11.57	≤40
Serum Aspartate Aminotransferase (U/L)	134.08 ± 42.64	≤40
Serum Bilirubin (mg/dl)	3.28 ± 2.90	0.3-1.2
Serum Albumin (g/dl)	2.91 ± 0.64	3.5-5.5
24 Hours Urinary Copper (µg)	746.03 ± 451.06	<40

A comparison of demographic and clinical characteristics concerning the Wilson Index Score was done and no statistically significant associations were found (p>0.05), as in table 3.

Table 2: Comparison of Demographic and Clinical Characteristics between Wilson Index Score among newly diagnosed Wilson's Disease cases (n=60)

Demographic and Clinical Characteristics		Wilson Index Score		p-Value
		<10 (n=29)	≥10 (n=31)	
Gender	Boys	21 (72.4%)	21 (67.7%)	0.539
	Girls	8 (27.6%)	10 (32.3%)	
Age	5-12	21 (72.4%)	26 (83.9%)	0.282
	13-18	8 (27.6%)	5 (16.1%)	
Residence	Urban	14 (66.7%)	11 (35.5%)	0.315
	Rural	15 (33.3%)	20 (64.5%)	
Child Score	A	18 (62.1%)	11 (35.5%)	0.103
	B	5 (17.2%)	7 (22.6%)	
	C	6 (20.7%)	13 (41.9%)	
Family History		7 (24.1%)	8 (25.8%)	0.409
Consanguinity		11 (37.9%)	16 (51.6%)	0.287

DISCUSSION

The present study analyzed 60 children with WD and we noted that 70.0% of children were boys, representing a boy-to-girl ratio of 2.3:1. A local study from Ali *et al.*, from Islamabad described 60.8% of children with WD to be male [14]. Current findings are consistent with Mahmud *et al.*, from Bangladesh who found a boys-to-girl ratio of 2:1 among 100 WD children [15]. Similar findings exhibiting male predominance have been documented in other parts of the world [16, 17]. Merle and colleagues found female predominance among WD cases [13]. No clear elaboration about the gender's association with WD exists in the literature. In this study, the mean age of children with WD was 10.13 ± 3.08 years ranging between 5 to 16 years while 78.3% of children were aged between 5-12 years. Mahmud et al from Bangladesh found the mean age of the children with WD to be 8.42 ± 2.6 years [15]. A local study by Aaraj and colleagues found the mean age of the children with WD as 9.74 years [16]. WD is not commonly observed before the age of 5, although there have been reports of its occurrence as early as 3 years of age [17]. The youngest participant in this study was a 5-year-old boy. Consanguinity of marriage was reported by 45.0% of WD cases in this study. Literature reports consanguinity to be an important feature of WD as it is known to be an autosomal recessive disorder. Literature reports more risk of WD among children with consanguineous parents [18-20]. The spectrum of WD is wide and varies geographically. It is important to find out certain clinical patterns dominating different parts of the world. The most frequent signs and symptoms were Jaundice, hepatomegaly, ascites, and coagulopathy, noted in 88.3%, 68.3%, 60.0%, and 45.0% of children respectively. Local data has previously recorded that hepatic symptoms are the

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commonest found in around 69% of WD cases while Jaundice is observed in 85.7% of these cases [14]. Day and colleagues observed that 58.3% of cases showed hepatic involvement, which was a significant finding in their study [5]. The primary hepatic symptoms were jaundice, hepatomegaly, and ascites. These findings are aligned with those reported in both national and international studies, reinforcing the consistency of the observed symptoms [21]. Additionally, neurological manifestations of WD are the second most common clinical presentation, particularly in individuals aged 10 to 15 years. Notably, this neurological aspect serves as the initial symptom in 40-60% of WD patients, statistics described in the literature [20]. KF rings were observed in 26.7% of WD cases in this study, primarily due to patients having hepatic WD. The present study found a positive family of WD in 25.0% of cases. The literature reports a positive family history of WD ranging between 25-41% [14, 21]. Present study adds important insights to present patterns of WD among children. Low ceruloplasmin levels (7.03 ± 7.51 mg/dL) in this study, are a hallmark of WD and reflect impaired copper metabolism due to mutations in the ATP7B gene, which disrupt copper incorporation into ceruloplasmin [22]. The normal range of ceruloplasmin is 20–40 mg/dL, and levels below 20 mg/dL strongly indicate WD, particularly in symptomatic patients [23]. Elevated 24-hour urinary copper levels, with a diagnostic cutoff >100 µg, further confirm the diagnosis by reflecting excessive copper excretion due to hepatocellular damage and reduced hepatic copper-binding capacity [24]. In this study, the mean 24-hour urinary copper level was 746.03 ± 451.06 µg. The findings of this study underline the importance of early recognition and diagnosis of WD, especially in children who present with unexplained liver dysfunction, neurological symptoms, or psychiatric changes. The demographic features, including the high male-to-female ratio and the common presence of consanguinity, provide valuable insight into genetic and environmental risk factors. The biochemical markers and clinical scores provide crucial diagnostic information that can guide management and early intervention to prevent severe liver and neurological complications.

CONCLUSIONS

It was concluded that hepatic manifestations are the most common among children with WD. The most frequent signs and symptoms among children were Jaundice, hepatomegaly, and ascites. There is a need to identify factors that contribute to early diagnosis and prompt treatment, thereby preventing severe brain damage and liver failures in affected patients.

Authors Contribution

Conceptualization: NS
Methodology: NS, HB, HSM, ZB, IA, KM
Formal analysis: NS, HB, ZB, IA, KM
Writing review and editing: NS, HB, ZB

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

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Comparative Analysis of Serum Vitamin D Levels in Newly Diagnosed Tuberculosis Patients versus Healthy Individuals

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ABSTRACT

Vitamin D deficiency has been implicated in the susceptibility to tuberculosis due to its crucial role in immune regulation and host defense mechanisms. **Objectives:** To compare serum Vitamin D levels between newly diagnosed TB patients and healthy individuals and assess their association with the nutritional-inflammatory profile. **Methods:** This comparative cross-sectional study was conducted over 1 year from Dec 2021 to Dec 2022. A total of 224 participants, comprising 112 newly diagnosed tuberculosis patients as cases and 112 healthy individuals as controls, were recruited. Cases included patients aged over 18 years with confirmed tuberculosis diagnosis GeneXpert MTB/RIF assay. Controls were individuals without tuberculosis symptoms and with serum vitamin D levels available. **Results:** Vitamin D levels were found to be lesser in TB patients with median levels of 14.35 ng/mL (interquartile range (IQR): 8.65–25.48) versus 19.08 ng/mL (IQR: 13.92–26.17; p=0.029) in normal people. A higher proportion of TB patients exhibited severe deficiency (<10 ng/mL) at 35.7% compared to 13.4% in controls (p=0.002). Similarly, deficiency (10–20 ng/mL) was more prevalent among tuberculosis patients (42.9%) than controls (26.8%). Vitamin D levels in tuberculosis patients had a positive correlation with BMI and albumin levels. **Conclusions:** It was concluded that tuberculosis patients exhibited poorer nutritional status, with lower BMI, albumin, hemoglobin, and Vitamin D levels compared to healthy controls with a significantly higher proportion of tuberculosis patients having severe Vitamin D deficiency.

INTRODUCTION

Vitamin D deficiency is a public health concern, with around one billion people estimated to have insufficient levels [1]. The prevalence varies geographically due to differences in sun exposure, dietary intake, cultural practices, and skin pigmentation. In many regions, particularly in South Asia, vitamin D deficiency is endemic [2]. In Europe, nearly 40% of the population is deficient, with even higher rates in elderly populations [3]. This widespread deficiency underscores the need for increased awareness and intervention. Tuberculosis (TB) remains one of the leading infectious diseases globally, caused by Mycobacterium tuberculosis. Recent evidence highlights its potential role in combating infections, including tuberculosis (TB), due to its ability to enhance macrophage function and upregulate the production of antimicrobial peptides like "cathelicidin and defensins" [4, 5]. The interaction between vitamin D and TB is well documented, with vitamin D deficiency identified as a risk factor for TB susceptibility. Studies suggest that individuals with low vitamin D levels have impaired macrophage activation, resulting in suboptimal bacterial clearance [6, 7]. A meta-analysis revealed that vitamin D deficiency is significantly more prevalent among TB patients than in healthy individuals [8]. Furthermore, supplementation with vitamin D in TB patients has been

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explored as an adjunct therapy, showing promise in enhancing treatment outcomes [9]. In Pakistan, TB remains a major public health challenge, with the country ranking fifth among high-burden TB countries [10]. Simultaneously, vitamin D deficiency is alarmingly prevalent, affecting approximately 7090% of the population, including all age groups [11, 12]. A 2019 study reported that over 80% of TB patients had vitamin D deficiency compared to 45% in healthy controls, highlighting the correlation between low vitamin D levels and increased TB risk [13]. Factors contributing to this deficiency include limited sun exposure due to cultural practices, inadequate dietary intake, and high rates of malnutrition [14]. Studies indicate that the majority of TB patients in Pakistan have insufficient vitamin D levels, potentially impairing immune response and bacterial clearance. Variations in Mycobacterium tuberculosis strain types, including the Beijing and East African-Indian lineages, further impact disease severity and treatment outcomes. While standard treatment regimens achieve high success rates in drug-sensitive TB, the growing threat of Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) necessitates prolonged, toxic therapies [13]. While global research has established a link between vitamin D deficiency and TB susceptibility, regional variations in prevalence and severity necessitate localized investigations. Pakistan's dual burden of TB and vitamin D deficiency offers a unique opportunity to explore this relationship further and help in the development of preventive and therapeutic strategies.

This study aimed to perform a comparative analysis of serum vitamin D levels between newly diagnosed TB patients and healthy individuals and assess their association with the nutritional profile.

METHODS

This comparative cross-sectional study was conducted over 1 year from Dec 2021 to Dec 2022 at Liaquat University Hospital, Hyderabad. A total of 224 participants, comprising 112 newly diagnosed TB patients as cases and 112 healthy individuals as controls, were recruited. The sample was calculated via an open epi sample size calculator by taking the percent of Vitamin D deficiency in exposed (TB patients) with the outcome as 68.96% percent of unexposed (healthy controls) with the outcome as 51.72% with 80% power of study and 90% CI [15]. The study was approved by the ERC of Liaquat University of Medical and Health Sciences, Jamshoro vide letter No. LUMHS/REC/-164. Cases included patients aged over 18 years with confirmed TB diagnosis through AcidFast Bacilli (AFB) smear microscopy or GeneXpert MTB/RIF assay. Controls were individuals without TB symptoms and with serum vitamin D levels available. Participants with chronic liver disease, chronic kidney disease, HIV-positive status, or ongoing vitamin D supplementation were excluded from the study. Pregnant individuals were also excluded to eliminate potential confounding factors related to pregnancy-induced changes in vitamin D metabolism. Vitamin D status was classified based on the clinical practice guidelines of the Endocrine Society Task Force [16]. Informed written consent was taken from every participant (cases and controls) before enrollment in the study. The study outcomes were assessed in terms of measuring the serum Vitamin D levels and their correlation with nutritional (BMI, Vitamin B12, Serum Ferritin, Hemoglobin, and Albumin) and inflammatory markers (ESR, Total Leucocyte Count, and Neutrophil-to-Lymphocyte Ratio) in TB patients and healthy controls. Data analysis was performed using SPSS version 21.0. Descriptive statistics were used to summarize demographic and clinical characteristics. An Independent t-test was applied to compare continuous variables between cases and controls, while the chi-square test assessed the relationship of the level of Vitamin D in cases and controls. Spearman's correlation was used to measure the association between Vitamin D levels and nutritional-inflammatory parameters. A p-value<0.05 was considered statistically significant.

RESULTS

The mean age was similar between TB patients (50 ± 16.46 years) and controls (49 ± 11.38 years) (p=0.43). A greater ratio of males was observed among TB patients (71.43%) compared to controls (55.36%). TB patients had a significantly lower mean BMI (21.34 ± 3.16 kg/m^2) compared to controls (26.53 ± 2.14 kg/m^2) (p=0.04). Mean albumin levels were lower in TB patients (3.03 ± 1.32 mg/dL) than in controls (4.3 ± 0.53 mg/dL) (p=0.013). Likewise, hemoglobin levels were lower in cases (10.52 ± 2.19 g/dL) than in controls (13.32 ± 1.56 g/dL) (p = 0.045). Differences in mean calcium, total WBC count, and platelet count were not significant (Table 1).

Table 1: Baseline Characteristics of Tb Patients (n=112) and Healthy Controls (n=112)

Variables	TB Patients (n=112)	Controls (n=112)	p-Value
Male	80 (71.43%)	62 (55.36%)	0.12
Female	32 (28.57%)	50 (44.64%)	
Mean BMI (Kg/m^2)	21.34 ± 3.16	26.53 ± 2.14	0.04*
Mean Albumin (mg/dL)	3.03 ± 1.32	4.3 ± 0.53	0.013*
Mean Calcium (mg/dL)	8.15 ± 1.27	10.21 ± 0.13	0.86
Mean ESR (mm/h)	67 ± 12.76	14.53 ± 6.31	0.003*
Mean Hemoglobin (g/dL)	10.52 ± 2.19	13.32 ± 1.56	0.045*
Mean Total WBC Count (10^3/L)	13642 ± 3281	6324 ± 1138	0.08
Mean Platelets (100,000/dL)	3.23 ± 1.51	2.21 ± 0.62	0.13

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*Statistically significant

Vitamin D levels were lesser in TB patients in comparison to healthy controls, with median levels of 14.35 ng/mL (IQR: 8.65–25.48) versus 19.08 ng/mL (IQR: 13.92–26.17; p=0.029). A higher proportion of TB patients exhibited severe deficiency (<10 ng/mL) at 35.7% compared to 13.4% in controls (p=0.002). Similarly, deficiency (10–20 ng/mL) was more common among TB patients (42.9%) than controls (26.8%). Opposite to that, Vitamin D sufficiency (>30 ng/mL) was observed in only 8% of TB patients compared to 24.1% of controls (Table 2).

Table 2: Comparison of Vitamin D Status Between Tb Patients (n=112) and Healthy Controls (n=112)

Variables	TB Patients (n=112)	Controls (n=112)	p-Value
Median (IQR) Serum Vitamin D3 Levels (ng/mL)	14.35 (8.65–25.48)	19.08 (13.92–26.17)	0.029*
Severe Deficiency (<10 ng/mL)	40 (35.7%)	15 (13.4%)	0.002*
Deficiency (10–20 ng/mL)	48 (42.9%)	30 (26.8%)	
Insufficiency (21–30 ng/mL)	15 (13.4%)	40 (35.7%)	
Sufficiency (>30 ng/mL)	9 (8.0%)	27 (24.1%)	

*Statistically significant

A significant positive correlation was observed between Vitamin D and BMI (r=+0.40, p=0.032) and albumin (r=+0.55, p=0.018), suggesting that better nutritional status may be associated with higher Vitamin D levels. While hemoglobin (r=+0.48, p=0.076) and Vitamin B12 (r=+0.15, p=0.162) showed positive correlations, they were not statistically significant. Conversely, ESR (r=-0.65, p=0.091), serum ferritin (r=-0.08, p=0.247), and NLR (r=-0.09, p=0.225) exhibited negative correlations with Vitamin D, though these associations lacked statistical significance (Table 3). While correlation of Vitamin D3 with Nutritional-Inflammatory Profile in Healthy Controls was not found to be statistically significant.

Table 3: Correlation Between Vitamin D3 and Nutritional-Inflammatory Profile in Tuberculosis Patients and Healthy Controls

PARAMETER	TB PATIENTS		CONTROLS	
	Correlation Coefficient (r)	p-Value	Correlation Coefficient (r)	p-Value
BMI	+0.40	0.032*	+0.22	0.148
Vitamin B12	+0.15	0.162	+0.09	0.312
Serum Ferritin	-0.08	0.247	-0.12	0.284
Albumin	+0.55	0.018*	+0.38	0.079
Hemoglobin	+0.48	0.076	+0.29	0.092
ESR	-0.65	0.091	-0.15	0.056
Total Leucocyte Count	+0.12	0.198	+0.07	0.367
Neutrophil-to-Lymphocyte Ratio (NLR)	-0.09	0.225	-0.05	0.419

*Statistically significant

DISCUSSION

The findings in the current study revealed a median serum Vitamin D level of 14.35 ng/mL among TB patients, significantly lower than the 19.08 ng/mL observed in controls (p=0.029). Severe Vitamin D deficiency was more prevalent in TB patients (35.7%) compared to controls (13.4%, p=0.002). Similarly, Vitamin D sufficiency was less common in TB patients (8%) than in controls (24.1%). A study by Balcells et al., showed that Vitamin D deficiency is consistently linked to active TB, likely owing to the immunomodulatory role in macrophage activation and granuloma formation [17]. TB patients had significantly lower BMI (21.34 ± 3.16kg/m^2) and serum albumin levels (3.03 ± 1.32mg/dL) compared to controls (26.53 ± 2.14kg/m^2 and 4.3 ± 0.53mg/dL, respectively, p=0.013). BMI and albumin were positively associated with Vitamin D levels in TB patients. This suggests that malnutrition exacerbates Vitamin D deficiency, which may worsen TB outcomes. Similar findings have been reported in India, where malnourished TB patients exhibited lower Vitamin D levels than their well-nourished counterparts, underscoring the need for nutritional interventions [18]. Malnutrition in TB patients likely arises from increased metabolic demands, poor appetite, and systemic inflammation. Low albumin levels, indicative of protein energy malnutrition, correlate with diminished Vitamin D binding protein, causing lower bioavailability of active vitamin D3 [19]. Elevated ESR levels in TB patients (67 ± 12.76mm/h) compared to controls (14.53 ± 6.31mm/h, p=0.003) indicate heightened systemic inflammation. However, no significant correlation was observed between Vitamin D levels and ESR (r=0.65, p=0.091). This contrasts with a study from China, where lower Vitamin D levels were linked to more severe inflammatory responses in TB patients [20]. The absence of such an association in our study could be due to variability in disease severity or differences in the inflammatory markers assessed. TB patients demonstrated lower hemoglobin levels (10.52 ± 2.19g/dL) compared to controls (13.32 ± 1.56g/dL, p=0.045), reflecting anemia of chronic disease. A positive relation between Hb levels and Vitamin D was observed (r=+0.48) but was non-significant (p=0.076). Anemia in TB is multifactorial, driven by chronic inflammation, nutritional deficiencies, and impaired erythropoiesis [21]. Studies from India have highlighted the synergistic impact of Vitamin D and iron deficiencies in exacerbating anemia among TB patients [22]. These findings reinforce the need to deal with Vitamin D deficiency and malnutrition in TB management. The WHO End TB Strategy emphasizes integrated nutritional support for TB patients, aligning with our observation that malnourished TB patients are prone to severe Vitamin D deficiency [23]. Vitamin D supplementation as adjunctive therapy has shown promise in enhancing sputum conversion rates and reducing treatment duration in

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randomized controlled trials conducted in India and Pakistan [24]. Variations in deficiency rates are influenced by dietary intake, sun exposure, genetic factors, and comorbidities. Comparative studies indicate that countries with higher latitudes experience more pronounced seasonal variations in Vitamin D3, potentially exacerbating TB risk during winter months [25].

CONCLUSIONS

Tuberculosis patients exhibited poorer nutritional status, with lower BMI, albumin, hemoglobin, and Vitamin D levels compared to healthy controls. A significantly higher proportion of TB patients had severe Vitamin D deficiency. Positive correlations were observed between Vitamin D levels and BMI as well as albumin, indicating a link between nutritional status and Vitamin D. However, inflammatory markers showed no significant association with Vitamin D levels. These findings suggest that nutritional deficiencies, particularly in Vitamin D, may be linked to TB, highlighting the importance of nutritional support in TB management.

Authors Contribution

Conceptualization: MAR
Methodology: MAR, MN, IJ, MS
Formal analysis: MAM, MZ
Writing review and editing: MN, IJ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

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Knowledge, Attitudes, and Practices towards Early Childhood Caries among Affluent Parents of Lahore

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ABSTRACT

Parents influence oral hygiene practices and children's health behaviours as young ones lack the comprehension and dexterity to maintain oral health. **Objectives:** To evaluate the knowledge, attitudes, and practices about early childhood caries among affluent parents of Lahore. **Methods:** A cross-sectional study was conducted from August 2024 to October 2024 using non-probability sampling with 203 participants. Revalidated questionnaires inquiring about knowledge, attitude, and practice were distributed to parents with children under 5 years old, enrolled in affluent schools within the city. Frequency and percentage distributions were obtained for each qualitative variable and mean, and standard deviation were acquired for quantitative variables. The differences between genders were analyzed using chi-squared statistics. A p-value of less than 0.05 was considered statistically significant. **Results:** Among 203 participants, the majority were mothers 56.2% and the sample comprised of most male children in age group 3-5 years. Among the participants, more than half of the parents had graduated from university; some had graduated from high school. Only a few had completed their primary-level education. The overall mean knowledge score was 52.77 ± 21.59, whereas the mean score for attitude and practice was 61.24 ± 25.49 and 65.61 ± 26.66 respectively. Mothers had significantly greater overall knowledge (p=<0.001), better attitudes (p=0.164), and practices (p-value=0.112) towards early childhood caries as compared to fathers. **Conclusions:** It was concluded that although affluent parents of 5-year-old children had good knowledge regarding the Early Childhood Caries, their attitude and practices were still lacking in keeping up with the recommended standards.

INTRODUCTION

The oral health of young children is threatened by early childhood caries (ECC), which is a complicated and multidimensional problem in pediatric dentistry [1]. Early childhood caries, which is defined as one or more primary teeth that are decaying, missing, or filled in children younger than six years old, is still a common and worrisome condition. This condition is significant not just because it affects dentition but also impacts on a child's general health. In this context, the roles that parents play become increasingly important in shaping their child's views and their habits toward oral hygiene [2]. Effective preventive measures and treatments depend critically on an understanding of the complex interactions between parental attitudes, knowledge, and ECC practices [3]. In addition to causing tooth pain and discomfort, ECC harms a child's general well-being, diet, and standard of living [4, 5]. Epidemiological studies highlight the prevalence rates of ECC around the world, which vary depending on factors such as access to oral healthcare, dietary patterns, and socioeconomic differences [6]. This article takes a critical

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look at the complex connection between parental involvement and the avoidance of early childhood development. It explores the nuances that affect parents' choices, actions, and perceptions about their children's oral health, going beyond the boundaries of simple statistics and clinical research. A child's early behaviours, including dental hygiene routines, are mostly shaped by their parents. A child's dental care regimen is based mostly on the interaction of parental attitudes, and actions [7]. Health can be understood in both macro and micro contexts. Aspects of behaviour, development, and biology are included in the micro context. While the community's structure and politics generate the macro context, which is influenced socially by the family, community, and environment. When it comes to ECC prevention, parents use different approaches, which are impacted by cultural, social, and educational variables, even if dental information is widely available [8,9]. Developing tailored interventions requires an understanding of the factors influencing parental knowledge and attitudes regarding early childhood education [9]. Moreover, parents' exposure to and assimilation of dental information may not result in the adoption of practical preventative actions. Even though parents have access to information, there are differences in how parents put oral hygiene routines into practice. These differences can be attributed to several impediments, including time restraints, budgetary limits, and contradicting information from several sources [10, 11]. Studies have shown differences in awareness of ECC among parents and their choice pf preventive actions. Fluoride use, dietary choices, tooth brushing regimens, and parental oral health behaviours are important contributions to preventing ECC. Furthermore, a variety of parental actions targeted at ECC prevention are influenced by misconceptions, a lack of knowledge about preventative strategies, and conflicting objectives [12, 13]. Parental attitudes toward early childhood education impact more than just one home. They are felt in the domains of public health campaigns, educational programs, and legislative frameworks designed to lessen the incidence of ECC in local communities. When creating focused interventions and customized strategies that appeal to a range of parental viewpoints, it is essential to acknowledge the complex interactions that exist between parental knowledge, attitudes, and practices [8, 14]. This research study begins a thorough investigation of the complex processes influencing parental involvement in ECC prevention. Even if the frequency and severity of ECC have been emphasized in earlier research, a deeper comprehension of parental attitudes, actions, and knowledge is required to create customized therapies that are acceptable in a range of parental circumstances. The topic of early childhood caries has become increasingly popular in the vibrant metropolis of Lahore, particularly among wealthy parents. As protectors of their offspring's health and welfare, these parents understand the significance of dental hygiene and how it affects their young charges. But even with their awareness and access to resources, there is still much to learn about the complex interactions between early childhood career knowledge, attitudes, and practices. This paper explores the complex attitudes and actions of wealthy parents in Lahore concerning this common dental issue, illuminating their convictions, routines, and the underlying causes that influence how they prevent and treat early childhood caries. The variables that affect parents' perceptions of early childhood caries (ECC) and how those perceptions affect the oral health of their kids. It seeks to comprehend the extent of parental knowledge and the elements influencing their perspectives regarding the use of dental hygiene products. To contribute to a more thorough approach to ECC prevention, the study seeks to close the knowledge, attitude, and practical implementation gap among parents.

This study aims to support a more all-encompassing strategy for preventing early childhood caries, one that recognizes and takes into account the many realities and viewpoints that parents have while attempting to protect their kids' oral health.

METHODS

The cross-sectional study was conducted from August 2024 to October 2024 using non-probability sampling with a sample size of 203 to comprehensively investigate the knowledge, attitude, and practices surrounding early childhood caries (ECC) among affluent parents in Lahore, Pakistan. After the approval, The Institutional Research and Ethics Committee provided ethical approval (UCD/ERCA/24/339). The study specifically targeted parents with children under the age of 5 who were enrolled in affluent schools within the city. The data for this study were collected using a self-administered questionnaire based on existing literature. To maintain data integrity, inclusion criteria required participants to be parents of children aged less than 5, and willing to actively participate in the study. On the other hand, language barriers and incomplete surveys were recognized as exclusion criteria, ensuring a rigorous analysis process. Utilizing a non-probability purposive sampling technique, participants were deliberately chosen to guarantee participation from a range of affluent schools. The self-administered questionnaire was adopted from the study by Al-Jaber et al., [15]. The sample size of 196 was calculated using a 95% confidence interval, a 50% prevalence of knowledge, attitudes, and practices (KAP), and a 5% margin of error [15]. The survey included thirty questions in all, organized

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into four categories. The initial section of the survey collected data on the participants' sociodemographic attributes, which included the gender of the parent, gender of the child, age of the child, age of parent, and level of education of the parent. In the second section of the questionnaire, thirteen questions concerning oral health knowledge of the parents were included and seven questions addressing attitudes toward professional dental care were included in the questionnaire's third section. Five items that analyzed oral hygiene practices and behaviours made up the fourth component. Information about aims and objectives was provided to the parents and informed consent was obtained before administration of the questionnaire. For analysis, each right response in the knowledge sections of the questionnaire received a score of "1", while incorrect and do not know answers obtained a score of "0". The level of knowledge was related to the correct answers and was classified as poor (<50%), moderate (50-75%), and good (>75%). Frequency and percentage distributions were obtained for each qualitative variable and mean, and standard deviation (SD) were acquired for quantitative variables. The differences between genders were analyzed using chi-squared statistics. A p-value of less than 0.05 was considered statistically significant. The data management and analysis were carried out, using the statistical software SPSS version 25.0

RESULTS

Total 203 responses were included in this analysis. The majority of participants in the study were mothers (56.2%) whereas participants who were fathers were 43.8%. More than half of parents (55.7%) had graduated from university, 29.6% had got higher education followed by 9.9% who had completed high school and lastly, 4.9% had done primary level. Male children included in this study were 51.20% and 48.80% were females. Out of these children, 51.7% were 3-5 years old followed by 34% of 1-2 years old, and lastly, 14.3% who were less than one year of age. The results were divided into three categories of questions asked about knowledge, attitudes, and practices. Regarding the first category "Knowledge" there were more than 70% "correct responses for the following questions: "Do you have knowledge or information about children's oral health", "Controlling the frequency of sugary intake can affect a child's dental decay" and "Proper care of oral hygiene is important for the health of permanent teeth". The overall mean knowledge score was 52.77 ± 21.59 (Table 1).

Table 1: Knowledge of Participants about Early Childhood Caries

Knowledge	Yes	No
	n (%)	n (%)
Do you have knowledge or information about children's oral health	156 (76.85%)	47 (23.15%)
The quantity of toothpaste in children <3 years is the size of a rice grain	99 (48.77%)	104 (51.23%)
Quantity of toothpaste in children >3 years is pea-sized	86 (42.36%)	117 (57.64%)
Effect on development of baby's teeth by Mother's diet during pregnancy	108 (53.20%)	95 (46.80%)
You can give canned juice regularly to your child	37 (18.23%)	166 (81.77%)
A dental checkup in your child's first year of life is essential even if the child does not suffer from tooth pain or dental caries	116 (57.14%)	87 (42.86%)
Bottle feeding at nighttime influences the child's baby teeth	133 (65.52%)	70 (34.48%)
Fluoridated toothpaste helps in preventing your child's dental decay	102 (50.25%)	101 (49.75%)
Controlling the frequency of sugary intake can affect a child's dental decay	150 (73.89%)	53 (26.11%)
The first signs of dental caries are the appearance of white spots or lines on the surfaces of teeth	98 (48.28%)	105 (51.72%)
Germs of dental caries can be transmitted from mother to her child by kissing on his/her lips or munching food herself before giving it to her child	88 (43.35%)	115 (56.65%)
Decay in baby teeth can harm the permanent teeth	111 (54.68%)	92 (45.32%)
Proper care of oral hygiene is important for the health of permanent teeth	159 (78.33%)	44 (21.67%)
Dental caries in children is inherited	57 (28.08%)	146 (71.92%)

The overall mean score for attitude was 61.24 ± 25.49. Approximately 80% correct responses were collected for the questions; "It is the parent's responsibility to maintain the child's oral health" and "Parents/caregiver should guide and help their children at the age of less than or equal to 5 years during brushing of their teeth" (Table 2).

Table 2: Attitude of Participants Towards Early Childhood Caries

Attitude	Yes	No
	n (%)	n (%)
It is the parent's responsibility to maintain the child's oral health	178 (87.7%)	25 (12.3%)
Your child's teeth get harmed if breast-feeding is done frequently and for a prolonged period	62 (30.5%)	141 (69.5%)
Providing fresh juices frequently during the day can harm your child's teeth	83 (40.9%)	120 (59.1%)
As soon as baby teeth erupt they should be cleaned	126 (62.1%)	77 (37.9%)
Dental check-up of your child as soon as his/her teeth erupt	124 (61.1%)	79 (38.9%)
Parents/caregivers should guide and help their children at the age of less than or equal to 5 years during brushing of their teeth	173 (85.2%)	30 (14.8%)
The overall mean of Attitude	61.24 ± 25.49	

Results related to practice depicted that more than 80% "correct" responses were collected when asked about questions, such as "Your child's oral health depends on a balanced diet" and "Parents should make an effort to improve their awareness about oral health". The overall mean practice score was 65.61 ± 26.66" (Table 3).

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Table 3: Information associated with child's oral health practices of parents

Practices	Yes	No
	n (%)	n (%)
Your child's oral health depends on a balanced diet	169 (83.25%)	34 (16.75%)
Providing breastfeeding/bottle feeding during bed-time could harm your child's teeth	98 (48.28%)	105 (51.72%)
Dental caries can be transmitted by sharing the utensils (i.e., spoons, forks)	80 (39.41%)	123 (60.59%)
Parents should make an effort to improve their awareness about oral health	175 (86.21%)	28 (13.79%)
Cleaning and brushing your child's teeth after each meal is necessary	144 (70.94%)	59 (29.06%)

Participants with higher education levels had significantly better overall knowledge scores than less educated ones (p=0.002)(Table 4).

Table 4: Comparison of Knowledge, Attitude, and Practice Score with Education level of Parents

Variables		n	Mean ± SD	p-Value*
Knowledge Score Percent	University	113	48.67 ± 22.08	0.002*
	Primary Level	10	71.42 ± 22.08	
	High School	20	59.64 ± 24.00	
	Higher Education	60	55.11 ± 17.25	
	Total	203	52.77 ± 21.59	
Attitude Score Percent	University	113	58.40 ± 25.88	0.116
	Primary Level	10	75.00 ± 25.15	
	High School	20	68.33 ± 32.39	
	Higher Education	60	61.94 ± 21.28	
	Total	203	61.24 ± 25.49	
Practice Score Percent	University	113	65.30 ± 26.99	0.185
	Primary Level	10	76.00 ± 18.37	
	High School	20	74.00 ± 33.77	
	Higher Education	60	61.66 ± 23.94	
	Total	203	65.61 ± 26.66	

Mothers had significantly better overall knowledge scores than fathers as shown in figure 1. Similarly, mothers showed a better attitude towards early childhood caries as compared to fathers however, the results were statistically insignificant (p=0.164). Also, more educated parents lacked the practices to prevent early childhood caries (p=0.185). Moreover, mothers were practicing preventive care for early childhood caries as compared to fathers (Figure 1).

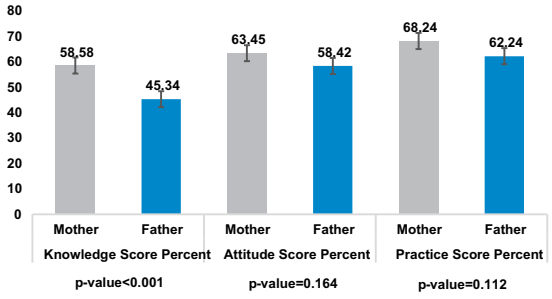

Figure 1: Comparison of Mean Scores of Knowledge, Attitude and Practice in Relation to Gender of Parents

DISCUSSION

The study provides valuable insights into the knowledge, attitudes, and practices of affluent parents in the Lahore region, regarding early childhood caries. These findings align with prior research that highlights the pivotal role of parents in influencing children's oral health behaviors. The mean knowledge score of 52.77% ± 21.59 reflects moderate awareness among parents about ECC. While many participants recognized the importance of controlling sugary intake (73.89%) and maintaining oral hygiene, critical gaps were observed in areas such as the appropriate amount of toothpaste for children under 3 years (48.77%) and over 3 years (42.36%). Interestingly the mothers in this study demonstrated higher knowledge scores than fathers (p<0.001). This is Gurunathan et al., findings suggesting that fathers are less involved in the daily care of their children and therefore less informed about their children's oral health practices [16]. Moreover, over half of the parents did not recognize white spots or lines on teeth as early indicators of dental caries [16]. In addition, parental education played a significant role, as those with higher education levels demonstrated better knowledge scores. This result is supported by studies such as Patil et al., which attributed higher knowledge levels to greater access to oral health resources through modern technology and the Internet [17]. However, contrary to findings from Qatar where 64% of the mothers were unaware of the recommended time for a child's first dental visit [18]. Our study found greater awareness among affluent parents in Lahore. Similarly, Saudi Arabian research reported that nearly half of the parents did not recognize the importance of a dental checkup for one-year-olds, whereas our study revealed better awareness in this demographic [18]. Parents exhibited a relatively positive attitude toward ECC prevention with a mean score of 61.24% ± 25.49. A majority (80%) agreed that maintaining oral health is the parents' responsibility and acknowledged the importance of assisting these children under 5 years of age during tooth brushing. These findings are consistent with studies in similar contexts where parents agreed that children's oral health is primarily a parental responsibility [18]. However, only 25% of the parents recognized that frequent and prolonged breastfeeding could harm a child's teeth aligning with findings from Muhammad et al., indicating a lack of awareness about specific ECC risk factors [3]. Similarly, only 50% correctly identified that regular intake of fresh juices could harm children's teeth. Although juices with added sugars are known to cause caries even natural juices can lead to demineralization and tooth wear when consumed excessively. Highly educated parents displayed more positivity compared to less educated ones, consistent with findings from a study conducted in Saudi Arabia [18]. The results point out the

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need for targeted interventions to address these attitudinal gaps and promote actionable preventive behaviours. Apart from the moderate knowledge and positive attitudes, parental practices towards ECC prevention showed mixed results. The majority of study parents recognized the importance of cleaning their child's teeth after every meal and maintaining a balanced diet which was consistent with other findings [19, 20]. However, some practices such as scheduling an early dental visit (57.14%) and avoiding nighttime bottle feeding (65.52%) require improvements in our population. A unique observation in this study was that the primary-level educated parents demonstrated better compared to other education categories. These findings contrast with Mohammed et al., which reported a direct correlation between higher education and better practices [3]. The difference may be that working parents in nuclear family's delegate childcare responsibilities to caregivers, resulting in less focus on oral hygiene. The suboptimal practice scores among educated parents indicate gaps in translating knowledge into behaviour, necessitating targeted interventions. The significantly better knowledge scores of mothers ($p<0.001$) highlight the role of maternal influence in shaping children's oral health behaviors. This underscores the need to improve fathers' knowledge through targeted interventions. Although the differences in attitude ($p=0.164$) and practice ($p=0.112$) scores between mothers and fathers were not statistically significant, the observed trends suggest a need for further exploration. These trends could inform targeted educational programs aimed at increasing fathers' involvement in oral health practices and the need for tailored educational campaigns targeting affluent parents to address knowledge gaps and encourage effective practices. Initiatives should highlight the importance of fluoride toothpaste, early dental visits, and recognizing early signs of dental caries. Purposive sampling is justified because it ensures that the study focuses on the most relevant participants, aligns with research objectives, and addresses practical constraints. However, the limitations (e.g., potential selection bias) should be discussed in the discussion section, emphasizing that the findings apply specifically to affluent parents in Lahore and may not be generalizable to all socioeconomic groups. Moreover, the results indicate a need for promoting cultural adaptation to enhance parental practices especially fathers and working parents.

CONCLUSIONS

It was concluded that affluent parents of 5-year-old children had a good knowledge of how to prevent ECC but their attitudes and practices fell short of recommended standards. Mothers were found to be significantly more knowledgeable than fathers. This study emphasized the need to improve father's involvement and knowledge regarding oral health.

Authors Contribution

Conceptualization: AC, KT
Methodology: AC, SS, MAA, KT, FR
Formal analysis: TNS, MAA
Writing review and editing: SS, AA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

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Exploring the Impact of Academic, Environmental, and Psychosocial Stressors on the Mental Well-Being of Medical Students

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ABSTRACT

Exploring the multifaceted impact of academic, environmental, and psychosocial stressors on students' overall mental well-being is necessary, identifying key areas for intervention and support. **Objectives:** To see the prevalence of different stressors in medical students. Also, to assess their mental well-being and the correlation of different stressors with it. **Methods:** An analytical cross-sectional study in a private medical college was done from July 2024 to December 2024. A questionnaire was developed through Google Forms and distributed through social media platforms, and quota non-purposive sampling was done. Stressors were assessed through the Likert scale, and mental well-being through the Kessler scale. Chi-square and independent sample T-tests were employed. P-value <0.05 was taken as significant. **Results:** Mild to moderate effects of academic, environmental, and psychosocial stressors were observed. Mostly, students were having severe mental distress, and an equal percentage were likely to be well. A moderate positive correlation between mental well-being and stressors was observed with significant p-values between mental well-being and academic stressors (r=0.497, p=<0.001), environmental stressors (r=0.432, p=<0.001), and psychosocial stressors (r=0.489, p=<0.001); depicting increased distress were associated with higher prevalence of stressors among participants. **Conclusions:** It was concluded that female, and students of final year MBBS were having more mental distress. Stressors were having a mild to moderate effect on participants. Establishing an academic culture that provides a haven for all, normalizes seeking help, and promotes collaboration over competition would go a long way toward alleviating some of the stressors that medical students face.

INTRODUCTION

This relates to the fact that obtaining a degree in medicine is widely considered to be among the most intellectually demanding of all educational achievements. While medical education provides students with the knowledge and expertise necessary to treat complicated health problems, the demands of this training usually encroach into serious stress [1]. Students enrolled in medical colleges or universities face a unique combination of academic, environmental, and psychosocial challenges that can adversely affect their mental health. Therefore, as the forces come into play, there are sufficient reasons to look at this whole issue from a comprehensive perspective of the role that these pressures play toward effective mental well-being for medical students [2]. When compared with other fields, medical students are more susceptible to mental health disorders. A high number of studies present rates that indicate a greater prevalence of depression, anxiety, and burnout in this group. Most importantly, some causes of mental health problems include an overwhelming academic workload, very malicious assessments, and a lot of requirements to do well academically. At the same time, environmental aspects would include inadequate recreation, having to adapt to new circumstances of existence, and lacking social support. The above-stated problems would further increase in levels with psychosocial aspects such as

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societal and family expectations, financial constraints, and strained interpersonal relationships [3]. It is, of course, student life and students' academic environment that is likely to be manifested as stressors in the lives of medical students, as it is the most perceptible aspect of stress. The students are expected to learn so much information in a very short period and mostly without external scrutiny. Frequent examinations and the overall need to perform exceptionally always create an environment of constant stress [4]. Many students have "imposter syndrome," in which even though they are performing, they do not trust their abilities, leading to self-doubt and feeling less worthy. The competition culture firmly infests all medical schools and has further created all the above problems while promoting the experience of competition-isolation among peers. Over time, this has created a strain on the mental health of students, resulting in poor academic performance and personal lives [5]. Environmental 'stressors' are another cardinal dimension in the aspect of mental well-being in medical students. Usually, the transition to medical school comes along with relocation and disruption of any present established support systems. Students also find it challenging to group themselves into unusual environments, thus exacerbating loneliness and homesickness [6]. Besides, students of medical education have a busy schedule, leaving little time for self-care, rest, or recreation. Other inadequacies include poor facilities and overcrowded living quarters, not to mention institutional limitations. The adverse attributes of all these environmental stressors are multiplied by the majority of poor-resource settings, where even more limitations, such as untimely access to mental health services, shall be experienced by students [7]. Psychological stressors are additional layers impeding the struggle toward mental well-being. Many such students come to medical school seeking the fulfilment of societal and family expectations, which do not necessarily correspond with or dovetail with their personal goals and ambitions. Another source of stress is financial since many medical students depend partly on loans or part-time jobs to fund their education. The competitive nature of the training further strains such relationships, alienating one from the other. So, students would rather suffer in silence than seek help from professionals because such help is often stigmatized [8]. The cumulative effect on the mental health of medical students is borne from the interaction of these academic, environmental, and psychosocial stressors. An example of this is the student who is having a challenge with college and maybe financially struggling, possibly even lacking a support system for aggregating the whole load on the student. Multipronged stress would be able to haunt the students as severe mental health outcomes such as anxiety disorders, episodes of depression, and burnout. Hence, these challenges can be ameliorated with a deeper insight into stressors unique to medical students and the inception of interventions aimed at ameliorating the consequences of the stressors [9]. An unattended mental health issue affects not only the well-being of a medical student but also the academic success, professionalism, and care of patients. Chronic stress and mental health disorders lead to burnout, lend themselves to unproductiveness, and hamper decision-making, impairing the operation of a future healthcare provider for quality care delivery. Thus, addressing mental health needs for students is individually concerning but, importantly, a stern public health issue [10]. To this end, the study intends to add to an emerging body of evidence relating to the mental health challenges of medical education. Hence, in establishing well-focused needs for addressing the multidimensional stressors faced by medical students, progress could then be made toward the systemic change that prioritizes well-being as a critical ingredient in medical training. This, therefore, builds resilient healthcare-providing personnel ready to meet the emerging demands of the ever-emerging health environment.

This study aims to assess the effects of academic, environmental, and psychosocial stressors on mental well-being among medical students. It would further elucidate the specific factors causing mental health problems in students so that unique stressors experienced in this population can be identified. The findings will direct efforts on efficient and specific strategies to enhance students' well-being, thereby improving the quality of education and the delivery of healthcare.

METHODS

An analytical cross-sectional study was conducted in a private medical college in Faisalabad from July 2024 to December 2024. Ethical approval was obtained from the institutional ethical committee, which had a reference number IEC/316-24. All students currently studying in the institute were included, and those who gave consent, while those who didn't give consent and non-MBBS students were excluded. A sample size of 300 was taken using non-probability quota sampling.[11] An equal percentage of students were taken from each MBBS class (60 each), including 30 males and 30 females. Quota sampling helped ensure proportional representation from each MBBS class. However, stratified random sampling would have introduced greater randomness in the selection process, thereby reducing selection bias. However, practical constraints of the study and the need to ensure representation from all academic years led to the choice of quota sampling. Nonetheless, to enhance the representativeness of our sample, it was ensured that participants within each quota were randomly recruited

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until the predefined sample size was reached. All those questionnaires were excluded from the final data analysis, which came after the 60 number of each class. Therefore, participants were randomly recruited in the study population to reduce any bias. The questionnaire was made on Google Forms after an extensive literature review, and a pilot study was done initially to check for any errors. Then, the questionnaire was distributed through social media platforms.It had five sections; 1st section had demographics; in the 2nd section, the Kessler psychological distress scale was used to assess the mental well-being of students, which is a validated questionnaire used for this purpose; and in the subsequent three sections, questions were asked regarding the academic, environmental, and psychosocial stressors on a Likert scale having scoring from 1(none of the time) to 5(all of the time). The Statistical Package for the Social Sciences (SPSS) version 22.0 was considered to analyze the data. Frequency and percentage were calculated to do scoring of the mental health scale to divide participants from 'likely well' to 'likely to have a severe disorder' category, and then a chi-square test was employed to assess gender-wise differences. Then, as per age group, gender, and class, comparisons were made among them, and mean + SD was calculated using independent sample t-test and ANOVA, and p-value<0.05 was taken as significant.

RESULTS

The sample size of our study was 300. It was divided into five equal halves, i.e. 60 students were taken from each MBBS class from 1st year to final year, having equal percentages of male and female students, i.e. 30 each. The mean age + SD of participants was 22.60 + 1.28 years. For analysis, age groups were made based on below and above 22 years of age, i.e. participants below 22 years of age were 142 (47.3%), and above 22 years were 158 (52.7%). The majority of the participants belonged to urban areas, i.e. 247 (82.3%), while 53 (17.7%) were from rural areas. The mean + SD of academic, environmental, and psychosocial stressors was 2.79 + 0.95, 2.54 + 0.83, and 2.54 + 0.98 depicting mild to moderate stress among participants in respect of these three variables. Table 1 shows the score interpretation of the Kessler Psychological Distress Scale, indicating that the majority, 98 (32.7%) of the participants were likely to have a severe disorder, an equal percentage of participants were likely to be well, followed by 64 (21.3%) were likely to have a moderate disorder. When a gender-wise comparison was made, female were more likely to have a moderate and severe disorder as compared to male, with a significant p-value of 0.002 (Table 1).

Table 1: Likelihood of Having a Psychological Distress

K10 Score	Frequency (%)	Interpretation		
10–19	98 (32.7%)	Likely to be Well		
20–24	40 (13.3%)	Likely to Have A Mild Disorder		
25–29	64 (21.3%)	Likely to Have A Moderate Disorder		
30–50	98 (32.7%)	Likely to Have A Severe Disorder		
Gender-Wise Comparison				
Variables	**Male**	**Female**	**Total**	**p-value**
No Distress	59 (19.7%)	39 (13%)	98 (32.7%)	0.002*
Mild	26 (8.7%)	14 (4.7%)	40 (13.3%)	
Moderate	28 (9.3%)	36 (12%)	64 (21.3%)	
Severe	37 (12.3%)	61 (20.3%)	98 (32.7%)	

The finding shows the age-group comparisons of mental well-being and stressors using an independent sample t-test. A significant association was seen between academic stressors and age groups. Also, the age group >22 years depicted more stress and was likely to have more distress as compared to those who were younger than 22 years (Table 2).

Table 2: Age-Group Comparisons with Mental Well-Being and Stressors

Variables	Age group	n	Score Range	Mean ± SD	95% Confidence Interval	p-value
Mental Wellbeing	<22 Years	142	10–50	2.45 + 1.21	-0.45–0.11	0.24
	>22 Years	158		2.62 + 1.28	-0.45–0.11	
Academic Stressors	<22 Years	142	1–5	2.67 + 0.87	-0.45–-0.02	0.02*
	>22 Years	158		2.91 + 1.01	-0.45–-0.02	
Environmental Stressors	<22 Years	142	1–5	2.47 + 0.81	-0.33–0.04	0.14
	>22 Years	158		2.61 + 0.84	-0.33–0.04	
Psychosocial Stressors	<22 Years	142	1–5	2.51 + 0.96	-0.28–0.16	0.59
	>22 Years	158		2.57 + 0.99	-0.28–0.16	

Note: *Significant p-value at <0.05

Results show gender comparisons with mental well-being and stressors using an independent sample T-test. A significant association was seen between gender and mental well-being; also, significant associations were seen with all stressors. Also, female depicted more stress and were likely to have more distress than male (Table 3).

Table 3: Gender Comparisons with Mental Well-Being and Stressors

Variables	Gender	n	Score Range	Mean ± SD	95% Confidence Interval	p-value
MentalWell being	Male	150	10-50	2.29 + 1.22	2.29 + 1.22	<0.001**
	Female	150		2.79 + 1.23	2.79 + 1.23	
Academic Stressors	Male	150	1–5	2.63 + 0.94	2.63 + 0.94	0.002*
	Female	150		2.97 + 0.93	2.97 + 0.93	
Environmental Stressors	Male	150	1–5	2.41 + 0.83	2.41 + 0.83	0.004*
	Female	150		2.68 + 0.81	2.68 + 0.81	
Psychosocial Stressors	Male	150	1–5	2.38 + 0.93	2.38 + 0.93	0.005*
	Female	150		2.7 + 1.01	2.7 + 1.01	

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Note: *Significant p-value at <0.05. ** Significant p-value at <0.01

This study shows class-wise comparisons with mental well-being and stressors using the ANOVA test. A significant association was seen between MBBS classes and mental well-being. Also, students of final year MBBS showed more psychological distress and stress than students of other classes. Post-hoc tests have been conducted to identify which class pairs differ significantly after checking the homogeneity of variance tests. The Games-Howell test was employed, and the following pairs differ significantly, i.e. 1st and 5th year, 3rd and 5th year, 4th and 5th-year MBBS students.Pearson correlation test was employed, and a moderate positive correlation between psychological distress and stressors was observed with significant p-values between distress and academic stressors (r=0.497, p=<0.001); environmental stressors (r=0.432, p=<0.001); and psychosocial stressors (r=0.489, p=<0.001); depicting increased distress were associated with higher prevalence of stressors among participants.

Table 4: Class-Wise Comparisons with Mental Well-Being and Stressors

Variables	Class	n	Score Range	Mean ± SD	95% Confidence Interval	p-value
Mental Wellbeing	1st Year	60	10–50	2.32 + 1.22	2 + 2.63	<0.001*
	2nd Year	60		2.62 + 1.12	2.33 + 2.91	
	3rd Year	60		2.37 + 1.27	2.04 + 2.7	
	4th Year	60		2.25 + 1.23	1.93 + 2.57	
	5th Year	60		3.15 + 1.2	2.84 + 3.46	
Academic Stressors	1st Year	60	1–5	2.78 + 0.97	2.51 + 2.92	0.1
	2nd Year	60		2.72 + 0.82	2.82 + 3.34	
	3rd Year	60		2.63 + 1.02	2.36 + 2.89	
	4th Year	60		2.78 + 0.85	2.56 + 3	
	5th Year	60		3.08 + 1.02	2.82 + 3.34	
Environmental Stressors	1st Year	60	1–5	2.58 + 0.76	2.38 + 2.77	0.21
	2nd Year	60		2.54 + 0.71	2.36 + 2.72	
	3rd Year	60		2.34 + 0.84	2.13 + 2.56	
	4th Year	60		2.54 + 0.85	2.33 + 2.76	
	5th Year	60		2.7 + 0.94	2.46 + 2.95	
Psychosocial Stressors	1st Year	60	1–5	2.47 + 1.01	2.22 + 2.74	0.23
	2nd Year	60		2.47 + 0.93	2.23 + 2.72	
	3rd Year	60		2.51 + 1.01	2.25 + 2.77	
	4th Year	60		2.44 + 0.89	2.21 + 2.66	
	5th Year	60		2.8 + 1.03	2.54 + 3.07	

Note: *Significant p-value at <0.01

The study finds evident indications of a difference in experience of moderate to severe psychological distress between the two genders: female was more likely than male to report having them. However, close observation of the stress and psychological distress from the correlation meanings leads to the conclusion that psychological distress increases when exposure to stressors increases because a moderate positive correlation exists between both variables. However, this does not ascertain resilience; it reflects the mere association between distress levels and stressors. Resilience is adaptability and recovery under stressors. The correlation does not directly assess resilience; it seems possible that higher levels of distress in female reflect increased exposure to stressors or better perception of stressors, perhaps from challenges peculiar to such female (for example, societal expectations, dual responsibilities, or barriers in medical education). All this connects, however, under the fact that resilience as a psychological construct may not have been the understood core of this study: the reflection of correlation was that of stressors with distress, leaving out delineation of protective factors that make resilience through the application of coping mechanisms, social support, or personality traits. Hence, having high levels of distress for women does not mean a lack of resilience; it can be indicative of a greater burden of stressors.

DISCUSSION

The study evaluated the mental well-being of medical students in a private medical institute and the different stressors that students faced in their lives. In our study, most students were having severe stress, and an equal percentage were likely to be well. A study done by Bartlett and Fowler al., showed that participants had significantly higher distress and among them, female showed more distress, which is similar to the results of our study, but in contrast, in our study, an equal percentage of students were also likely to be well [12]. A study by Al-Tammemi *et al.*, showed severe distress among participants, which is similar to the results of our study [13]. A study conducted by Noreen *et al.*, showed higher psychological distress as in our study, but in contrast, the mental well-being was more compromised in male students as compared to female in our study [11]. A study by Alfayez and AlShehri *et al.*, also showed severe stress among medical students, more prevalent in females, which is similar to our study results [14]. A study by Alotaibi *et al.*, also showed that severe distress was more prevalent in medical students than in our study [15]. All these studies showed a higher prevalence of stress among participants, signifying the role of different stressors in medical students, which need to be addressed. In our study, students of higher MBBS classes, i.e. final year, showed more distress and stress, but a study by Al-Rouq showed that stress decreased with each senior year, which is in contrast to our results [16]. A study by Slimmen *et al.*, showed that academic and psychosocial stressors were acting negatively on mental well-being, similar to our results [17]. Research by Li *et al.*, showed that academic stressors had a positive correlation with mental health, in contrast to our study results [18]. A study by Srivastava *et al.*, showed that various demographics like age and year of

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study and academic, environmental, and psychosocial stressors had a distress effect on students, affecting their mental well-being similar to our study [19]. A study by Tran *et al.*, showed that academic satisfaction had a significant role in improving students' mental well-being, while in our study, similar results were seen where less academic stress was associated with better mental well-being [20]. Research by Satpathy *et al.*, showed that academic and psychosocial stressors were associated with better students' mental well-being, in contrast to our study results [21]. A study by Ragab *et al.*, showed that female students of senior MBBS classes were having more mental distress as compared to male and junior MBBS class students, similar to our results [22].

CONCLUSIONS

It was concluded that mild to moderate academic, environmental, and psychosocial stress was found in students; also, an equal percentage of students had moderate mental distress, and the same percentage was also likely to be well. One must incorporate mental health and wellness programs in medicine curricula to mitigate the challenge. Programs such as stress management workshops, peer mentoring systems, counselling services, and other such provisions may help access resolution. Establishing an academic culture that provides a haven for all, normalizes seeking help, and promotes collaboration over competition would go a long way toward alleviating some of the stressors that medical students face.

Authors Contribution

Conceptualization: AA
Methodology: HA, I, QB, FA
Formal analysis: MUD
Writing review and editing: MUD, HA, I, FA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Distribution of Radial Root Position of Maxillary Central Incisors on Cone Beam Computerized Tomography

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ABSTRACT

Knowledge about the radial root position before possible replacement of central incisors for immediate implant is of pivotal importance to clinician. It varies among different populations. **Objective:** To determine distribution of radial/sagittal root position in maxillary central incisors in patients reporting to 2 tertiary care hospitals of Lahore, Pakistan using CBCT. **Methods:** Sample size of 110 individuals between 20-50 years, strictly falling in inclusion criteria was used. Cross sectional study with non-probability consecutive sampling technique was applied in Department of Periodontology at Fatima Memorial Hospital and University college of Medicine and Dentistry, from Jan 2023 to Sep 2023. The position of maxillary central incisor roots was determined using CBCT. Chi-square test was used for stratification based on age and gender. **Results:** The mean age was 33.67 ± 8.68 and sample consisted of females 50 (45.45%) and males 60 (54.55%). The most common root position was class I, 79 (71.82%), followed by class II, 20 (18.18%), then class IV, 7 (6.36%) and least was class III, 4 (3.64%). The difference among genders (p=0.272) and age (p=0.161) were insignificant statistically. **Conclusions:** Most common incidence of radial root spatial position for maxillary central incisor is buccal (class 1), followed by II (middle) but class IV and III also existed and must analyzed CBCT to determine the radial root position before any immediate implant in esthetic zone for optimal esthetic and functional outcome.

INTRODUCTION

When a single tooth has to be replaced in anterior maxilla, immediate dental implant is a popular treatment of choice after it was introduced in 1990s. Loss of both soft and hard tissue can be prevented by immediate implant placement [1]. Restoration with Immediate implant placement is the most patient friendly procedure as this not only reduces the treatment time but also protects the alveolar bone and soft tissues and yields superior esthetic results [2]. But immediate placement of implant in pre-maxilla is a challenging modality of treatment as it has more chances of complications. Incorrect angulation of drill during osteotomy preparation may lead to facial/palatal wall perforation, dehiscence or bony defects, misplaced implant and incorrect emergence profile [3]. Thus, the osteotomy preparation and implant placement has to be in accordance to the root morphology (width and length), radial root position, and the osseous housing morphology so that the implant is placed in palatal or buccal wall and 4-

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5mm beyond the root apex, thus achieving primary stability [4]. Current guidelines suggest the placement of implant in the sloping palatal wall of socket [5]. This guideline is not applicable to every clinical situations as root can be placed close to the palatal wall yielding a thin palatal wall. So, the radial or sagittal root position must be known before hand in order to make a decision. Cone beam computerized tomography is the method of choice to check the sagittal root position before immediate implant placement [6]. The landmark study by Joseph Kan was reported in 2011, predominantly in a Caucasian ethnic population [7]. They categorized the relationship between the alveolar process and radicular tooth structures as class I (root positioned against labial cortex), II (root positioned between buccal and palatal cortex), III (root is positioned against the palatal cortical plate), and IV (At least two thirds of the root engaging both the labial and palatal cortical plates). Out of 100 CBCT examinations meeting the inclusion criteria, he found that majority of central incisors to be type I (86.5%). Type II, type III and type IV were found to be 5%, 0.5% and 8%. Another study was conducted by Lau *et al.*, in 2011 in Hong Kong. He reported buccal type to be 78.8%, palatal to be 1.8% and middle to be 19.4% [8]. Similar study was done in 2014 by Chung *et al.*, in Korean population concluded buccal type to be 94%, middle to be 5.6% and palatal to be 0.4% [9]. Issa N studies also showed significant variations among various populations. Issa *et al.*, in 2020 found that in Egyptian population, the prevalence of the 4 types and were found to be 60.7% for class I, 33%, 4.7 % and 1.7% for class II, III and IV [10]. Jung *et al.*, in Korean population found that 92.2 % of population had buccal type sagittal root position, 7.8% had middle root position and 0% had palatally positioned root for central incisor [11]. In 2016, Radzewski R and Osmola K studied radial root position in Chinese population and found buccal type predominant 95.4%. The middle type was 4.4% and 0.2 % had palatal type radial root position [12]. In 2019, Petaibunlue et al., studied Thai population and found 79.6% population had buccally placed root (type I), rest of the population had type II radial root position and found the types III and IV to be non-existent [13].The radial/sagittal root position distribution varies significantly among different populations in the studies done in past.This factor is vital for treatment planning with immediate implant. Each type of sagittal/radial root position poses ease and difficulties in immediate implant placement.CBCT is the only and the most reliable tool for its assessment and determination. Computerized tomographic scans are another option but CBCT produced images of greater resolutions with lesser radiation doses to patient.The distribution of central incisor roots in Pakistani population is different than the previously studied populations of Americans, Chinese, Korean and Egyptians and the Sagittal distribution of these populations cannot be applied to Pakistani Population. Therefore, this study aimed to determine the distribution of sagittal/radial root position in central incisors for immediate implant placement using CBCT in patients reporting to tertiary care hospital.

METHODS

It was a cross-sectional study with non-probability consecutive sampling technique conducted at Department of Periodontology at Fatima memorial Dental hospital Lahore and University College of Medicine and Dentistry, The University of Lahore from Jan 2023 to Sep 2023. A sample size of 110 cases was calculated with 95% confident level, 5% margins of errors and expected percentage of middle root position as 7.8% [14]. Approval from Institutional Review board (IRB) of Fatima Memorial Hospital was taken. A detailed synopsis including study design, sample size, inclusion and exclusion criteria was sent to Research Evaluation Unit of College of Physicians and Surgeons Pakistan. The synopsis was approved with reference no CPSP/REU/DSG-2019-060-2752. Only the patients falling into the inclusion criteria were included in the study. The demographics of all subjects were recorded and every subject was asked to sign a consent form. Inclusion criteria was as follows; Individuals between age 20-50 years with no history of tooth root manipulation i.e., no orthodontic treatment, no fixed prosthesis and no history or radiographic signs of trauma in anterior segment of maxilla. ALADA Principle was followed. No subject was exposed to unnecessary radiations. Subjects prescribed cone beam CT scan as dictated by their treatment plan and subjects who had not undergone CBCT in past 6 months. Female patients were excluded if they were Pregnant or lactating. Secondly patients were also excluded if they had history of previous surgery in maxilla such as orthognathic surgery, apicectomies or internal fixation following trauma to maxilla. Patients with developmental disorders/Growth anomalies and history of chemotherapy and radiotherapy were also excluded. Radiology department of dental hospital has Planmeca Romexis 3D machine for CBCT. Cone beam computed tomography (CBCT) was taken in Planmeca Romexis 3D Mid (60-120 kV; 9-33 s; 200µm voxel size) of all subjects. As per existing literature, buccally positioned roots (class I), middle positioned roots (class II), palatally positioned roots (class III) and pedunculated roots (class IV) was recorded in each patient. In order to address any bias, all readings were taken by only one doctor and CBCT from only one system was included in the study. All data analysis was done in SPSS 22 qualitative variables like gender and position of maxillary central incisor (bucally placed, middle positioned, palatally placed, and pedunculated) was presented as frequency and

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percentages. Quantative variable like age was presented as mean ± SD. Data were stratified as age and gender. Chi-square test was used taking p-value less than or equal to 0.05 as significant level.

RESULTS

The mean age of the participants were 33.67 ± 8.68 years with range from 20 to 50 years. The females were 50 (45.45%) and males were 60 (54.55%). The common age group was 20-30 years 46 (41.82%) followed by 31-40 years 33 (30.00%) and least was 41-50 years 31 (28.18%). The most common root position was class I (buccally positioned root) found in 79 (71.80%), followed by class II (middle position root) in 20 (18.18%), then class IV (pedunculated maxillary base) in 7 (6.36%) and least was class III (palatally placed root) in 4 (3.64%) (Figure 1).

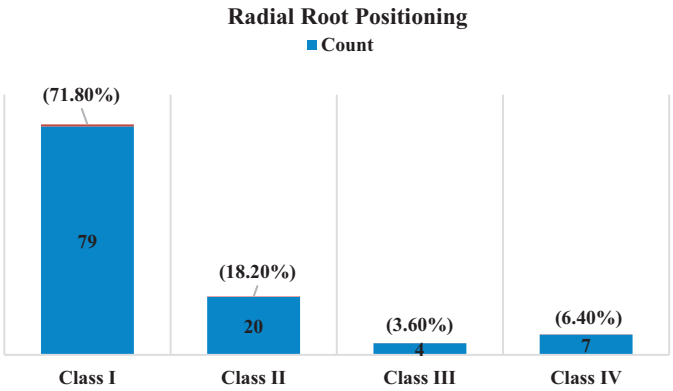

Figure 1: Distribution of Radial Root Positioning

Class III of radial root position of maxillary central incisor was 3 (5%) in males and in females was 1 (2%). Class IV was 6 (10%) and in females was 1 (2%). The distribution of radial root positions of the maxillary central incisor among genders showed no statistically significant difference (p=0.272), indicating that gender does not influence the root position (Table 1).

Table 1: Comparison of Radial Root Position of Maxillary Central Incisor among Genders

Characteristics	Radial Root Position of Maxillary Central Incisor Frequency (%)		p-Value[2]
	Female N = 50[1]	Male N = 60[1]	
Class I	39 (78.00%)	40 (66.67%)	0.272
Class II	9 (18.00%)	11 (18.33%)	
Class III	1 (2.00%)	3 (5.00%)	
Class IV	1 (2.00%)	6 (10.00%)	

[1]n (%), [2]Fisher's Exact Test

There was no statistically significant association between age groups and radial root position of the maxillary central incisor (p=0.161), suggesting that age does not significantly impact root positioning. Class III was found in only age group 20-30 years 4 (8.7%). Class I (buccally positioned root) was the most common radial root position overall, found in 71.82% of participants, regardless of gender or age group (Table 2).

Table 2: Comparison of Radial Root Position of Maxillary Central Incisor Among Age Groups

Characteristics	Radial Root Position of Maxillary Central Incisor Frequency (%)/Range			p-Value[2]
	20-30, N = 46[1]	31-40, N = 33[1]	41-50, N = 31[1]	
Class I	30 (65.22%)	24 (72.73%)	25 (80.65%)	0.161
Class II	10 (21.74%)	5 (15.15%)	5 (16.13%)	
Class III	4 (8.70%)	0 (0.00%)	0 (0.00%)	
Class IV	2 (4.35%)	4 (12.12%)	1 (3.23%)	

[1]n (%), [2] Fisher's exact test

DISCUSSION

These findings showed that the most common root position was class I (buccally positioned root) found in 79 (71.82%), followed by class II (middle position root) in 20 (18.18%), then class IV (pedunculated maxillary base) in 7 (6.36%) and least was class III (palatally placed root) in 4 (3.64%). There was no statistical difference among age groups and gender for the type of /radial root position in central incisors for immediate implant placement. Biologically, the palatal part of alveolar bone of the maxillary anterior teeth, is thicker in quantity also qualitatively it has a cortical nature [15-17]. So, it presents a superior site both qualitatively and quantitatively for implant placement than the labial bone. Class I sagittal root position (SRP) provides these ideal conditions. This also leads to minimum insult in the labial bone leading to lesser resorption of labial bone which is critical for esthetic outcome and the gap between implant and the buccal socket wall can be grafted using bone substitutes [18]. Kan *et al.*, classification for root spatial distribution in relation to osseous housing was used in this study [7]. The classification is as follows; Class I: The root is found along the labial cortical plate leaving a thick palatal bone and apical bone. Class II: The root lies in the middle of the alveolar housing. It does not engage buccal/palatal cortices in the apical third. Class III: the entire radicular apparatus runs along the palatal alveolar cortex and there is thick buccal bone. Class IV: two thirds of the root are engaging both labial and palatal cortical plates and apical bone is insufficient for primary stability. The study reported greater incidence of class I radial root position (71.82% population). These results supported that mostly teeth were suitable contenders for implant and provisional loading. 95% incidence of sagittal root position was found in another study done on Chinese population, further supporting the motion [19]. A similar study was done by Issa *et al.*, in Egyptian population. 100 patients both male and female underwent CBCT were included in study sample. Root positions were classified into Classes I-IV. The results were similar to previous studies indicating the

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predominance of class I (60.7%), and others reported were class II (33%), class III (4.7 %) and class IV (1.7%). The cross sectional root position in relation to alveolar process of anterior upper teeth (canine to canine) on CBCT was further assessed in another study and reported. A sample size of 100 included both genders with mean age 53.1 was selected and the results were interpreted as Class I, II, III, or IV. Out of sample size of 600, 81.1%, 6.5%, 0.7%, and 11.7% were reported as Class I, II, III, and IV. Class IV radial root position reported in Kawala B *et al.*, studies in which these results had a remarkable prevalence of 11.7%.This challenging situation has two thirds of the root is engaging both labial and palatal cortical plates and apical bone is thin [20].The socket enclosing the root is pedunculated from alveolar bone proper. Such cases are a contradiction for immediate implant placement.It is necessary to augment the hard tissues with bone substitutes prior to implant placement and during the placement to increase the predictability of the treatment [21] Treatment trends today demand dental implant with optimal esthetics.To meet this increasing demand, treatment planning considerations are extremely important.CBCT evaluation prior to these cases and such classifications are pivotal in interpretation of literature guidelines before planning these cases [22-24]. Gluckman H *et al.*,studies indicated a greater incidence of mechanical and biological complication if CBCT is not done before implant placement [25].

CONCLUSIONS

It can be concluded that most common class for radial root locality of upper central incisor is class I (The root is found along the labial cortical plate leaving a thick palatal bone and apical bone) followed by II (root position is in the middle of the osseous housing without engaging the labial and palatal cortical plates at the apical third). Increasing demand of immediate implant treatment to shorten treatment time increase the importance of knowledge about sagittal root position on CBCT for treatment planning in the anterior maxilla.

Authors Contribution

Conceptualization: KA
Methodology: AD, MK, TA, UM
Formal analysis: MH, ZAK, KA
Writing, review and editing: AD, MH, ZAK, MM, KA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Effect of Hemodialysis on Intraocular Pressure (IOP) and Ocular Perfusion Pressure (OPP)

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ABSTRACT

Hemodialysis is a routine procedure in patients on renal replacement therapy. It carries risk of intraocular pressure and ocular perfusion pressure derangement. With proper monitoring of IOP and blood pressure, visual impairment can be minimized. **Objective:** To study the effect of hemodialysis on intraocular pressure (IOP) and ocular perfusion pressure (OPP). **Methods:** Cross sectional observational study after getting ethical approval was carried out in a Tertiary Care Hospital Rawalpindi from Aug 2021 to Apr 2022. Sixty patients with CKD on HD were included. A pneumotonometer was used to measure IOP twice at every time point. IOP was measured Pre-HD, during HD, and Post-HD. After measuring IOP and BP the value of OPP, MAP, SOPP and DOPP were calculated. Statistical analysis was done using SPSS version 21.0. **Results:** The value of IOP at pre-HD was 18.82 ± 0.57, during HD was 20.73 ± 0.55 and post-HD was 21.55 ± 0.60. Similarly, the value of MAP at pre-HD was 93.48 ± 4.26, during HD was 88.25 ± 4.71 and post-HD was 84.63 ± 5.20. The value of OPP at pre-HD was 74.70 ± 4.23, during HD was 67.50 ± 4.80 and post-HD was 63.13 ± 5.19. Pre-HD to post-HD the value of IOP increased significantly to 2.73 mmHg, MAP decreased significantly to -8.85 mmHg and OPP decreased significantly to -11.57 mmHg. **Conclusion:** During HD, there is a significant rise in IOP and reduction in OPP, both of which enhance the risk of glaucoma progression and development. Even when IOP is effectively managed, clinicians must evaluate HD history in patients with glaucoma progression.

INTRODUCTION

Patients with CKD "chronic kidney disease" are typically treated with hemodialysis (HD) i.e. blood-filtration technique. Numerous metabolic markers, such as glucose levels, potassium, sodium and blood urea, might vary during HD. Osmotic shifts in blood, vitreous and aqueous humour, and other extracellular fluids come from these fluctuations [1]. During or after dialysis, however, few patients can develop symptoms like headache, eye discomfort and blurred vision. The question of whether high intraocular pressure caused by the long-term dialysis causes glaucoma or visual problems in the patients on hemodialysis has piqued ophthalmologists' interest, prompting more investigation [2]. It can also impact intraocular pressure (IOP), visual acuity and retinal thickness [3]. Patients with CKD and renal replacement treatment may experience visual loss because of the original disease, such as diabetic retinopathy and hypertension, or because of dialysis-related complications [4]. Ocular complications include endogenous endophthalmitis, occipital lobe blindness, ischaemic optic neuropathy and reduced cell density of corneal endothelium. In literature during or after the HD changes in

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IOP have been reported widely. Glaucoma is caused by an increased IOP and decreased ocular perfusion pressure (OPP)[5]. In the USA, 871000 patients got therapy for ESRD, with 26.0 % of which patients being over "60. years old", as per NIH "National Institutes of Health". As Age increases the chances for developing glaucoma. Older patients on hemodialysis who have end-stage renal illness are more probable to develop glaucoma [6, 7]. IOP is main risk' factor in the progression & development of glaucoma. Transitory elevations in Intra Ocular Pressure have been documented while HD in the patients without or with glaucoma. However, the effect of large but brief rise in IOP during HD sessions, its relations to the progression of glaucomatous illness, is not understood [8]. Maintenance of the OPP via system adjustment of blood pressure' and general control of IOP is required for adequate oxygenation of ocular tissues. Vascular dysregulation is thought to cause irregular perfusion of eyes leading to ischaemic damage of optic nerve, which is thought to be the underlying cause of glaucoma [9]. Researchers discovered that hypoxia of optic nerve develops when the IOP rises beyond 40 mmHg or OPP falls under 50 mmHg, indicating that autoregulation is no longer able to adjust. However, it was found by Stefánsson et al that "optic nerve" may withstand "OPP" over 50 mmHg, but hypoxia resulted when OPP went below 30 mmHg in variety of human and animal trials [10]. Low OPP has been linked to OAG "open angle glaucoma" in humans, according to multiple population-based epidemiologic studies [11]. According to the findings of the Early Manifest Glaucoma Trial, low baseline pressure of systolic perfusion elevated hazard ratio for development of glaucomatous illness was the up to 1.42. Every such epidemiologically studied research mentioned low OPPs that were stable and constant throughout time; HD may only cause a transitory alteration in OPP [12]. Significant IOP rise or OPP decrease that goes unnoticed during HD may lead to glaucomatous optic nerve injury and vision loss. The link between variations in IOP and HD has been studied for over 50 years. CKD patients have inadequate general blood supply to eyes [13, 14], and hemodialysis-induced changes in the IOP can worsen this state or potentially cause irreparable ischemia and hypoxic damage to retina and optic nerve. As a result, to safeguard visual function in hemodialysis patients, it is vital to examine variations in IOP during hemodialysis and research associated causes.

The study aimed to evaluate the changes in IOP and OPP that were linked to increased risk of the vision impairment in patients on HD.

METHODS

After getting approval of the ethical review approval, under letter ID A/28/EC/447/20, a cross-sectional prospective study was carried out as at Tertiary Care Hospital Rawalpindi from Aug 21 to Apr 22. Informed written consent was also obtained from each patient. Using convenience sampling technique, according to WHO sample calculator sixty (60) patients with CKD who were on HD were included. Dialysis was done three times a week for three to five hours each time. Patients who had a previous Corneal defect, past corneal intervention /surgery, topical anesthetics drugs allergies and having present eye illness /infection were excluded for study. A pneumotonometer was used to measure IOP twice at every time point. Two observations were averaged into single reading with a variation of <0.5 mmHg. At each of following time intervals, IOP was measured with patient seated: Pre-HD, around 20 minutes before commencing HD; During HD, roughly 2 hours after the starting HD; and Post-HD, around 20 minutes after terminating HD. For calculating the "Mean Arterial Pressure" MAP, at each time following formula was used:

MAP = diastolic B.P + 1/3(systolic B.P – diastolic B.P).

By using automated sphygmomanometer BP was checked in terms of SBP and DBP with patient sitting in upright position around brachial artery. The OPP, DOPP, SOPP and MOPP were calculated using following equations:

O.P.P = MAP – I.O.P

S.OPP = Systolic B.P – I.O.P

D.OPP = Diastolic B.P – I.O.P

MOPP = 2/3(MAP – I.O.P)

Descriptive statistics were used to describe quantitative and qualitative variables. Comparisons among mean O.P.P, MAP & I.O.P before, during and after HD were made using the paired samples. For analyzing the data, SPSS "statistical package for social sciences" version 22.0 was used and 'p< 0.05' was taken as statistically significant.

RESULTS

In this study, 60 patients were enrolled after fulfilling the selection criteria. The mean age of patients in our study was 51.57 ± 12.04 years with 33(55.0%) patients were male and 27(45.0%) patients were female. Of 60 patients, 25(41.7%) had urban residential status and 35(58.3%) had rural residential status. The causes of ESRD in our study were diabetes mellitus (26.7%), hypertension (25.0%), focal segmental glomerulosclerosis (8.3%) and others (40.0%).

Table 1: Baseline Results of Parameters of Study Patients

Parameters	Results
Age (Years)	51. 57 ± 12.04
Sex	
Male	33 (55.0 %)
Female	27 (45.01 %)

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Residential Status	
Urban	25 (41.7 %)
Rural	35 (58.3 %)
Causes of CKD	
DM	16 (26.7 %)
HTN	15 (25.0 %)
FSGS	05 (8.3 %)
Others	24 (40. %)

The pre and post results of weight, plasma osmotic pressure and blood pressure were given in table 2. Also, no patient was observed any adverse event.

Table 2: The Hemodialysis Effect on Weight, BP and Plasma Osmotic Pressure.

Different Variables	N	Mean ± SD
Pre-Hemodialysis Weight (kg)	60.00	68.05 ± 4.76
Post-HD Weight (kg)	60.00	66.05 ± 4.78
Pre-HD Plasma Osmotic Pressure ($mOsm/kgH_2O$)	60.00	277.27 ± 4.51
Post-HD Plasma Osmotic Pressure ($mOsm/kgH_2O$)	60.00	264.62 ± 3.23
Pre-HD SBP	60.00	136.52 ± 10.83
Pre-HD SBP	60.00	72.00 ± 2.90
During HD SBP	60.00	122.37 ± 10.26
During HD SBP	60.00	71.10 ± 5.19
Post-HD SBP	60.00	117.75 ± 11.02
Post-HD SBP	60.00	68.10 ± 4.82

In this study, the value of IOP at pre-HD was 18.82 ± 0.57, during HD was 20.73 ± 0.55 and post-HD was 21.55 ± 0.60. Similarly, the value of MAP at pre-HD was 93.48 ± 4.26, during HD was 88.25 ± 4.71and post-HD was 84.63 ± 5.20. The value of OPP at pre-HD was 74.70 ± 4.23, during HD was 67.50 ± 4.80 and post-HD was 63.13 ± 5.19. The mean values of IOP, OPP and MAP were significantly changed in the session of HD. From pre-HD to post-HD the value of IOP increased significantly 2.73 mmHg ($p<0.0001$), MAP decreased significantly -8.85 mmHg ($p<0.0001$) and OPP decreased significantly -11.57 mmHg ($p<0.0001$). Others pressure of perfusion was also decreased significantly from baseline values. Independent T-test was applied. $p<0.05$ is considered significant. These results are given in Table 3.

Table 3: Measurement of Pressure and Calculation in Hemodialysis

Measurement (mmHg)	Mean ± SD			Change From					
	Before-HD	While-HD	After-HD	Before HD to During HD		While HD to Post-HD		Pre- to post-HD	
				Mean + SD	p-value	Mean + SD	p-value	Mean + SD	p-value
IOP	18.82 ± 0.57	20.73 ± 0.55	21.55 ± 0.60	1.91 ± 0.76	0.0000	0.82 ± 0.81	0.0000	2.73 ± 0.86	0.000
MAP	93.48 ± 4.26	88.25 ± 4.71	84.63 ± 5.20	-5.23 ± 5.77	0.0000	-3.62 ± 7.85	0.0007	-8.85 ± 7.01	0.000
OPP	74.70 ± 4.23	67.50 ± 4.80	63.13 ± 5.19	-7.20 ± 5.73	0.0000	-4.37 ± 7.95	0.0001	-11.57 ± 6.98	0.000
SOPP	117.69 ± 10.79	101.64 ± 10.34	96.20 ± 10.93	-16.06 ± 15.32	0.0000	-5.43 ± 15.86	0.0102	-21.49 ± 15.42	0.000
DOPP	53.17 ± 2.87	50.37 ± 5.18	46.55 ± 4.85	-2.81 ± 5.90	0.0005	-3.82 ± 8.34	0.0008	-6.62 ± 5.56	0.000
MOPP	49.80 ± 2.82	45.00 ± 3.20	42.09 ± 3.46	-4.80 ± 3.82	0.0000	-2.91 ± 5.30	0.0001	-7.71 ± 4.65	0.000

*DOPP "diastolic ocular perfusion pressure (OPP)"; I.O.P "intraocular pressure"; MAP "mean arterial pressure"; MOPP "mean OPP" SOPP "systolic OPP"

DISCUSSION

Impact of Hemodialysis on the OPP is not thoroughly investigated. The impact of HD on IOP, on the other hand, has been thoroughly researched, but the findings are mixed, and no definitive solution has evolved. Findings of current study show a notably increased Intra Ocular Pressure and reduction in almost all the parameters of perfusion pressure. The OPP has risen to levels that increased the chances of developing glaucomatous illness and its progression. Most of the early research looking at the impact of HD on the IOP found increase in the "IOP", which was accredited to a quick drop in the Osmolarity of plasma along with relative increase in the intra-cellular urea concentration in comparison to the extra-cellular urea concentration. A pressure difference is formed between' the eye and the plasma compartments as consequence of rapid change, causing extracellular fluid to migrate from blood to anterior chamber [6,15]. Recent research has shown that during HD, IOP does not alter or decreases, and OPP does not change [13,16]. These results contradict present findings, which demonstrated a large rise in IOP and a considerable reduction in OPP during HD. Current HD approach was not sufficiently different from that employed in this other research to account for the disparities in outcomes. As previously stated, a drop in the plasma osmolarity can cause a rise in the Intra-Ocular Pressure, whereas a rise in the colloid osmotic, pressure causes a decrease in IOP. So, it is evidenced that Instability in BP & IOP are related to glaucoma. Therefore, Ocular Perfusion Pressure alterations owing to I.O.P or B.P variations can play a significant part in illness progression. Two observations back the concept. First, individuals with generally proper controlled IOP but increasing POAG "primary open angle glaucoma" or general tension glaucoma experienced a substantial drop in the SBP

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throughout 24-hour duration. 2nd was in comparison with the well persons. People with the POAG showed significantly less MOPP as well as larger diurnal MOPP changes [17]. Also, more investigations revealed, changes in MOPP within 24-hour duration can be risk in progression and normal-tension glaucoma development [18]. These investigations suggest that individuals with glaucoma show more variation in 'passive' OPP than in well individuals. Present investigation indicated oscillations in 'OPP' throughout the HD, which is known to be associated with BP alterations related to shifting of fluids. Consequently, Hemodialysis patients could be having greater active changes in 'IOP' and/or 'OPP' during repeated hemodialysis sessions, which can ultimately enhance their chances for the progression and glaucomatous illness development. Wang *et al.*, [2] investigate how the influence of hemodialysis on intra-ocular pressure changes with anatomy of the anterior eye chamber, similar to other findings [6]. They find that an increase in intra-ocular pressure in individuals with highly narrow angles is linked with alterations in anterior chamber anatomy. After a single hemodialysis session, a study found that ophthalmological observations, including IOP was consistent and significant in patients undergoing this therapy owing to ESRD. During ophthalmologic checkup of patients receiving hemodialysis, keep in mind that there may be dry eye findings than in the general population, and the condition may worsen after hemodialysis session. The low values of IOP after hemodialysis suggest that a thorough eye examination should be performed the same day. It seems that evaluating IOP before or after hemodialysis is more suitable for these individuals. Furthermore, since axial length fluctuates with hemodialysis, be cautious while measuring it [19]. A prospective, observational, comparative 24-hour trial was performed on consecutive subjects with normal IOP undergoing maintenance HD 3 days a week between 13:00 and 17:00 hours in an academic setting. Trial suggests that HD significantly impacts 24-hour IOP characteristics in normotensive eyes. The long-term significance of these findings requires further elucidation in normotensive patients and, predominantly, in patients with glaucoma undergoing HD [20]. Current research includes strengths and drawbacks. The key strength of present research is that this is the first study that was undertaken in current circumstances. The initial limitations of the current investigation are limited number of the patients. Second, while OPP and IOP were evaluated in single session, it is uncertain if observed higher Intra Ocular pressure & lower Ocular Perfusion Pressure are repeatable for every patient over additional sessions of Hemodialysis. In the future, investigations with large size of the sample that including repeated measurements throughout numerous Hemodialysis sessions is required in corroboration with present findings. Third, the function of this temporary rises in Intraocular Pressure and reductions in Ocular Perfusion Pressure is uncertain. Thus, alterations in the OPP identified in current investigation, happening throughout span of 5 hours, thrice weekly, can be inconsequential regarding chance of glaucoma development. Prospective research related specifically to the chance of glaucoma development following Hemodialysis with 'examination of visual fields' abnormalities will adequately answer the query.

CONCLUSIONS

It is concluded that during HD, there is a significant rise in IOP and a reduction in OPP, both of which enhance risk of glaucoma progression and development. Even when IOP is effectively managed, clinicians must evaluate the history of hemodialysis in the patients with glaucoma aggravation. During HD sessions, such individuals can benefit from monitoring of IOP and as well as BP to reduce OPP alterations caused by spikes in IOP spikes and/or reduced BP.

Authors Contribution

Conceptualization: MO, MI
Methodology: SM, KM
Formal analysis: MA[1]
Writing, review and editing: JM, Ma[2]

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Comparative Efficacy of Occlusal Splint Therapy and Conservative Physiotherapy in the Treatment of Temporomandibular Joint Pain: A Longitudinal Study

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ABSTRACT

Temporomandibular joint disorders significantly impact patients' quality of life. Occlusal splint therapy and conservative physiotherapy (Transcutaneous Electrical Nerve Stimulation (TENS) and Electrical Muscle Stimulation (EMS)) are common treatments for temporomandibular joint disorders. However, their comparative long-term efficacy remains unclear.**Objectives:** To compare the efficacy of occlusal splint therapy and conservative physiotherapy (TENS and EMS) in improving mouth opening and reducing pain in temporomandibular joint disorder patients over six months.**Methods:** A longitudinal quasi study of 12 months was conducted with 112 patients randomly assigned to occlusal splint therapy (n=56) or conservative physiotherapy (n=56). Pre-operative and post-operative mouth opening and Visual Analog Scale (VAS) pain intensity scores were measured at 3 weeks, 6 weeks, 12 weeks, and 6 months. Independent sample t-tests and repeated measures Analysis of Variance (ANOVA) were used for statistical analysis.**Results:** Both groups showed significant improvements in mouth opening and visual analogue scale scores over time. The occlusal splint group demonstrated superior long-term outcomes, with greater improvements in mouth opening and pain reduction at 12 weeks and 6 months. RM-ANOVA revealed significant time effects for both treatments.**Conclusions:** It was concluded that occlusal splint therapy provides greater long-term improvement in mouth opening and pain reduction compared to TENS and EMS. These findings suggest the importance of considering treatment duration and follow-up in managing temporomandibular joint disorders.

INTRODUCTION

Temporomandibular joint (TMJ) disorders are a group of disorders that include the issues arising in TMJ, jaw muscles and associated structures. Common outcomes of these disorders are pain and tenderness, limited mouth opening and decreased voluntary bite force resulting in decreased chewing efficacy significantly impacting the quality of life of patients [1]. The etiology of TMJ disorders includes malocclusion, parafunctional habits, stress-induced muscle tension, trauma and sometimes iatrogenic causes like 3rd molar extraction, inferior alveolar nerve block or other dental surgical procedure [1, 2]. Common treatment offered for acute TMJ disorders of non-traumatic origin is occlusal splint therapy, physiotherapy which includes transcutaneous electric nerve stimulation (TENs) and Electrical muscle stimulation (EMS) combined with pharmacological help like muscle relaxants, anti-

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inflammatory drugs and pain killers [3, 4]. Occlusal split therapy is a commonly used treatment modality for TMJ disorders due to its established effectiveness in pain relief and other symptomatic improvement. The treatment includes the provision of a hard-occlusal splint commonly known as stabilizing split or Michigan splint. It works by redistributing occlusal forces more favourable thereby decreasing stress and strain on jaw muscles and TMJ leading to the resolution of symptoms and a decrease in pain. It was confirmed that occlusal splints are an effective treatment for TMJ disorders in both the long term and the short-term. List and Axelsson also reported that if splint therapy is properly conducted it can result in sustained pain reduction and long-term functional benefits [5]. Conservative physiotherapy techniques include TENS and EMS. TENS is effective in providing immediate pain relief and works by stimulating nerve fibers reducing pain perception, while EMS is effective in providing deep muscle stimulation leading to improvement in muscle function strength and endurance. Hassan et al., reported that TENS and EMS are good and recommended treatment modalities in the reduction of pain and symptomatic relief of TMJ disorder particularly in the acute phase [3]. While both treatment modalities are prevalent, their comparative long-term efficacy in managing TMJ disorders remains underexplored. The findings will help clinicians make informed treatment decisions, potentially leading to improved patient outcomes, reduced pain, enhanced jaw function, and better overall quality of life for individuals suffering from TMJ disorders.

This study aims to fill this gap by evaluating the effectiveness of occlusal splint therapy versus TENS and EMS in improving mouth opening and reducing pain over six months. This study provides comparative evidence on the effectiveness of occlusal splint therapy versus conservative physiotherapy (TENS and EMS) in treating temporomandibular joint disorders.

METHODS

A longitudinal quasi experimental study with 12 months' follow-up was employed to compare the efficacy of occlusal splint therapy and conservative physiotherapy (TENS and EMS). Recruitment of patients started from Feb 2022 and all the patients had their one-year follow-up till Feb 2023. The study was approved by the institutional review board Ref # UCD/ERCA/21/10ab. Patients of age 18-40 having temporomandibular joint pain with more than one month's history were included. Patients in pain with complaints of TMJ clicking, limited mouth opening (MO) and/or jaw deviation were also included. However, patients with a history of treatment with TENS, EMS or occlusal splint therapy were excluded. Patients with TMJ disorders of non-muscular origin (e.g., arthritis, structural abnormalities) or a history of acute trauma leading to TMJ problems were also excluded. Participation in the study was voluntary, though patients who had known allergies to acrylic were also excluded. The study was performed on patients reporting to the prosthodontics clinic of Fatima Memorial Hospital and the private dental clinics of the investigators of this study. A sample size of 112 was calculated using the reference article [6]. 120 participants (considering some dropouts) were enrolled in the study over one year. 3 participants took consent back after 3 weeks while 5 participants stopped responding during different times of data collection. The total number of participants lost during the study was 8. All the patients had to sign the voluntary consent form after which they picked a slip from a jar that contained 120 slips (60 physiotherapies and 60 occlusal splint therapy) using the lottery method. Patients were then referred for initiation of the treatment, and the assigned doctor treated the patient for a full 6 months. Investigators who evaluated the outcomes were completely blind to the grouping of the participants. Physiotherapy (TENS and EMS) group was named Group A and the occlusal splint therapy group was named Group B. Data were collected from 112 patients with TMJ disorders, 54 in Group A and 58 in Group B. Group A was given TENS therapy 20 minutes' session three times a week and EMS therapy 20 minutes' therapy three times a week. Each therapy was given on alternative days and Sunday was kept therapy free. All the patients in Group A bought a portable TENS-EMS rechargeable device and instructions about the frequency setting, mode setting duration setting and treatment schedule were given to the patients in written form by the specialist physiotherapist according to the protocol. Group B was provided with a custom-made hard acrylic stabilizing occlusal splint with canine and incisal guidance such that centric relation becomes equal to centric occlusion in the splint occlusal scheme. All the splints were made such that freeway space is not violated. Patients were advised to wear a splint for all the sleep time and 6 hours in the day along with the nightwear. Patients were evaluated every week by the relevant doctor but data were collected at the following interval; pre-operatively and then post-operatively on 3 weeks, 6 weeks, 12 weeks and 6-month intervals by the investigators. Mouth Opening (MO) was recorded from inter-incisal opening measured in millimetres using a caliper. Whereas, the Visual Analog Scale (VAS) for Pain was noted on a 10-point scale to assess pain intensity. Descriptive statistics were calculated for baseline characteristics and follow-up measurements. Independent sample t-tests and Repeated Measures ANOVA (RM-ANOVA) were performed to assess between-group and within-group differences over time respectively.

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RESULTS

Out of 112 samples, 61 male and 51 female were part of the study. Both treatment groups had similar MO and VAS scores pre-operatively (p>0.05), however showed significant improvements in MO and VAS scores over time with therapy. Group A has a higher mean MO at 3, 6, and 12 weeks compared to the occlusal splint therapy group. At 6 months, Group B shows a higher mean MO than the TENS and EMS groups. The descriptive statistics for mouth opening (MO) at various time points are provided in Table 1.

Table 1: Comparison of Mouth Opening (MO) as Outcome Variable

Variables	Pre-Op MO Mean	3 Weeks Post Op MO Mean	6 Weeks Post Op MO Mean	12 Weeks Post Op MO Mean	6 Months Post Op MO Mean
Total Mean	31.82 ± 4.33	35.52 ± 4.74	37.1 ± 3.93	39.07 ± 3.2	39.71 ± 3.36
TENS And EMS (n=54)	31.70 ± 4.2	37.89 ± 3.7	38.96 ± 56	39.68 ± 3.1	37.85 ± 3.0
Occlusal Splint (n=58)	31.89 ± 4.4	33.16 ± 4.4	35.25 ± 3.8	38.46 ± 3.2	41.57 ± 2.6
p-value	0.862	<0.001	<0.001	0.045	<0.001

OP=operation. Independent t-test was used to evaluate inter-group comparison. p>0.05 was considered significant.

Group A had lower mean VAS at 3 and 6 weeks compared to the occlusal splint therapy group, however, the VAS scores improved drastically in Group B at 12 weeks and 6 months. The descriptive statistics for Visual Analog Scale (VAS) scores at various time points are provided in Table 2.

Table 2: Comparison of VAS Scores as Outcome Variable

Variables	Pre-Op VAS	3 Weeks Post-OP VAS	6 Weeks Post-OP VAS	12 Weeks Post-OP VAS	6 Months Post-OP VAS
Total Mean	7.62 ± 0.92	5.8 ± 1.3	5.07 ± 1.13	3.8 ± 1.16	3.1 ± 1.86
TENS And EMS (n=54)	7.6 ± 0.9	4.85 ± 0.99	4.41 ± 0.96	4.2 ± 1	4.6 ± 1.1
Occlusal Splint (n=58)	7.64 ± 0.94	6.75 ± 1.03	5.43 ± 1.18	3.43 ± 1.15	1.75 ± 1.19
p-value	0.839	<0.001	<0.001	<0.001	<0.001

Independent t-test was used to evaluate inter-group comparison. p>0.05 was considered significant.

The study revealed that both treatment groups show a consistent increase in MO over time. Group A has a higher mean MO at 3, 6, and 12 weeks compared to the occlusal splint therapy group. At 6 months, Group B shows a higher mean MO than the TENS and EMS groups. Regarding VAS scores, both treatment groups show a consistent decrease in VAS scores over time. Group A has lower mean VAS at 3 and 6 weeks compared to the occlusal splint therapy group. At 12 weeks and 6 months, Group B shows lower mean VAS than the TENS and EMS group in Figure 1.

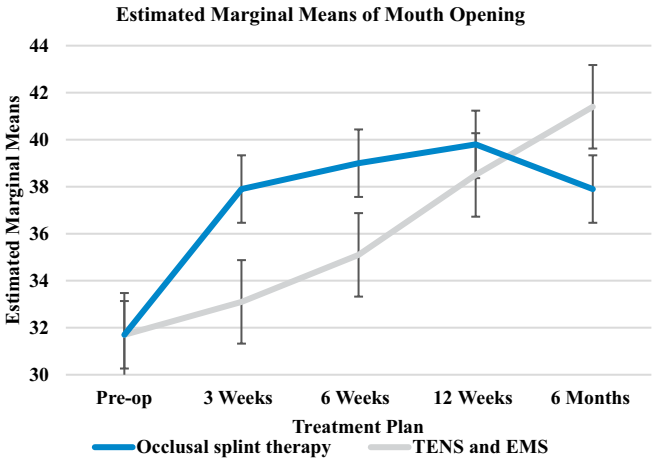

Figure 1: MO with Treatment Plan

RM-ANOVA tests of within-subject effects for MO and VAS both have p-values of <0.001, indicating significant changes over time. The p-value for between-subject effects is 0.061 for MO and 0.161 for VAS, suggesting no significant difference between the two treatment groups overall, despite significant changes over time. The VAS scores over time are illustrated in Figure 2.

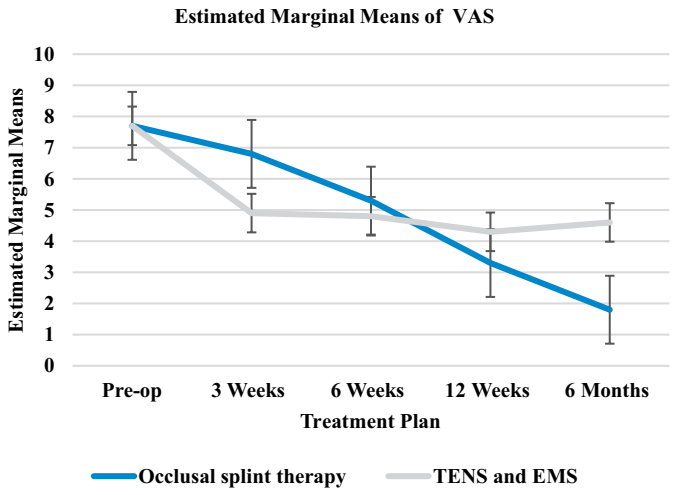

Figure 2: VAS Score Graph with Treatment Plan

DISCUSSION

Occlusal splint therapy has been shown to effectively reduce pain and improve jaw function by stabilizing the occlusal relationship and redistributing forces across the TMJ [7].In this study, patients using occlusal splints experienced significant improvements in MO and VAS scores over the 12-week and 6-month follow-up periods.

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This aligns with previous research indicating that occlusal splints are beneficial in the long-term management of TMJ disorders [8]. Interestingly, while the occlusal splint group showed less improvement in MO and VAS scores during the initial 3 and 6 weeks compared to the TENS and EMS group, they demonstrated superior outcomes at 12 weeks and 6 months.This suggests that occlusal splint therapy may have a more gradual, yet sustained effect on TMJ disorder symptoms [9, 10].This delayed but steady improvement highlights that the splint therapy improves the muscle forces, creates occlusal harmony provides mutually protected occlusion, reducing any parafunctional habit by acting as a habit breaker and providing adequate time for the muscle to heal and gain strength [11].ENS and EMS therapies are effective non-invasive treatments for TMJ pain and dysfunction, primarily through pain modulation and muscle stimulation [6, 12]. In this study, the TENS and EMS group showed significant initial reductions in VAS scores and improvements in MO during the first 6 weeks, outperforming the occlusal splint group. These findings are consistent with existing literature, which supports the immediate analgesic effects of TENS and the muscle-strengthening benefits of EMS [9, 13]. However, the observed decline in effectiveness beyond the 6-week mark, culminating in less favourable outcomes at 12 weeks and 6 months compared to occlusal splint therapy, suggests that while TENS and EMS are effective in the short term, their long-term benefits may not be as robust [14]. This might be due to the need for ongoing sessions to maintain therapeutic effects, highlighting a potential limitation in the sustainability of conservative physiotherapy or maybe muscles not responding beyond a specific means [3, 15].There can be another because which can be investigated but within the scope of the study occlusal splint therapy shows better results in long-term than conservative physiotherapy [16, 17]. A similar finding was observed by Madani and Mirmortazavi, who compared TENS with occlusal splints, highlighting both treatments' effectiveness, with variations in short-term and long-term benefits.They found that while TENS provided more immediate pain relief, occlusal splints showed better long-term outcomes in terms of pain reduction and functional improvement [18].The comparative efficacy of conservative physiotherapy and occlusal splint therapy remains an area of interest. Fouda AA in 2020 gives a systematic review emphasized the need for a holistic approach, incorporating both physical and psychological interventions for optimal TMJ disorder management [19]. Similarly, Greene and Obrez questioned the importance of changing the occlusion while managing TMJ disorders [20]. Huttunen *et al.*, underscored the role of a multidisciplinary approach in achieving better outcomes, suggesting that combining different treatment modalities could be more effective in managing complex cases of TMJ disorders. These studies underscore the importance of considering both short-term and long-term outcomes when evaluating treatment efficacy [12]. The current study considers both short-term and considerably long-term outcomes of both treatment modalities with parameters like MO and VAS. Significant improvements in MO and VAS scores were observed over time for both treatment groups. Statistical data analysis indicates that the effectiveness of the treatments varies over time. The initial superiority of TENS and EMS in reducing pain and improving MO is followed by the greater long-term benefits of occlusal splint therapy. This underscores the importance of treatment duration and follow-up in managing TMJ disorders [21]. The treatment can be highly effective if conservative physiotherapy is used as a treatment modality to reduce the VAS score and increase MO in the acute phase while occlusal splint therapy is used for long-term improvement of symptoms. These findings suggest that clinicians should consider the time-dependent effects of these treatments when developing management plans for TMJ disorders. Occlusal splint therapy may be more suitable for patients seeking long-term relief, whereas TENS and EMS could be recommended for immediate pain relief and short-term improvements. Combining these therapies could potentially offer both immediate and sustained benefits, optimizing patient outcomes.

CONCLUSIONS

It was concluded that both occlusal splint therapy and conservative physiotherapy (TENS and EMS) are effective in managing TMJ disorders, with each treatment demonstrating unique strengths over different periods. Occlusal splint therapy provides significant long-term benefits, while TENS and EMS offer effective short-term relief. These findings can guide clinicians in tailoring treatment plans based on individual patient needs and treatment goals, ultimately improving the quality of care for patients with TMJ disorders.

Authors Contribution

Conceptualization: MSN, MH[1], SZ, SS
Methodology: MSN, MH[1], MH[2], MS, SZ, SS
Formal analysis: MSN, MH[2], MS, SZ
Writing review and editing: MSN, MH[1], MH[2], MS, SZ, SS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Evaluation of Nutrition Awareness of Rural Women Concerning Cardiovascular Disease

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ABSTRACT

Cardiovascular disease is the leading component of non-communicable diseases. Atherosclerotic and hypertensive diseases, mostly ischemic heart disease and stroke together with heart failure are the main Cardiovascular disease entities and signify threats to population health. In Pakistan, the incidence of Cardiovascular disease is more common among female as compared to male. The ratio of male to female patients is 1:3. Nutrition plays a significant role in the development and prevention of heart diseases. **Objective:** To evaluate of Nutrition Awareness of Rural Women Concerning Cardiovascular Disease. **Methods:** A descriptive cross-sectional study was carried out to assess the nutritional knowledge and health-related behaviour regarding cardiovascular disease of rural women aged 35 to 45. The research was a survey based with a well-established interview-based questionnaire was used to collect data. The sample was selected using random sampling and comprised of 300 respondents. **Results:** The results revealed rural women had little knowledge regarding good nutrition practices like consumption of high fat, low fiber, high amount of red meat, full-fat milk, and low amount of fruits and vegetables can lead to heart disease. **Conclusions:** It was concluded that assessment of nutritional knowledge regarding Cardiovascular disease of rural women age 35 to 45 gave statistical evidence of increasing risk factors for heart diseases. Results were useful in the development of gender-specific messages to increase awareness about heart disease and to promote lifestyle behaviours to decrease risk.

INTRODUCTION

Cardiovascular diseases are the leading cause of mortality and morbidity in developing countries. The term cardiovascular disease includes stroke, coronary heart disease, peripheral vascular disease and heart failure. Coronary heart disease (known as coronary artery disease or ischemic heart disease) is the most common form of heart-related disease and results from atherosclerosis or accumulation of fatty plaque in the artery walls that causes narrowing of the artery lumen [1]. Coronary artery disease which includes coronary syndrome, atherosclerosis, and other form of chronic ischemic disease, is responsible for many deaths. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality especially in developing countries, despite advances in treatment and diagnostic procedures [2]. Knowledge about the risk factors of cardiovascular disease is considered to be important for adopting healthy lifestyle behaviours. One out of four deaths is because of cardiovascular disease [3]. Those who are not good in their behavioural factor have more chances of developing cardiovascular diseases. Underlying societal influences and socioeconomic parameters increase the chances of cardiovascular disease [4]. Socioeconomic status which is assessed by education, income level and occupation is directly related to diet quality. Socioeconomically disadvantaged people are associated with an increased prevalence of CVD mortality [5]. Atherosclerotic cardiovascular disease has a substantial impact on women's lives. Stroke and coronary heart disease, types of CVD, are responsible for the first and third causes of mortality in the world [6]. Among

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women, more deaths are because of CVD as compared to chronic lower respiratory disease, cancer, Alzheimer's disease and accidents. CVD is because by modifiable and non-modifiable factors. Gender, age and family history are non-modifiable factors. The risk of stroke and heart disease is decreased by as much as 80% by controlling cholesterol, smoking status, weight and hypertension. CVD modifiable risk factors are unhealthy diet, obesity, and sedentary lifestyle, harmful use of alcohol, stress and diabetes. The most vulnerable group to heart disease and stroke are people living in rural areas. In rural areas, major health-related issues are diabetes, tobacco use, obesity and low availability of doctors and hospitals [7]. Increased knowledge of the resident's CVD risk factors would be beneficial for public health-related programs and for the primary care provider and what would be the ways to increase health-promoting behaviors to decrease CVD risk factors [8]. Approximately 75% of risk factors are because of unhealthy lifestyle choices. Modification of risk factors focuses on three main lifestyle-related risk factors: diet/weight management, smoking cessation and physical activity. Women believe that osteoarthritis, arthritis and cancer are more common in women as compared to Coronary Artery Disease (CAD) whereas most of the deaths are because of heart diseases. Pakistanis 15.9% have a minimum of one factor of heart disease risk. Pakistani women have more heart disease risk factors than men [9]. The most common risk factors of heart disease in men are higher low-density lipoprotein (LDL) and cholesterol levels than in women. Common risk factors among women are high triglycerides and low high-density lipoprotein (HDL). The metabolic syndrome prevalence among Pakistani female was 49%. 30% of women who have metabolic syndrome are affected with CAD [10]. Coronary heart disease is the most common cause of death worldwide approximately it is the cause of 25–30 % of deaths. In Pakistan, a lack of knowledge about proper nutrition and risk factors for heart disease combined with a sedentary lifestyle and increased cigarette smoking are the major causes of heart disease.

This study aims to find out the awareness of rural women about the diet and knowledge about the heart disease risk factors. The proposed study was about the assessment of nutritional knowledge and health behaviour regarding CVD of rural women aged 35 to 45 years.

METHODS

The research was conducted for the assessment of nutritional knowledge and health-related behaviours regarding CVD in rural women aged 35 to 45 and was based on a survey in a hospital so the data were collected through the questionnaire.The research design was descriptive cross-sectional, in which data were analyzed and collected from the population at a specific point in time. Study data were used to measure the prevalence of chronic and acute conditions in the population. The universe of this study was rural women. The period of data collection was of 6 months, form Jan 2023 to Jun 2023. The sample was collected from Ghurki Trust Teaching Hospital Jallo Morr, Lahore. The people visiting the hospital were coming from the various nearby villages and were selected conveniently to collect the data. Inclusion criteria included rural women between 35 to 45 years of age, visiting the Gurki Teaching Hospital. Those who had gone through a surgical operation up to 3 months earlier than the date of data collection were not included. Participants aged less than 35 and over 45 were excluded from the study. The sample size of this study was calculated by using standard formula [7] and 300 rural women were selected of 35-45 age. Informed consent was taken. The non-probability convenience sampling technique was used in this study. A questionnaire was used to assess the nutritional knowledge related to cardiovascular disease in rural women. The demographic section consists of the following variables name, age, residence, education, income, marital status and occupation. The second section contains questions about the nutritional knowledge of rural women. This section consists of questions regarding fiber, fat, vegetables, fruits, meat, weight and fatty foods. The questionnaire was administered to rural women after obtaining permission from college authorities. The researcher selected a hospital located in the village, Ghurki Trust Teaching Hospital, Jallo Morr and after acquiring formal permission from the hospital the researcher collected data from the rural women. The questionnaire used for data collection was self-administered by the researcher. The personal information of respondents was kept confidential. They were given 15 minutes to answer questions. The queries about any questions were explained in detail. The three months' duration was required by the researcher to collect data and multiple visits were held. For the present study, the data were analyzed by SPSS software (Statistical Package for the Social Sciences); Version 23.0 and Microsoft Excel 2010. The data were presented in the form of frequencies and percentages by using tables and bar charts.

RESULTS

The present study was intended to assess nutrition knowledge and health behaviours regarding cardiovascular disease of rural women aged 35-45 years. The data of this study has been presented using descriptive analysis of the demographic information that was collected in the first section of the questionnaire. The heart disease-related nutrition knowledge of the respondents is statistically analyzed in the form of percentages and frequencies by using bar charts and tables. The demographic section includes age of the respondent, education, marital status,

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and occupation. The nutritional knowledge section includes the following sections: fiber, fat, weight, fruits and vegetables, meat, fatty food and salt. 51% of rural women were in the range of 40-45 of age. 54.5% of rural women were illiterate. 68% of women had an income of less than 10,000. 65.4% of women were married. 52.6% of women were unemployed (Table 1).

Table 1: Demographics of the Respondents

Characteristics	n (%)
Age	
30-34	56 (18%)
35-39	86 (27.6%)
40-45	158 (51%)
Education	
Less than Matric	58 (16.8%)
Matric	31 (9.9%)
Intermediate	22 (7.1%)
BS	14 (4.5%)
Higher	5 (1.6%)
None	170 (54.5%)
Income	
less Than Rs. 10,000	212 (67.9%)
Rs. 11000-30000	64 (20.5%)
Rs. 31000-50000	23 (7.4%)
Rs. 51000 above	1 (0.3%)
Marital Status	
Married	204 (65.4%)
Widow	52 (16.7%)
Divorced	30 (9.6%)
Unmarried	14 (4.5%)
Occupation	
Unemployed	164 (52.6%)
Self-Employed	10 (3.2%)
Employed By the Government	29 (9.3%)
Employed By Individual	97 (31.1%)

The nutritional knowledge questionnaire is further divided into parts which include fiber, fat, weight, fruits and vegetables, meat, salt and fatty food consumption. Results show that 44% of rural women did not know the role of fibre in decreasing the chances of risk factors for heart disease. 41% disagree that major health diseases are related to low consumption of fibre. 46% agree that white flour is better for health than brown flour. 57% disagree that brown bread is good for heart health (Table 2).

Table 2: Fiber Related Knowledge

Questions	n (%)
Increasing the fiber in your diet reduces the chances of heart disease	
Strongly Disagree	28 (9.0%)
Disagree	41 (13.1%)
Neutral	137 (43.9%)
Agree	73 (23.4%)
Strongly Agree	21 (6.7%)
Major health diseases are related to low consumption of fiber	
Strongly Disagree	34 (10.9%)
Disagree	128 (41%)
Neutral	87 (27.9%)
Agree	41 (13.7%)
Strongly Agree	10 (3.2%)
White flour is better for health than brown flour	
Strongly Disagree	12 (38%)
Disagree	46 (14.7%)
Neutral	79 (25.3%)
Agree	143 (45.8%)
Strongly Agree	20 (6.4%)
Brown bread is good for heart health	
Strongly Disagree	14 (4.5%)
Disagree	177 (56.7%)
Neutral	71 (22.8%)
Agree	26 (8.3%)
Strongly Agree	12 (3.0%)

The finding shows that 43% are not aware that reducing the fat in your diet decreases the chances of heart disease. 53% of rural women were neutral that margarine contains less fat as compared to butter. 50% disagree that vegetable oil is better than ghee (Table 3).

Table 3: Fat Related Knowledge

Questions	n (%)
Reducing the fat in your diet decreases the chances of heart disease	
Strongly Disagree	11 (3.5%)
Disagree	62 (19.9%)
Neutral	132 (42.3%)
Agree	86 (27.6%)
Strongly Agree	9 (2.9%)
Margarine contains less fat as compared to butter	
Strongly Disagree	26 (8.3%)
Disagree	42 (13.5%)
Neutral	164 (52.6%)
Agree	61 (19.6%)
Strongly Agree	7 (2.2%)
Vegetable oil is better than ghee	
Strongly Disagree	8 (2.6%)
Disagree	155 (49.7%)
Neutral	101 (32.4%)
Agree	24 (7.7%)
Strongly Agree	12 (3.8%)

Results show that 59% disagreed that overeating is the main cause of obesity. 34% agreed that reducing food intake is helpful in reducing body fat. 33% disagreed that being overweight is one of the main causes of heart disease. 52% gave a neutral answer to the question that is the brown sugar better than white sugar. This means they do not know about it (Table 4).

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Table 4: Weight-Related Knowledge

Questions	n (%)
Overeating is the main cause of obesity	
Strongly Disagree	21 (6.7%)
Disagree	183 (58.7%)
Neutral	46 (14.7%)
Agree	42 (13.5%)
Strongly Agree	8 (2.6%)
Reducing food intake helps reduce body fat	
Strongly Disagree	41 (13.1%)
Disagree	56 (34%)
Neutral	75 (24%)
Agree	106 (17.9%)
Strongly Agree	22 (7.1%)
Being overweight is one of the main causes of heart disease	
Strongly Disagree	27 (8.7%)
Disagree	102 (32.7%)
Neutral	95 (30.4%)
Agree	63 (20.2%)
Strongly Agree	1 (0.3%)
Brown sugar is better than white sugar	
Strongly Disagree	29 (9.3%)
Disagree	37 (11.9%)
Neutral	163 (52.2%)
Agree	69 (22.1%)
Strongly Agree	2 (0.6%)

41% agreed that eating less than 2 servings of fruits is good for health. 44% disagreed that eating more vegetables helps reduce heart disease. 51% strongly disagreed that eating a minimum of 5 servings of fruits and vegetables per day can lower your blood pressure. 39.1% disagreed that Almonds are good for heart health (Table 5).

Table 5: Fruits and Vegetables Related Knowledge

Questions	n (%)
Eating less than 2 servings of fruits is good for health	
Strongly Disagree	27 (8.7%)
Disagree	58 (18.6%)
Neutral	69 (22.1%)
Agree	128 (41%)
Strongly Agree	18 (5.8%)
Eating more vegetables helps reduce heart disease	
Strongly Disagree	9 (2.9%)
Disagree	137 (43.9%)
Neutral	55 (17.6%)
Agree	86 (27.6%)
Strongly Agree	13 (4.2%)
Eating a minimum of 5 servings of fruits and vegetables per day can lower your blood pressure	
Strongly Disagree	159 (51%)
Disagree	28 (9%)
Neutral	73 (23.4%)
Agree	32 (10.3%)
Strongly Agree	8 (2.6%)
Almonds are good for heart health	
Strongly Disagree	29 (9.3%)
Disagree	122 (39.1%)
Neutral	85 (27.2%)
Agree	61 (19.7%)
Strongly Agree	3 (1%)

Finding show 35% disagreed that eating too much meat is not good for health. 45% agreed that Red meat is better for health than chicken. 39% disagreed that Fish is good for heart health. 32% strongly disagreed that Egg yolk contain more fat as compared to egg white (Table 6).

Table 6: Meat Related Knowledge

Questions	n (%)
Eating too much meat is not good for health	
Strongly Disagree	61 (19.6%)
Disagree	108 (34.6%)
Neutral	66 (21.2%)
Agree	52 (16.7%)
Strongly Agree	13 (4.2%)
Red meat is better for health than chicken	
Strongly Disagree	23 (7.4%)
Disagree	29 (9.3%)
Neutral	104 (33.3%)
Agree	114 (45.2%)
Strongly Agree	3 (1%)
Egg yolk contains more fat as compared to egg white	
Strongly Disagree	99 (31.7%)
Disagree	51 (16.3%)
Neutral	94 (30.1%)
Agree	52 (16.7%)
Strongly Agree	4 (1.3%)
Fish is good for heart health	
Strongly Disagree	37 (11.9%)
Disagree	122 (39.1%)
Neutral	77 (24.7%)
Agree	56 (17.9%)
Strongly Agree	8 (2.6%)

This shows that 45% did not have any knowledge that eating fatty foods does not affect blood cholesterol levels. 49% disagreed that steamed chicken is better than red meat. 39% agreed that fried foods are better for heart health (Figure 1).

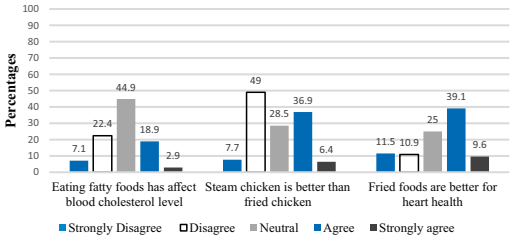

Figure 1: Graphical Representation of Rural Women's Perception Regarding Fatty Food Consumption

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This shows that 38% disagreed that eating too much salt is not good for health. 46.2% disagreed that less salt is good for controlling blood pressure. 54% did not know that processed foods contain more salts than non-processed food(Figure 2).

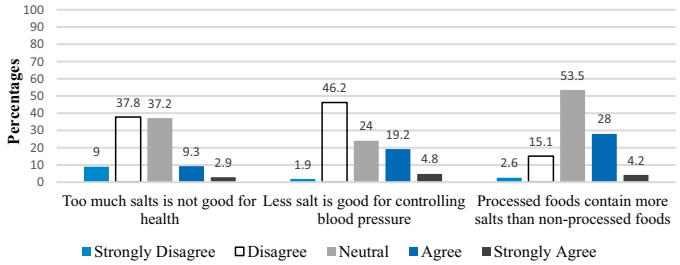

Figure 2: Graphical Representation of Rural S Perception Regarding the Salt

DISCUSSION

The study mainly aimed to assess the nutritional knowledge of rural women regarding CVD. Heart disease-related nutrition knowledge is precise and significant for behaviour change. Improper nutrition and unhealthy dietary habits are the leading causes of heart disease among rural women [11]. This study would be helpful in the development of a nutrition education plan about CVD. Awareness regarding CVD risk factors and nutrition play a significant part in healthy heart-associated actions of women [4]. The diet plays a noteworthy part in preventing and developing heart disease. There is a direct connection between CVD and unhealthy dietary patterns [12]. The proper knowledge about the nutrition is essential for the upgrading of lifestyle that averts heart diseases. High intake of saturated fat, Trans fat, cholesterol and sodium can lead to heart disease. Low intake of fruits, vegetables and whole grains increases the risk factors for heart disease [13]. Results showed that the knowledge of rural women regarding fiber intake is inadequate. Four questions were asked about the fiber intake of rural women they had negative Responses. 44% of rural women did not know the role of fiber in decreasing the chances of risk factors for heart disease. 41% of women disagree that major health diseases are related to low consumption of fiber. 46% of women think that white flour is better than brown flour. 57% strongly disagree that brown bread is good for heart health. This finding shows that they do not know the benefits of fiber. These findings are similar to the study that concludes that less intake of fiber is one of the causes of heart disease. In the end, it was concluded that the predominant diet and lifestyle patterns in the study are related with excessive intake of saturated fats and cholesterol associated with cardio-metabolic disease. The Fruits, nuts, Vegetables, and Legumes pattern related to the component proline betaine has been associated with reduced risk. The Animal Protein intake pattern was related to ceramides, NAPEs, sphingomyelins, and short-chain acylcarnitines. Moreover, Animal Protein and sweets, Fried Snacks, and High-Fat Dairy patterns had contrary associations with omega-3 fatty acids, which have been associated with a lesser risk of cardiovascular disease. [14]. High intake of fat is one of the reasons for heart disease particularly saturated fat which mostly comes from animal sources. Results depicted the knowledge of rural women about fat intake. 50% of women disagree that vegetable oil is better than ghee. 44.2 % agree that high-fat food prevents the chances of heart disease. 53% of rural women were neutral that margarine contains less fat as compared to butter. 43% are not aware that reducing the fat in your diet decreases the chances of heart disease. These findings show that rural women are unaware of the connection between fat intake and cardiovascular disease. These findings are in line with the comparable study which accomplishes that rural women do not have healthy dietary habits. The respondent's fat consumption is greater because they have less knowledge about heart disease and the role of nutrition in its development. The results concluded that Diet is a risk factor for coronary artery disease and can be attuned to decrease the risk. Consumption of beef, chicken, eggs and junk food is related to a high threat of CVD. Ingestion of vegetables, yoghurt, and fruits, on the other hand, has a protective effect against coronary artery disease. Anthropometric methods such as BMI, WHR and WC can also show an augmented risk of coronary artery disease [15]. High fat can lead to atherosclerosis, particularly saturated fat. Saturated fat is typically present in whole milk, cheese and yoghurt. Results characterized that 46.2% had given a neutral response to the question that is more calcium in whole milk than skimmed milk. 46.2% agreed that full-fat yoghurt is better for health than low-fat yoghurt. 53% agreed that a glass of whole milk is better than skimmed milk. These results verdicts are in line with another study which exhibited that saturated fat is one of the main causative factors of heart problems. Total dietary fiber intake was linked with a lesser long-term CVD risk, particularly in the 20–39 and 40–59 age groups, where the decrease was most momentous [16]. Overweight is the leading cause of heart disease. Results exhibited the knowledge of rural women about overweight is insignificant. 33% of women consider that overweight is not the cause of heart disease. 59% disagree that overeating can cause obesity. 34% agreed that reducing food intake helps reduce body fat. 52% gave a neutral answer to the question that is the brown sugar better than white sugar. This means they do not know about it. Rural women do not consider the overweight as a risk factor for heart disease. Another study also got similar results. Among the participants, half of the patients had awareness concerning heart-healthy choices, 37% were

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consuming a healthy diet, 50% were partially following and 4.4% were not taking at all. It concluded that the awareness of participants regarding healthy diet and lifestyle was insufficient and also their dietary practices were of inferior quality and not in harmony with the medical references. There is an essential requirement to increase awareness in heart patients concerning healthy diet selections so that their risk of CVD progression can be reduced [17]. Increased intake of fruits and vegetables is important for the prevention of heart disease. Findings indicated the knowledge of rural women about fruits and vegetables about heart disease [18]. 41% agree that eating less than two servings of fruits is good for health this means their dietary habits are not good as they have insufficient knowledge. 44% disagree that eating more vegetables helps reduce heart disease. 51% strongly disagree that eating a minimum of 5 servings of fruits and vegetables per day can lower your blood pressure. 39.1% disagree that Almonds are good for heart health. Another comparable study has similar results that the knowledge about fruits and vegetables about heart disease in rural women is insufficient [19]. Salt increases the blood pressure of the body which is the risk factor of heart disease. Results illustrated that 38% disagree that eating salt is not harmful which means they do not know the damaging effects of high consumption of salt on health. 46.2% disagreed that less salt is good for controlling blood pressure. 54% did not know that processed foods contain more salts than non-processed foods. Another study presented that rural women consume high amounts of salt and they have no knowledge regarding the bad effects of salt on health [20]. High meat consumption increases the risk factors for heart disease. Animal sources contain saturated fat which increases the lipid profile of blood. Results disclosed the knowledge of rural women regarding the meat group. 35% agreed that eating red meat is good for health. 39% disagreed that fish is good for the health of the heart. 32% strongly disagreed that Egg yolk contains more fat as compared to egg white. All of these findings showed rural women have inadequate knowledge regarding meat groups which is the main reason for obesity and heart disease among them [21]. Increased consumption of fatty foods increases the fat consumption of people. Mostly saturated and Trans fat leads to heart disease. 45% did not have any knowledge that eating fatty foods does not affect blood cholesterol levels. 49% disagreed that steamed chicken is better than red meat. 39% agreed that fried foods are better for heart health. These findings indicated that participants did not know fatty foods and their role in the development of heart disease. In another study results depicted that Conferring to the BMI, the maximum number of the respondents were overweight. The respondents' practice level of healthy diet and lifestyle was lower than their knowledge and attitude level toward CAD. A positive correlation originated among the respondents' attitude, knowledge and practice [22]. Most of the CVD patient's BP levels and troponin values were estimated higher than the standard limit. Along with that lipid profile level was higher than the normal value. Most of the participants were in borderline risk condition of CVD and some had great risk. The patients who consumed a higher amount of egg, red meat, cheese, soft drinks, fast food, and snacks had increased LDL and TG levels in blood which were the main risk factors of CVD than the patients who take fish, pulse, chicken, nuts, vegetables, and fruits in their diet habitually. the research thus concluded that the majority of participants were not aware of nutrition knowledge regarding heart health. The lack of awareness has affected their health-related behaviour adversely. They are ignorant about the foods that increase their risk of CVD. The proper nutrition education intervention must be conducted in rural areas [23]. They must be made aware of the bad aspects of the consumption of high amounts of fatty foods [24]. Seminars and workshops should be held in rural areas regarding healthy dietary habits and health behaviours for the prevention of CVD. Media should play a pivotal role in the provision of nutritional knowledge regarding heart health and the promotion of healthy lifestyle behaviours.

CONCLUSIONS

It was concluded that the majority of rural women are not aware of nutrition knowledge regarding heart health. The lack of awareness has affected their health related behavior adversely. They are ignorant about the foods that increases the risk of heart disease. The proper nutrition education intervention must be conducted in the rural areas. They must be made aware about the bad aspect of consumption of high amount of fatty foods. Seminars workshops should be held in rural areas regarding healthy dietary habits and health behaviors for the prevention of CVD. Media should play pivotal role in in provision of nutritional knowledge regarding heart health and in the promotion of healthy lifestyle behaviors.

Authors Contribution

Conceptualization: AS
Methodology: AS
Formal analysis: MNK
Writing review and editing: SS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Association of Different Formulation with Oral Contraceptive Agents in Lipid and Carbohydrates Metabolism in Women

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ABSTRACT

Oral contraceptives impact lipid and carbohydrate metabolism differently based on formulation. **Objectives:** To assess the association between Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives and key metabolic markers, including lipid profile and carbohydrate metabolism, in women using these formulations. **Methods:** A cross-sectional study recruited women aged 18–45 using one of these contraceptives for at least 6 months. Exclusion criteria included metabolic disorders, cardiovascular disease, and recent medication use affecting metabolism. Demographic and health data (BMI, blood pressure, waist-to-hip ratio) were collected. Metabolic markers—including cholesterol, LDL, HDL, triglycerides, Apolipoproteins A1/B, fasting glucose, fasting insulin, HOMA-IR, OGTT, and HbA1c were measured. Statistical tests included One-Way ANOVA, Kruskal-Wallis, and Tukey's post-hoc ($p<0.05$). **Results:** Significant metabolic differences were observed. Ethinylestradiol-Levonorgestrel users had higher total cholesterol ($p=0.002$) and increased insulin resistance (HOMA-IR, $p=0.019$), suggesting a potential long-term cardiovascular risk. Ethinylestradiol-Norgestimate users exhibited higher Apo-lipoprotein A1 levels ($p=0.005$), indicating a possible cardio-protective effect in reducing atherosclerosis risk. HOMA-IR was also higher in Progestin-Only users compared to Ethinylestradiol-Norgestimate ($p=0.006$). No significant differences were found in fasting glucose or HbA1c. **Conclusions:** It was concluded that Ethinylestradiol-Norgestimate may have a more favourable metabolic profile, with lower cholesterol and insulin resistance.Tailored contraceptive selection could reduce metabolic risks, particularly in women with cardiovascular concerns. Further research is needed to assess long-term effects. However, the exclusion of women with pre-existing metabolic disorders limits the generalizability of these findings. Future studies should include these subgroups to provide a broader understanding of metabolic responses to oral contraceptives.

INTRODUCTION

Oral contraceptives are extensively used worldwide, both for effective birth control and for the management of hormonal and reproductive health issues [1]. Combinations of ethinylestradiol with progestins like levonorgestrel or norgestimate are frequently prescribed, as they replicate natural hormonal cycles, aiding in contraception and providing additional benefits like cycle regulation, reduction in menstrual pain, and lowered ovarian cyst. Progestin-only formulations, which omit estrogen, offer an alternative for women who cannot use estrogen, providing similar contraceptive efficacy through progestin's influence on ovulation risk [2]. However, these oral contraceptives are known to change certain metabolic activities, most notably lipid and carbohydrate metabolism, which is important for cardiovascular and metabolic health. Long-term oral contraceptives, especially among women already predisposed to metabolic problems, may promote the development of cardiovascular

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disease through long-term dysregulation of lipid and carbohydrate metabolism. Other studies suggest that combined contraceptives containing ethinylestradiol can increase triglyceride and low-density lipoprotein (LDL) levels with a concomitant decrease in high-density lipoprotein (HDL), thus raising the risk for cardiovascular diseases. More importantly, progestin-only formulations appear to have this neutral or varying impact on lipid metabolism, as several different progestins could be used. Furthermore, another component of metabolic syndrome, insulin resistance, has been associated with the chronic use of androgenic progestins such as levonorgestrel. These effects are important for determining the women who need special care while using hormonal contraceptives [3]. In most contraceptives, formulations that have ethinylestradiol along with either levonorgestrel or norgestimate and also progestin-only contraceptives affect lipid markers like total cholesterol, LDL, HDL, Apo-lipoprotein A1 and B, and triglycerides. Ethinylestradiol-based formulations are likely to increase the total cholesterol and triglyceride levels as well as the LDL, and HDL levels, thus increasing cardiovascular risks [4]. The combination methods, the progestin-only choice may have unique metabolic effects because of the lack of estrogen. The metabolic impacts caused by progestin-only contraceptives are different from those of combined formulations because ethinylestradiol, which has a proestrus effect, is absent in those formulations. The progestin-only methods of contraception are lipid a sedentary form of energy storage arthritis through androgenic receptors. There is net deposition of LDL cholesterol reduced HDL cholesterol and altered triglyceride levels due to the different types of progestin used, and also diabetic partial inhibition of lipid metabolism. In addition, increased doses of various progestins may enhance the insulin effects and activity of pancreatic β-cells which aid in insulin resistance. Some studies suggest that certain progestins which have a reputation for higher insulin-resistance setting androgenic activity, such as levonorgestrel, seem to worsen insulin resistance which results in higher homeostasis model assessment-estimated insulin resistance (HOMA-IR) levels. Others with lower androgenic activity, like desogestrel, may have a neutral effect in disposition tissues and free fatty acids. These considerations all suggest a need for more in vivo studies. There seems to be limited understanding regarding its long-term effects on subjects using progestin-only contraceptives [5]. Oral contraceptives (OCP) alter the metabolism of carbohydrates as well. The variables, 'fasting insulin, HOMA-IR (a measure of insulin resistance), fasting blood glucose, and OGTT (oral glucose tolerance test)' results are relevant in determining glucose metabolism within the body with different formulations. In addition, the impact of OCP use on blood glucose control over time can be estimated from HbA1c, an indicator of average blood glucose levels over some time. This information is crucial as it highlights shifts in lipid and carbohydrate metabolism that occur after extensive periods and tends to predispose one to cardiovascular and other metabolic abnormalities. Because women respond to various forms of contraception differently within the metabolism, behavioural contraceptive management is important. Underlying metabolic disorders or conditions that predispose an individual towards increased insulin resistance may benefit from low androgenic weight Ethinylestradiol-Norgestimate which, as proposed, has more favourable effects on lipid and carbohydrate metabolism. On the other hand, people who have a lower metabolic should be exposed to a wider variety of contraceptive options. Metabolic screening, including lipid levels, glucose level after fasting, and insulin resistance (HOMA-IR), assists clinicians in choosing the most appropriate contraceptive method for the patient. This may reduce the burden of long-term metabolic risks that arise from using hormonal contraception.

This study aims to assess the association between Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives and key metabolic markers, including lipid profile (total cholesterol, LDL, HDL, triglycerides, Apo-lipoprotein A1/B) and carbohydrate metabolism (fasting glucose, insulin resistance, HbA1c, and HOMA-IR), in women using these formulations. By evaluating changes in 'cholesterol, triglycerides, apolipoproteins, insulin levels, glucose tolerance, and HbA1c', this research seeks to provide a broad view of how different hormonal combinations in contraceptives influence metabolic health, helping to guide informed contraceptive choices for women.

METHODS

A cross-sectional study recruited 84 women aged 18–45 who had been using one of these contraceptives for at least six months at Sheikh Khalifa Bin Zayed Al Nahyan Hospital/ Azad Kashmir (AK) Combined Military Hospital (CMH) Rawalakot, from January 2023 to July 2023. The study focused on three commonly used contraceptive formulations: 1. Ethinylestradiol-Levonorgestrel, 2. Ethinylestradiol-Norgestimate, and 3. Progestin-Only. The ethical approval was obtained from the 'institutional review board (IRB)' of Sheikh Khalifa Bin Zayed Al Nahyan Hospital/ AK CMH Rawalakot (375-A/SKBZ/CMH/RKT) before the start of the study. The sample size analysis was conducted with a significance level of 0.05 and a power of 80% to detect significant differences among groups. Based on estimated effect sizes from previous studies [6], a

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minimum sample size of 80 participants was required. To account for potential data inconsistencies and dropouts, a total of 84 participants were recruited. While purposive sampling ensured the inclusion of participants actively using the contraceptive formulations under study. The study population may not fully represent different age groups, ethnicities, or metabolic backgrounds. 'Participants were fully informed of the study's purpose, procedures, risks, and benefits'. Written informed consent was obtained from each participant, and they were assured of confidentiality and their right to withdraw from the study at any time without any negative consequences. The inclusion criteria were age: 18 to 45 years, Consistent use of Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, or Progestin-Only for at least six months, Willingness to complete a 12-hour fasting period before sample collection and agreement to participate, indicated by providing written informed consent after a full explanation of study details. The exclusion criteria history of diabetes, polycystic ovary syndrome (PCOS), any lipid disorder, known cardiovascular conditions that could independently affect lipid or carbohydrate metabolism, Recent use of medications impacting metabolic profiles, antidiabetic drugs, lipid-lowering agents, or corticosteroids, Current pregnancy or breastfeeding and switches in contraceptive type or formulation within the past six months, to maintain stable exposure. Additionally, potential confounders such as diet, physical activity, and family history were not explicitly controlled, participants with a history of metabolic syndrome or recent major dietary interventions (extreme diets, weight loss programs) were excluded to reduce variability. Data Collection and Biochemical Assessment, data were gathered through structured interviews and clinical assessments, focusing on demographic and health information relevant to the study's aims. Upon enrolment, participants were interviewed to collect baseline 'demographic data, including age, body mass index (BMI)', duration of contraceptive use, systolic and diastolic blood pressure, and waist-to-hip ratio. BMI was calculated from measured height and weight, and waist-to-hip ratio was determined to assess body fat distribution. Blood pressure measurements were conducted using an Omron HEM-7121 which has been calibrated. To enhance reliability, every reading was documented two times and a mean was taken. To mitigate bias from self-reported contraceptive use, participants were asked to provide medical records or prescriptions detailing the contraceptive type and duration of use. Self-reported data were checked against other structured interviews. Only women on the same contraceptive formulation for at least six months were included, assuring they had the same hormonal context and less variability. To assess the biochemical parameters of lipid and carbohydrate metabolism, blood samples were obtained from participants after an overnight fasting 12 hours. This was performed to ensure accurate ground-level metabolic measures are taken without the inflating impact of food intake. Samples were taken by qualified phlebotomists through venepuncture to maintain the quality of the samples. The samples, post-collection, were separated into plasma and serum, the samples were then stored under strictly controlled temperatures until they were analyzed for any deviations. For the analysis of lipid profiles, a Roche Cobas 6000 Analyzer equipped with enzymatic colourimetric assays was used to determine total cholesterol, LDL, HDL, and triglycerides. These methods ensured precise quantification due to the enzyme reactions that are unique to each lipid parameter. An immune-turbidimetric assay on the Roche Cobas 6000 was used to measure Apolipoprotein A1 and Apolipoprotein B by utilizing antibodies to measure the concentration of each Apo-lipoprotein in serum. These measurements help analyse the profile of cardiovascular risks associated with various contraceptive formulations, which is the reason these specific lipid measurements were significant.

The carbohydrate metabolism assessment, including 'fasting blood glucose, HbA1c, fasting insulin, HOMA-IR, and OGTT' results, were also analysed. 'Fasting blood glucose was measured with the glucose oxidase method on the Roche Cobas 6000', known for precise glucose quantification in serum. HbA1c levels, reflecting average blood glucose over the past 3 months, were analysed using high-performance liquid chromatography (HPLC) on the Tosoh G8 HPLC Analyser. The levels of fasting insulin were measured using an immunoassay on the (Abbott Architect i2000SR) analyser, antibodies identify insulin concentrations, providing insights into pancreatic function and insulin sensitivity. HOMA-IR was measured based on fasting insulin and glucose values, offering an estimate of insulin resistance, an important factor in evaluating the metabolic effects of the contraceptives. Additionally, participants underwent an Oral Glucose Tolerance Test (OGTT), where they consumed a standard glucose solution followed by blood glucose measurements at intervals using the Roche Cobas 6000. OGTT results highlight glucose handling over time, allowing assessment of glucose tolerance potentially influenced by the contraceptive formulations. Statistical analysis was performed with SPSS version 22.0, to examine the effects of different oral contraceptive formulations on metabolic and demographic variables, data were initially assessed for normality using the Shapiro-Wilk test. Potential confounding factors, diet, physical activity, and genetic predisposition to metabolic disorders, were not explicitly

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controlled in this study. However, to minimize bias, participants with pre-existing metabolic disorders and recent medication use affecting lipid and carbohydrate metabolism were excluded. While this approach reduced some variability, future studies should incorporate more detailed assessments of lifestyle factors to refine these associations Variables that were normally distributed (p>0.05) were summarized using mean and standard deviation, while non-normally distributed data were summarized with median and interquartile ranges (IQR). For demographic variables, normally distributed variables (Age, BMI, Duration of Contraceptive Use, Systolic Blood Pressure, Diastolic Blood Pressure, Waist-to-Hip Ratio) were compared across the three contraceptive groups (Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only) using One-Way ANOVA. In analysing lipid metabolism variables, One-Way ANOVA was used for between-group comparisons, followed by Tukey's post-hoc test when significant differences were detected. For carbohydrate metabolism variables, normally distributed data were analyzed using One-Way ANOVA with Tukey's post-hoc test for pairwise comparisons. Non-normally distributed data (e.g., Fasting Blood Glucose and HbA1c) were evaluated with the non-parametric Kruskal-Wallis test to identify 'any significant differences between groups'. 'All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant'.

RESULTS

The normality of each variable was assessed using the Shapiro-Wilk test. Variables with p-values greater than 0.05 in all groups were considered normally distributed and analyzed with parametric tests (One-Way ANOVA). These normally distributed variables included Age, BMI, Duration of Contraceptive Use, Systolic Blood Pressure, Diastolic Blood Pressure, Waist-to-Hip Ratio, Total Cholesterol, LDL, HDL, Triglycerides, Apo-lipoprotein A1, Apo-lipoprotein B, Fasting Insulin, HOMA-IR, and OGTT Result. For these variables, group comparisons were conducted using One-Way ANOVA. Moreover, Fasting Blood Glucose and HbA1c had p-values below 0.05 in at least one group, indicating non-normal distribution. As a result, these variables were analyzed using the non-parametric Kruskal-Wallis test. The One-Way ANOVA test revealed significant differences in BMI (p=0.05), Duration of Contraceptive Use (p=0.001), Systolic Blood Pressure (p=0.03), and Waist-to-Hip Ratio (p=0.003) across contraceptive groups. Specifically, Ethinylestradiol-Norgestimate users had a longer duration of contraceptive use compared to other groups, and Ethinylestradiol-Levonorgestrel users exhibited a higher waist-to-hip ratio. No significant differences were observed in age or diastolic blood pressure between groups. Demographic variables are shown in Table 1.

Table 1: Demographic Variables between Groups

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	p-value
Age (Years)	31.65 ± 4.3	31.60 ± 5.9	31.17 ± 6.1	0.92
BMI (kg/m^2)	26.67 ± 2.95	24.42 ± 4.27	25.98 ± 3.88	0.05
Duration of Contraceptive Use (months)	22.77 ± 6.90	29.58 ± 9.40	16.67 ± 5.98	0.001
Systolic Blood Pressure (mmHg)	119 ± 8.7	113 ± 11.7	117 ± 9.3	0.03
Diastolic Blood Pressure (mmHg)	119.95 ± 6.20	77.7 ± 8.66	78.31 ± 6.47	0.27
Waist-to-Hip Ratio	0.850 ± 0.47	0.816 ± 0.43	0.834 ± 0.24	0.003

In lipid metabolism variables, One-Way ANOVA indicated significant group differences for Total Cholesterol (p=0.004) and Apo-lipoprotein A1 (p=0.007). Tukey's post-hoc test showed that Total Cholesterol levels were significantly higher in the Ethinylestradiol-Levonorgestrel group compared to Ethinylestradiol-Norgestimate (p=0.002), and Apolipoprotein A1 was higher in Ethinylestradiol-Norgestimate compared to Progestin-Only (p=0.005). No significant differences were found in LDL, HDL, Triglycerides, or Apolipoprotein B. Lipid Metabolism Variables are shown in Table 2.

Table 2: Lipid Metabolism Variables between Group

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	ANOVA p-value	Significant Group Differences
Total Cholesterol (mg/dL)	31.65 ± 4.3	31.60 ± 5.9	193.10 ± 25.94	0.92	Ethinylestradiol-Levonorgestrel vs. Ethinylestradiol-Norgestimate (p=0.002)

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LDL (mg/dL)	118.75 ± 23.81	114.70 ± 17.62	111.82 ± 21.20	0.403	None
HDL (mg/dL)	50.60 ± 10.85	53.88 ± 8.03	54.26 ± 8.38	0.207	None
Triglycerides (mg/dL)	157.48 ± 33.79	142.00 ± 23.09	147.17 ± 41.92	0.174	None
'Apo-lipoprotein A1 (g/L)'	1.38 ± 0.18	1.46 ± 0.23	1.31 ± 0.15	0.007	Ethinylestradiol-Norgestimate vs. Progestin-Only (p=0.005)
'Apo-lipoprotein B (g/L)'	0.98 ± 0.17	0.97 ± 0.09	0.91 ± 0.14	0.109	None

For normally distributed carbohydrate metabolism variables, One-Way ANOVA revealed a significant difference in HOMA-IR (p=0.004). Tukey's post-hoc analysis showed that HOMA-IR levels were higher in both Ethinylestradiol-Levonorgestrel and Progestin-Only groups compared to Ethinylestradiol-Norgestimate (p value 0.019 and p value 0.006, accordingly). Fasting Insulin and OGTT Results showed no significant differences across groups (p value=0.378 and p value 0.247, respectively). For the non-normally distributed variables, Fasting Blood Glucose (p=0.566) and HbA1c (p=0.086), the Kruskal-Wallis test indicated no statistically significant differences among groups. Carbohydrate metabolism variables are shown in Table 3.

Table 3: Carbohydrate Metabolism Variables between Groups

Variables	Ethinylestradiol-Levonorgestrel (Mean ± SD)	Ethinylestradiol-Norgestimate (Mean ± SD)	Progestin-Only (Mean ± SD)	ANOVA p-value	Significant Group Differences
Fasting Insulin (µIU/mL)	14.73 ± 4.58	14.25 ± 6.83	16.00 ± 4.02	0.378	None
HOMA-IR	3.14 ± 1.08	2.50 ± 0.95	3.23 ± 0.78	0.004	Ethinylestradiol-Levonorgestrel vs. Ethinylestradiol-Norgestimate (p=0.002)
OGTT Result (mg/dL)	135.58 ± 26.95	132.80 ± 18.11	141.63 ± 19.88	0.247	None
Fasting Blood Glucose (mg/dL)	87.29 [IQR 84.36–95.64]	90.05 [IQR 81.59–98.93]	90.06 [IQR 86.40–96.85]	0.566	None
HbA1c (%)	5.46 [IQR 5.26–5.83]	5.46 [IQR 5.08–5.65]	5.66 [IQR 5.25–5.88]	0.08	None

DISCUSSION

This study examined the metabolic effects of different oral contraceptive formulations on lipid and carbohydrate markers in women, specifically comparing Ethinylestradiol-Levonorgestrel, Ethinylestradiol-Norgestimate, and Progestin-Only contraceptives. Our findings reveal differences in lipid profiles and insulin resistance indicators among these formulations, offering insights into how various hormonal compositions can impact metabolic health, potentially influencing cardiovascular and metabolic risk factors. In lipid metabolism, significant differences were found in total cholesterol and Apo-lipoprotein A1 levels among the groups. The Ethinylestradiol-Levonorgestrel formulation showed a higher level of total cholesterol compared to the Ethinylestradiol-Norgestimate. This finding was consistent with prior research indicating that contraceptives containing levonorgestrel may increase lipid levels due to its relatively higher androgenic activity compared to other progestins, which can affect lipid synthesis and cholesterol levels [7, 8]. Such outcomes were consistent with other longitudinal studies that have shown an increase in total cholesterol levels with sustained use of Ethinylestradiol-Levonorgestrel contraceptive

Dragoman et al., a meta-analysis was conducted, and it was revealed that the sustained use of Levonorgestrel-containing Oral Contraceptives for over 12 months led to an increase in LDL cholesterol levels with a mean difference of 10.2 mg/dL (95% CI: 6.2-14.2) [9]. This indicates that prolonged use of Levonorgestrel may have multi-faceted detrimental consequences on the lipid profile, increasing the chances of cardiovascular risks in certain populations. In the future, more focus should be placed on long-term cohort studies to see if these metabolic changes level off, worsen, or improve over time. There are studies which argue that Levonorgestrel's androgenic activity could affect total cholesterol levels and cardiovascular health [10, 11]. But Ethinylestradiol-Norgestimate, which is known to be less androgenic, had lower cholesterol levels which makes influencing cardiovascular health more favourable to women who desire to maintain a healthy lipid profile. Levels of Apo-lipoprotein A1 were greater in the Ethinylestradiol-Norgestimate group than the Progestin-Only group, suggesting a possible cardio-protective effect of this formulation. Apo-lipoprotein A1 is an HDL molecule involved in the cardiovascular protective processes. The increase of Apo-lipoprotein A1 in the Ethinylestradiol-

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Norgestimate group is consistent with data that show non-androgenic contraceptives tend to have a better influence on HDL and chances of Apo-lipoproteins [12]. On the other hand, Progestin-Only formulations have much less favourable effects on lipid markers because there is no estrogen which is important in preserving HDL [13]. The variability in lipid metabolism observed among Progestin-Only contraceptive users may be influenced by individual genetic factors and baseline health conditions. Polymorphisms associated with lipid metabolism, such as perilipin 1 (PLIN1) and lipoprotein lipase (LPL), have been found to affect body composition and lipid profiles. Andrade-Mayorga *et al.*, reported that some polymorphisms of the PLIN1 gene were associated with greater decreases in fat mass after 12 weeks of the intervention, indicating that certain genes did predispose one to factors affecting lipid metabolism [14]. Further, baseline health conditions such as insulin resistance, obesity, and pre-existing dyslipidemia may also help explain the observed inter-individual differences. Our study did not analyse these genetic and metabolic factors, highlighting the necessity for future studies to include genetic testing along with detailed health assessments to understand the altered responses to Progestin-Only contraceptive pills. When analysing carbohydrate metabolism, "there was a marked difference in HOMA-IR between the groups, whereby the Ethinylestradiol-Levonorgestrel and Progestin-Only formulations had higher HOMA-IR compared with Ethinylestradiol-Norgestimate." This aligns with previous research showing that certain contraceptives, particularly those with more androgenic progestins, can reduce insulin sensitivity, increasing the risk of insulin resistance over time [15]. Studies have shown that androgenic progestins, levonorgestrel can exacerbate insulin resistance in some women, which may contribute to metabolic risks, particularly with long-term use [16, 17]. In contrast, Ethinylestradiol-Norgestimate, which has a milder androgenic profile, may be less likely to disrupt glucose and insulin regulation, thus presenting a more favourable option in terms of glycemic control [18]. Fasting blood glucose and HbA1c did not show statistically significant differences among groups, suggesting that short- to medium-term use of these contraceptives may not significantly impact overall glycemic control in healthy women without pre-existing metabolic disorders. Although our study did not find significant differences in fasting blood glucose and HbA1c among the contraceptive groups, it is important to consider that specific subgroups, such as women with a family history of diabetes or metabolic syndrome, may exhibit different metabolic responses. Maria-Elina *et al.*, found that former long-term use of combined hormonal contraceptives was associated with an increased risk of prediabetes in perimenopausal women [19].This suggests that individuals with a predisposition to glucose metabolism disorders might experience more pronounced effects when using certain hormonal contraceptives. Future studies should consider stratifying participants based on metabolic risk factors to better understand these individualized responses 'However, it is worth noting that other studies have shown mixed results regarding the effect of hormonal contraceptives on glucose metabolism', with some findings indicating a potential increase in fasting glucose and HbA1c with prolonged use, particularly in formulations containing higher estrogen doses [20, 21]. Present results support the hypothesis that these formulations, especially when used at lower doses and for limited periods, may not have substantial adverse effects on glucose levels in otherwise healthy women.Nevertheless, 'further research is needed to clarify the long-term impact of these contraceptive types on glucose metabolism'. In conclusion, this study highlights that different oral contraceptive formulations may have distinct effects on lipid and carbohydrate metabolism, with Ethinylestradiol-Norgestimate appearing to offer a more favourable metabolic profile in terms of cholesterol, Apo lipoprotein A1, and insulin sensitivity. These findings indicate hormonal contraceptive choices might be customised to align with individual metabolic profiles, especially for women who prioritise women with metabolic and cardiovascular health concerns.

CONCLUSIONS

It was concluded that this study highlights the diverse metabolic impacts of different oral contraceptive formulations. Ethinylestradiol-Norgestimate demonstrated the most favourable effects on cholesterol and insulin sensitivity, whereas Ethinylestradiol-Levonorgestrel and Progestin-Only formulations exhibited varying influences on lipid markers. These findings underscore the importance of personalised contraceptive choices based on metabolic risk assessments. Long-term studies are needed to evaluate the sustained metabolic effects over extended durations, particularly in women with pre-existing cardiovascular or metabolic risks. Implementing metabolic screening tools in clinical practice could enhance safer contraceptive prescribing and improve long-term metabolic health outcomes.

Authors Contribution

Conceptualization: SMH
Methodology: SMH, SMSAB, JZ
Formal analysis: SN, NF
Writing review and editing: SAK, SN, JZ

All authors have read and agreed to the published version of the manuscript

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Conflicts of Interest

All the authors declare no conflict of interest.

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Analysis of Hematological and Biochemical Parameters in Rheumatoid Arthritis Patients from Faisalabad, Punjab

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ABSTRACT

Rheumatoid Arthritis (RA) is a long-term autoimmune disease that causes inflammation and joint degeneration. It can lead to significant impairment and a loss in quality of life for millions of people worldwide. When diagnosing and treating RA, hematological and biochemical indicators are frequently assessed. These data are essential for monitoring the disease's progression, identifying organ involvement, and making treatment decisions. **Objectives:** To come up with some significant differences in hematological and biochemical indicators between patients with RA and healthy controls for the diagnosis of RA. **Methods:** Three hundred blood samples were taken in total from the population of Faisalabad City; 150 blood samples were drawn from people who have been confirmed diagnosed with RA, and 150 blood samples were collected from healthy people without any disease. The significant levels between the two groups were ascertained by calculating descriptive statistics and statistical comparisons using independent t-tests for continuous variables. **Results:** Among assessed parameters, erythrocyte sedimentation rate (ESR) and white blood cells (WBCs) were hematological parameters found to be highly elevated in RA patients, whereas hemoglobin (Hb) and alkaline phosphatase (ALP) are biochemical parameters that have been demonstrated significantly low in RA patients as compared to healthy. **Conclusions:** Deferentially expressed parameters ESR, WBCs, Hb, and ALP can be used for the diagnosis of RA.

INTRODUCTION

Rheumatoid Arthritis (RA) is a systemic autoimmune disease that damages joint and is characterized by a persistent, symmetrical inflammation of the afflicted joints, which leads to osteoporosis and other impairments. Even though just a small number of joints are impacted at first, extra-articular symptoms are frequently seen as more joints become affected [1, 2]. Joint cartilage and bone are both severely damaged by RA, resulting in severe synovitis [3]. RA is classified as non-inflammatory joint (osteoarthritis) and inflammatory due to crystal formation (pseudogout and the basic calcium phosphate disease, Gout), or by bacteria or viruses (Staphylococcus aureus Neisseria Gonorrhea, Parvovirus and Enterovirus), or due to auto-immune processes. It can also cause damage to other organs, such as the kidney, heart and lungs, the eye, the digestive system, the nervous system, and skin [4]. Rheumatoid factor and antibodies against post-translational modified proteins such as citrullination (ACPA) and carbamylation (anti-CarP antibodies) are among the autoantibodies that are indicative of the condition. Immune cells may be drawn to the joint as a result of these autoantibodies forming immune complexes. Patients with RA can be classified as either autoantibody-positive or autoantibody-negative based on the presence of these autoantibodies [5]. The effects of RA include significant morbidity, a rise in mortality, and annual

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expenses in the billions [6]. Women are more likely than males in the same age group to get RA, and the condition's incidence increases with age [7]. The systemic character of RA leads to a significantly shorter life expectancy than the general population, worse quality of life, and decreased social and occupational functioning [8]. Between 0.1% to 2.0% of persons globally are thought to have RA. Self-reported data from the National Health Survey (NHS) for the years 2014–2015 indicates that, in terms of RA prevalence (2%), Australia has the largest population worldwide [9]. Pakistani patients are 44 years old on average [10]. Globally, the prevalence of RA varies, with industrialized nations typically having a greater prevalence. This can be attributed to a variety of variables, including genetics, demographic differences, and underreporting in other regions of the world, as well as exposure to environmental risk factors [2]. There are no established diagnostic criteria for RA. To be diagnosed with RA, a patient must have at least one clinically swollen joint and receive at least six out of ten points on an evaluation test [11]. The primary diagnostic tools are the findings from imaging and blood testing. The rheumatoid factor test is one of the many blood tests used to identify RA [12].

The aim aimed to potential biomarkers associated with RA, so the CBC and biochemical chemistry of RA patients were compared to those of a control group in this study.

METHODS

This study was a prospective, cross-sectional study. The formula for comparing two independent means was used to get the study's sample size, taking into account important statistical factors, such as research power (0.84 for 80% power) and the standard normal variate for the significance level (1.96 for a 95% confidence interval). It was calculated that in order to guarantee sufficient statistical power, each group needed at least 150 participants. As a result, the study involved 300 people in total—150 RA sufferers and 150 healthy controls. The Safi Teaching Hospital of Riphah International University in Faisalabad, Pakistan, analyzed the samples from April to August 2023. The hematological and biochemical parameters were compared. Simple random sampling technique was used to enroll the participants. Rheumatoid arthritis patients and healthy controls from the Faisalabad area made up the study population. The American College of Rheumatology's diagnostic and clinical standards were met by the patients. Rheumatoid arthritis and other inflammatory or autoimmune disorders were not present in the participants in the healthy control group, nor had they ever been. Those who had recently undergone major surgery or blood transfusions were nursing or pregnant, had a history of medication use, or had co-occurring medical disorders were among the exclusion criteria. Written, informed consent was taken by each participant. The research protocol was approved by the Research Ethical Committee, Riphah International University, Faisalabad, Pakistan. Reference No. Res/RcRAHS/23/126 to ensure adherence to accepted ethical guidelines. Together with the complete blood count (CBC), the following parameters were measured: erythrocyte sedimentation rate (ESR), rheumatoid factor (RA factor), and c-reactive protein (CRP). In addition, aspartate transaminase (AST), alanine transaminase (ALT), blood urea, creatinine, total bilirubin, direct bilirubin, indirect bilirubin, alkaline phosphatase (ALP), gamma GT (gGT), and anti-CCP tests were performed to assess organ function. Red vacutainers without anticoagulants were used to collect serum samples from fasting subjects while EDTA-containing vacutainers were used for CBC samples. The equipment underwent quality control testing and was calibrated following the manufacturer's instructions. For serum collection For the collection of serum The blood was collected in a sterile test tube, and the serum was separated by centrifuging 5 ml of each sample for 5 minutes at 3500 rpm. Tests were carried out 24 hours after the collection. A hematology analyzer was used to perform a CBC to evaluate several parameters, such as the RBC, WBC, platelet, Hb level, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), and DLC. SLECTRA MINI and ROCHE COBAS c 311, were used to measure the levels of RA factor and CRP in plasma or serum. Enzyme-linked immunosorbent assay (ELISA) was utilized to identify the existence of antibodies directed against CCP in blood samples. SPSS version 23.0 was used to analyze the data. For every variable, descriptive statistics (mean ± standard deviation) were computed. The means of the RA group and the healthy control group were compared using the independent t-test. Relationships between independent predictors (such as hemoglobin, WBC count, and ESR) and dependent variables (such as CRP and anti-CCP) were investigated using regression analysis. Boxplots were used to depict only statistically significant parameters for better interpretability, and all statistical tests were set at a significance level of $p<0.05$.

RESULTS

The mean ± SD of each parameter for both groups and the p-value. Only the statistically significant parameters are shown in boxplot graphs. The Hb level is 13.2 ± 0.86 g/dL in healthy individuals but is significantly lower in patients (12.10 ± 1.16 g/dL) due to a statistically significant difference ($p=0.000$). The red blood cell count in healthy individuals is 4.22 ± 0.40 million/µL, whereas in patients, it is somewhat higher at 4.43 ± 0.33. The statistically significant difference in RBC counts between the two groups ($p=0.000$) suggests a potential alteration in RBC turnover or patient generation.

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In healthy persons, the mean WBC count is 7860.93 ± 1486.73/µL, while in patients, it is 8595.86 ± 2592.07/µL. The variation in WBC counts is statistically significant (p=0.003), indicating a sickness or immune response. With a p-value of less than 0.0001, it was discovered that there was a significant difference in the mean number of eosinophils between the two groups: 3.49 ± 1.98 in the RA patients and 2.61 ± 1.99 in the control group. The mean platelet count in patients is somewhat lower, at 247086.66 ± 74730.74/µL with a p-value of 0.055, than the platelet counts in healthy individuals, which is 264646.66 ± 82754.51/µL. The ESR is considerably greater in patients at 39.66 ± 12.55 mm/hr than in healthy individuals at 12.30 ± 3.11 mm/hr. A significant difference between the two groups (p=0.000). Between healthy individuals and patients, there are no appreciable variations in the neutrophil, lymphocyte, monocyte, and basophil parameters (Table 1).

Table 1: Descriptive Statistics of Biochemical Parameters

Parameter	Healthy	Patients	p-value
Hb	13.2 ± 0.86	12.10 ± 1.16	0.000
RBCs	4.22 ± 0.40	4.43 ± 0.33	0.000
WBCs	7860.93 ± 1486.73	8595.86 ± 2592.07	0.003
Neutrophils	60.74 ± 8.49	60.41 ±10.52	0.767
Lymphocytes	29.18 ± 7.99	30.28 ± 9.79	0.287
Monocytes	6.46 ±1.52	6.20 ± 1.42	0.129
Eosinophils	3.49 ±1.98	2.61 ± 1.99	0.000
Basophils	0.29 ± 0.17	0.31 ± 0.19	0.625
Platelets	264646.66 ± 82754.51	247086.66 ± 74730.74	0.055
ESR	12.30 ± 3.11	39.66 ± 12.55	0.000

A descriptive statistical analysis of the biochemical parameters, p=0.139 shows that the difference in urea levels between patients (25.75 ± 6.79 mg/dL) and healthy people (26.93 ± 6.97 mg/dL) is not statistically significant. The mean creatinine levels of patients are significantly higher (0.73 ± 0.22 mg/dL) than those of healthy individuals (0.64 ± 0.19 mg/dL), with a p-value of 0.001, suggesting a potential kidney malfunction in the patient group. The p-value 0.000 indicates that patients' mean uric acid levels are significantly higher (6.57 ± 2.41 mg/dL) than those of healthy people (5.66 ± 0.92 mg/dL). The RA factor levels in patients were found to differ significantly from those in healthy individuals (8.01 ± 1.72 IU/ml) by 83.83 ± 166.92 IU/ml, with a highly significant p-value of 0.000. Patients' CRP levels are significantly higher than those of healthy individuals (7.21 ± 1.51 mg/L) at 22.33 ± 72.31 mg/L, with a p-value of 0.011, indicating higher inflammatory activity in the patient group. The mean uric acid levels of patients are significantly higher (6.57 ± 2.41 mg/dL) than those of healthy individuals (5.66 ± 0.92 mg/dL), as indicated by p=0.000. With a highly significant p-value of 0.000, it was discovered that the RA factor levels in patients differed significantly (8.01 ± 1.72 IU/ml) from those in healthy individuals by 83.83 ± 166.92 IU/ml. With a p-value of 0.011, the CRP levels of patients are significantly higher at 22.33 ± 72.31 mg/L than those of healthy individuals (7.21 ± 1.51 mg/L), suggesting higher inflammatory activity in the patient group. The mean ALP (90.39 ± 37.56 IU/L) and gGT (40.66 ± 26.21 IU/L) of the patients are significantly different from the healthy individuals' (ALT: 57.73 ± 87.52 IU/L; gGT: 33.36 ± 24.31 IU/L) values (p-values of 0.000 and 0.013, respectively). However, there are no significant differences between the ALT (p=0.896) and AST (p=0.658) values of the two groups. Patients with rheumatoid arthritis exhibit a substantial relationship with their mean Anti-CCP level of 221.60 ± 143.24 U/ml, which is significantly higher than that of healthy individuals. The relationship is highly significant, with a p-value of 0.000 (Table 2).

Table 2: Descriptive Statistics of Biochemical Parameters

Parameter	Healthy	Patients	p-value
Urea	26.93 ± 6.97	25.75 ± 6.79	0.139
Creatinine	0.64 ± 0.19	0.73 ± 0.22	0.001
Uric Acid	5.66 ± 0.92	6.57 ± 2.41	0.000
RA Factor	8.01 ± 1.72	83.83 ± 166.92	0.000
CRP	7.21 ±1.51	22.33 ± 72.31	0.011
Total Bilirubin	0.39 ± 0.13	0.46 ± 0.51	0.069
Direct Bilirubin	0.34 ± 0.57	0.22 ± 0.40	0.032
Indirect Bilirubin	0.30 ± 0.19	0.26 ± 0.17	0.100
ALT	57.73 ± 87.52	58.88 ± 63.68	0.896
ALP	125.96 ± 56.84	90.39 ± 37.56	0.000
gGT	33.36 ± 24.31	40.66 ± 26.21	0.013
AST	35.69 ± 30.84	34.31 ± 22.65	0.658
Anti-CCP	7.63 ± 1.46	221.60 ± 143.24	0.000

The relationships between hematological and biochemical variables and specific RA-specific biomarkers like anti-CCP, CRP, uric acid, and RA factor was also conducted. There is a statistically significant positive association based on regression coefficients between uric acid levels and ESR based on the p-value of 0.012 and the coefficient of 0.023. The association between urea levels and uric acid is statistically significant, as indicated by the regression coefficient of 0.081 and p-value of 0.000. Lower hemoglobin levels and higher levels of RA Factor are associated, as indicated by the p-value of 0.034 and regression coefficient of -15.146. Additionally, platelets showed a significant positive association with increased levels of RA Factor and decreased platelet counts, with a p-value of 0.022 and a regression coefficient of 0.000. ESR also showed a significant positive association, with a regression coefficient of 1.987 and a p-value of 0.001. WBCs demonstrated a positive association with a p-value of 0.001 and a regression coefficient of 0.005, suggesting a relationship between elevated WBC counts and elevated CRP levels. Notably, a substantial negative association with a p-value of 0.000 and a coefficient of -30.916 was discovered between anti-CCP levels and Hb. This implies a relationship between elevated anti-CCP levels and

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decreased Hb levels. Furthermore, a noteworthy positive association with a p-value of 0.002 was observed between the WBC and anti-CCP levels. The regression coefficient of this connection was 0.011. This implies an association between elevated WBC counts and elevated anti-CCP levels. With a regression coefficient of 4.649 and a p-value of 0.000, ESR also showed a significant positive link, suggesting a potential association between elevated ESR levels and elevated anti-CCP levels. Additionally, a statistically significant negative association between the levels of anti-CCP and urea was discovered, with a regression coefficient of -2.815 and a p-value of 0.015. This suggests a connection between reduced urea levels and elevated anti-CCP levels. ALP's regression coefficient is -0.323. This means that Anti CCP should drop by 0.323 units for every unit increase in ALP. ALP and Anti-CCP levels may be inversely associated, based on the negative regression coefficient (Table 3).

Table 3: Regression Analysis Results

Dependent Variable	Independent Variable	Coefficient (B)	Standard Error	Significance
Uric Acid	ESR	0.023	0.009	0.012
Uric Acid	Urea	0.081	0.018	0.000
RA Factor	Hb	-15.146	7.113	0.034
RA Factor	Platelets	0.000	0.000	0.022
RA Factor	ESR	1.987	0.607	0.001
CRP	WBCs	0.005	0.002	0.001
Anti-CCP	HB	-30.916	6.339	0.000
Anti-CCP	WBCs	0.011	0.003	0.002
Anti-CCP	ESR	4.649	0.497	0.000
Anti-CCP	Urea	-2.815	1.155	0.015
Anti-CCP	ALP	-0.323	0.147	0.028

DISCUSSION

It is thought that the most significant improvement index is early diagnosis. Yet early diagnosis is still challenging since it relies entirely on clinical data from the patient's health record, physical examination, and blood and imaging examinations [13]. Many autoimmune rheumatic diseases can present as hematologic disorders, such as anemia, coagulopathy, WBC and platelet abnormalities, and hematologic malignancies [14]. This study indicated the systemic characteristics of Rheumatoid and its effect on hematopoiesis by identifying substantial variations in several hematological markers between RA patients and healthy controls. Anemia, a common consequence linked with chronic inflammatory disorders like RA, was seen in RA patients' significantly lower HB levels; similarly, low levels have previously been observed in previous investigations [15, 16]. RA patients showed a considerably higher mean RBC, which was unexpected. According to reports, inflammatory cytokines may inhibit RBC maturation [17]. Consequently, we propose that aberrant red cell indices could be the reason for low HB even in cases where the RBC count is larger. It is essential to carry out additional studies into the underlying mechanisms triggering RBC changes in RA. The WBC counts of RA patients were considerably higher, suggesting increased immune-mediated activity or a possible infection [18]. Moreover, leukocytes might be drawn to inflammatory synovial tissues as a result of systemic inflammation in RA, which would further raise WBC levels [19]. The systemic inflammatory burden associated with RA is further emphasized by the noticeably higher ESR levels seen in these patients [20]. ESR is a non-specific inflammatory marker that is influenced by red cell aggregation and plasma protein concentration. It assesses how quickly erythrocytes settle in an anticoagulated blood vertical column [21]. Elevated ESR levels in RA are indicative of increased production of acute phase reactants in response to cytokine-mediated inflammation [21]. Elevated ESR readings in RA patients correlate with disease activity, making them a helpful tool for monitoring treatment response and disease progression [22]. Patients with RA had lower platelet counts, however not to a statistically significant degree. All these results point to a considerable difference between the hematological features of RA patients and healthy individuals. This is in line with the systemic inflammatory aspect of the illness and how blood cell counts are affected by it. Notably, RA patients had higher uric acid levels, which may indicate a metabolic disease [23]. Elevated amounts of uric acid can be caused by medication adverse effects or increased purine breakdown in patients with RA. Since raised uric acid levels are associated with an increased risk of gout, a common comorbidity in persons with RA, monitoring uric acid levels and treating hyperuricemia is essential to preventing complications from the condition. Serum uric acid elevation is more common in RA patients and may serve as an inflammatory marker for the degree of joint inflammation. Furthermore, there is mounting evidence that suggests larger steroid doses might result in hyperuricemia. Therefore, it is important to implement suitable preventative measures for these individuals [24]. The autoimmune origin of RA was confirmed by the significantly higher levels of RA factor in RA patients as compared to healthy controls. Most RA patients' serum contains RA factor, an autoantibody that targets the Fc region of immunoglobulin G (IgG) and is a crucial diagnostic sign for the condition. RA factor contributes to synovial inflammation, cartilage deterioration, and joint degeneration in RA by promoting immune complex formation and complement activation [25]. Patients with RA have elevated CRP values, which are indicative of both the disease activity and systemic inflammatory burden. Elevated CRP is correlated with extra-articular symptoms, joint destruction, and synovial inflammation in RA, making

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it a useful biomarker for monitoring disease activity and directing treatment approaches. In contrast to earlier research, increased bilirubin levels were also noted in RA patients [26, 27]. These findings indicate notable variations in several biochemical indicators, pointing to possible anomalies in renal function, inflammation, and autoimmune activity in individuals with RA.

CONCLUSIONS

Raised ESR, WBCs, and low HB were the patients' differential hematological markers; correlation studies also showed a relationship between these parameters and particular diagnostic tests. Biochemical tests revealed elevated creatinine and gGT, low direct bilirubin and ALP. Regression analysis revealed a link between ALP and anti-CCP as well. Thus, high WBCs, low HB, low ALP, and elevated ESR can all be utilized as indicators of rheumatoid arthritis. The study's overall findings emphasize how crucial thorough hematological and biochemical profiling is for comprehending the pathogenesis of RA and formulating effective clinical care plans. The study's shortcomings, including its cross-sectional methodology and comparatively small sample size, must be acknowledged. Future research will consider this strategy in the hopes of finding unique markers linked to every stage of RA. To sum up, the intricate relationship between hematological and biochemical indicators in RA highlights the disease's systemic character and diverse pathogenesis. To improve patient outcomes, advance our understanding of the disease, and improve diagnostic accuracy and treatment options, more study is needed into the complex interactions between hematological and biochemical parameters in RA.

Authors Contribution

Conceptualization: SKR
Methodology: RA, FMW, UBM, MA, AR
Formal analysis: RA, FMW, UBM, MA, AR
Writing review and editing: SKR
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Frequency of Subclinical Hypothyroidism (SCH) among Patients of Polycystic Ovarian Disease (PCOD) Presenting in Outpatient Department of Tertiary Care Hospital

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ABSTRACT

Subclinical hypothyroidism is a prevalent endocrine disorder, often associated with polycystic ovarian disease both of which share a complex interplay of hormonal imbalances, contributing to significant metabolic and reproductive disturbances. **Objectives:** To determine the frequency of subclinical hypothyroidism among patients of polycystic ovarian disease presenting in an outpatient setting. **Methods:** This descriptive cross-sectional study was conducted at the Obstetrics and Gynaecology Department of Fatima Memorial Hospital, Lahore, from December 2022 to June 2023. 155 female having polycystic ovaries were enrolled using non-probability consecutive sampling. Blood samples of the patients were sent to the pathology lab for measurement of serum thyroid-stimulating hormone (TSH) level and frequency of subclinical hypothyroidism (thyroid-stimulating hormone>5mIU/L despite normal serum free thyroxin (0.8 to 1.8 ng/dL) was noted. Data were entered and analyzed using SPSS version 26. **Results:** In the current study mean age and BMI of participants having polycystic ovarian disease were calculated as 28.31 ± 7.7 years and 29.5 ± 5.8 kg/m2, respectively. Among 155 participants 43.2% were married and most of them belonged to the urban population and middle socioeconomic class. Subclinical hypothyroidism was found in 14.8% of female suffering from polycystic ovarian disease. **Conclusions:** It was concluded that this study underscores the high prevalence of subclinical hypothyroidism among patients with polycystic ovarian disease, highlighting the need for routine thyroid function screening in this population. Early detection enables timely interventions and supports a comprehensive approach to managing polycystic ovarian disease and its related comorbidities.

INTRODUCTION

Polycystic ovarian disease is a common endocrine disorder; that affects 4-20% of women [1]. This syndrome is characterized by hyperandrogenism, oligo-amenorrhea and polycystic ovaries. Insulin resistance and hyperandrogenism are amongst the most common endocrine irregularities encountered in polycystic ovarian disease (PCOD) [2]. More than half of females with PCOD are associated with insulin resistance, hyperglycemia, weight gain, and metabolic syndrome [3]. Thyroid disorders are also commonly observed in patients with PCOD, with subclinical hypothyroidism (SCH); affecting 5% to 10%. SCH contributes to subfertility and unfavourable pregnancy outcomes [4, 5]. The relationship between subclinical hypothyroidism (SCH) and PCOD has been reported in the literature, but the mechanisms are still unclear [6, 7]. Thyroid hormones function as insulin agonists in muscles and as antagonists in the liver. Consequently, deficiency in thyroid hormone reduces glucose production and

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utilization. Some researchers have proposed that insulin resistance, a key factor in the pathogenesis of PCOD, might arise as a result of hypothyroidism [7]. Additionally, hypothyroidism may impair gonadal function, and contribute to anovulatory cycles [8]. While previous studies have reported the coexistence of SCH and PCOD, data on the exact frequency of SCH in PCOD patients remain inconsistent, and there is limited research focusing on its implications for metabolic and reproductive health.

This study aims to determine the frequency of SCH among PCOD patients to better define its burden in our local population. Identifying this prevalence could guide targeted screening and management strategies, ultimately improving reproductive and metabolic outcomes in affected individuals.

METHODS

This descriptive cross-sectional study was done at the Department of Obstetrics and Gynecology, Fatima Memorial Hospital, Lahore, from December 2022 to June 2023 after obtaining synopsis approval from CPSP (REU No: 47315). Using the single-proportion formula, sample size of 155 female was calculated using a 95% confidence level, 5% margin of error and taking an expected percentage of subclinical hypothyroidism as 11.3% in female presenting with PCOD [9]. Power of 80% was assumed to detect meaningful differences in SCH prevalence within the study population. Sample selection was using a non-probability, consecutive sampling technique. In this study, female aged 16-45 years, presenting with PCOD were included. PCOD was diagnosed based on Rotterdam Criteria (2003) criteria: 1. Ovulatory dysfunction, 2. Clinical (hirsutism oligo-menorrhoea/amenorrhea, infertility, acne and acanthosis nigricans) or biochemical signs of hyperanderogenism (normal or low follicle-stimulating hormone, elevated luteinizing hormone), 3. Polycystic ovaries on ultrasonography (follicle number per ovary ≥20, and/or ovarian volume ≥10 mL, ensuring no corpora luteal cysts or dominant follicles are present). Pregnant females, females already diagnosed with overt hypothyroidism or hyperthyroidism, renal disease (creatinine>1.2mg/dl) or liver disease (Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) >40IU, hepatitis B or C), Hypertension (HTN) (Blood Pressure (BP)≥140/90mmHg), diabetes mellitus (DM)(BSR>186mg/dl), hyperprolactinemia (prolactin >30ng/ml), females receiving hormonal therapy or steroids during last 6 months were excluded. Informed consent was obtained from all patients. Demographic data (name, age, marital status, BMI, duration of symptoms, area of residence, and socioeconomic status) was recorded. Then blood samples of all participants were taken using 5cc disposable syringe under aseptic measures and sent to the laboratory of the hospital for assessment of thyroid function test. Reports were assessed and subclinical hypothyroidism was labelled as positive if thyroid-stimulating hormone (TSH)>5mIU/L despite normal levels of serum-free thyroxin (0.8 to 1.8 ng/dL). Patients diagnosed with subclinical hypothyroidism were referred to an endocrinologist. The data were analyzed through SPSS version 26. Mean and standard deviation were calculated for age, duration of symptoms and BMI. Frequency and percentage were calculated for marital status, area of residence, socioeconomic status and subclinical hypothyroidism. Data were stratified for age, marital status, BMI, duration of symptoms, area of residence and socioeconomic status. Post-stratification, a chi-square test was applied and a p-value <0.05 was taken as significant.

RESULTS

The mean age, duration of symptoms and BMI of female was calculated as 28.31 ± 7.7 years, 11.26 ± 6.7 months and 29.5 ± 5.8 kg/m2, respectively. Out of 155 participants, 43.2% were married, 58% of female had an urban residence 28.5% of women belonged to the poor and 45.8% belonged to the middle socioeconomic class (Table 1).

Table 1: Patient-Related Demographic Characteristics

Parameters		n=155
Age (Mean ±S D) Years		28.31 ± 7.7 Years
Duration of Symptoms (Mean ± SD) Months		11.26 ± 6.7 Months
BMI (Mean ± SD) kg/m^2		29.5 ± 5.8 kg/m^2
Marital Status n (%)	Married	67 (43.2%)
	Unmarried	88 (56.8%)
Residence n (%)	Rural	65 (42%)
	Urban	90 (58%)
Socioeconomic Status n (%)	Low	44 (28.4%)
	Middle	71 (45.8%)
	High	40 (25.8%)

The pie chart shows that the frequency of subclinical hypothyroidism was noted as 14.8% among female suffering from PCOD (Figure 1).

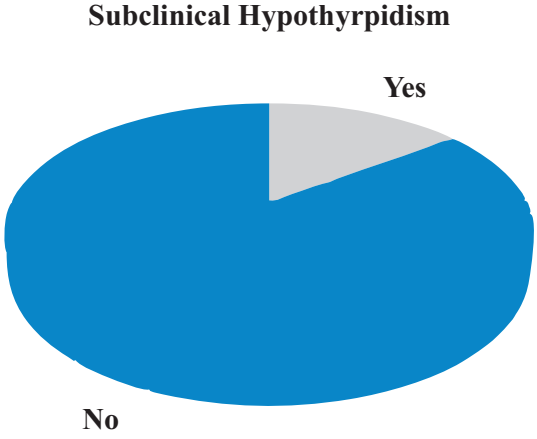

Figure 1: Frequency of Subclinical Hypothyroidism

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Patient data were stratified to analyse the association between SCH and various patient characteristics. A statistically significant association was observed between BMI and SCH ($p<0.001$), indicating a higher prevalence of SCH in patients with BMI <30 compared to those with BMI >30. Other factors, including age, marital status, duration of PCOD, residence, and socioeconomic status, were not significantly associated with SCH ($p>0.05$) (Table 2).

Table 2: Subclinical Hypothyroidism About Patient's Characteristic

Parameter		Subclinical Hypothyroidism		p-value
		Yes	No	
Age	16-30 Years	16 (16.2%)	83 (83.8%)	0.538
	31-45 Years	7 (12.5%)	49 (87.5%)	
Marital Status	Married	8 (11.9%)	59 (88.1%)	0.376
	Unmarried	15 (17%)	73 (83%)	
BMI	<30	21 (25.3%)	62 (74.5%)	<0.001
	>30	2 (2.8%)	70 (97.2%)	
Duration of PCOD	<6 Month	10 (16.9%)	49 (83.1%)	0.562
	>6 Months	13 (13.5%)	83 (86.5%)	
Residence	Rural	9 (17.3%)	43 (82.7%)	0.407
	Urban	11 (13.9%)	68 (86.1%)	
Socioeconomic Status	Poor	4 (91.%)	40 (90.9%)	0.264
	Middle	14 (19.7%)	57 (80.3%)	
	High	5 (12.5%)	35 (87.5%)	

DISCUSSION

In the current study, subclinical hypothyroidism was found in 14.8% of female having PCOD [10]. Comparable results were obtained in a similar study conducted recently in Pakistan by Abdullah *et al.*, in which among 136 patients studied, 19.1% were found to have SCH [11]. Another locally conducted study by Fatima *et al.*, found similar results [12]. In contrast, a study by Raj *et al.*, found a higher frequency of SCH 43.5% among women diagnosed with PCOD vs 20.5% among those without PCOD [13]. However, Rojhani *et al.*, suggest that its prevalence was similar between PCOD patients and controls [14]. Furthermore, previous studies investigating this association have yielded mixed results [15]. While most clinical studies have reported a higher prevalence of SCH in women with PCOS. Zhang *et al.*, in a study, found that SCH does not increase the risk of PCOD after adjusting for confounding factors [16]. A meta-analysis by Ding *et al.*, revealed a significant combined odds ratio of 3.59 for SCH risk in PCOD patients compared to controls, with the TSH cutoff value taken being ≥4 mIU/L [15]. Hypothyroidism is commonly observed in PCOD patients, suggesting a significant correlation and risk of thyroid disorders in this vulnerable population [17, 18]. Furthermore, it was collectively suggested a higher prevalence of metabolic syndrome among SCH patients, indicating that it may exacerbate lipid and glucose-related metabolic disturbances in females with PCOD [19]. Early identification and management of SCH through comprehensive thyroid profiling can play a crucial role in mitigating the metabolic and reproductive complications associated with PCOD, thereby improving patient outcomes and overall quality of life [20]. This study suggests that lower TSH levels may also be clinically significant, particularly in women of reproductive age or those planning pregnancy. Future research should consider evaluating SCH using alternative TSH thresholds to provide a more comprehensive understanding of its role in PCOS.

CONCLUSIONS

It was concluded that this study underscores the high prevalence of subclinical hypothyroidism among patients with PCOD, highlighting the need for routine thyroid function screening in this population. Early detection enables timely interventions and supports a comprehensive approach to managing PCOD and its related comorbidities.

Authors Contribution

Conceptualization: IG, SG, SK
Methodology: AA
Formal analysis: SK
Writing review and editing: IG, SG, AA, AZ, NS, NA, SK
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Comparison of Single Port Laparoscopic Ingulinal Hernia Repair versus Open Herniotomy in Term of Recurrence and Postoperative Scrotal Hematoma

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ABSTRACT

Hernia repair is common surgical procedures, with techniques evolving to improve outcomes. Comparing laparoscopic and open approaches is crucial for determining the optimal method to reduce complications such as recurrence and postoperative scrotal hematoma. **Objective:** To compare the frequency of hematoma and recurrence in laparoscopic assisted inguinal hernian repair versus open herniotomy. **Methods:** This quasi experimental study was conducted after approval from CPSP (Ref No: CPSP/REU/PSG-2017-068-339, REU 37362) at Pediatric Surgery Department Services Hospital, Lahore, from October 2020 to March 2021 on 254 patients. Patients were divided into two equal groups; Group-A (single port needle assisted laparoscopic repair) and Group-B, (open repair). Patients were assessed after 24 hours to see scrotal hematoma and regular follow up for 3 months to see the recurrence. Data were analyzed using SPSS version 26.0. Independent sample t-test and chi square was applied to compare quantitative and qualitative variables between groups; p-value ≤0.05 as significant. **Results:** Postoperative hematoma formation was found among 2 patients (1.6%) of Group-A and in 13 patients (10.2%) of Group-B, (p=0.003). Postoperative recurrence between two groups was comparable and statistically insignificant (Group A 6.3% vs Group B 4.0%, p=0.393). (p=0.393). **Conclusions:** In conclusion, laparoscopic-assisted hernia repair and open herniotomy demonstrate comparable recurrence rates. However, laparoscopic-assisted repair is associated with a significantly lower incidence of postoperative hematoma. These findings indicate that laparoscopic repair may be a safer option with fewer postoperative complications, making it a favorable choice for pediatric inguinal hernia surgery.

INTRODUCTION

Inguinal Hernia (IH) is a common presentation to pediatric surgeons, with an incidence ranging from 0.8%-4.4% [1]. It is typically caused by incomplete closure of the processus vaginalis [2]. Given the risk of incarceration and potential complications, surgical intervention is recommended for all children diagnosed with inguinal hernia [3]. For IH, open herniotomy serves as the basic modality of care for children. This method is renowned for its ease of performance, high success rate, and low rate of complications [4, 5]. According to a survey conducted in 2014 on the management of IH, 83% of participants favored the open approach for treating pediatric inguinal hernia [6]. However, recently, laparoscopic hernia repair has become common practice in many centers. Laparoscopic herniorrhaphy was introduced by Montupet in 1993. Recent advancements in technology and surgical instruments have highlighted the advantages of laparoscopic herniorrhaphy, including reduced post-operative pain, shorter surgery duration, minimal tissue damage, easier identification of contralateral patent processus vaginalis,

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and improved cosmetic outcomes [7]. However, there are ongoing debates about whether laparoscopic herniorrhaphy is superior due to concerns over potentially higher recurrence rates and the risk of testicular vessel injury leading to atrophy [8, 9]. While open herniotomy remains the gold standard according to some authors, laparoscopic herniorrhaphy has been shown to be equally safe and offers additional benefits. These advantages suggest that pediatric surgeons should consider it as part of their routine practice, rather than limiting its use to selected cases. This conclusion is supported by an analysis conducted by Isabel Bada-Bosch et al [10]. Given the ongoing debate regarding the safety of various surgical approaches, previous data on the subject has been controversial.

Therefore, this study was being conducted with the objective of comparing the frequency of hematoma and recurrence between laparoscopic-assisted inguinal hernia repair and open herniotomy.

METHODS

This quasi experimental study was performed at Paediatric Surgery Department, Services Hospital Lahore from October 2020 to March 2021 after taking synopsis approval from CPSP (Ref No: CPSP/REU/PSG-2017-068-339, REU 37362). 254 patients (127 in each group) sample size was planned at 5% significance level, 80% power of test, and frequency of scrotal hematoma taken as after single port laparoscopic repair 1.5% and 8.2 % after open herniotomy [11]. Patients were enrolled using non-probability consecutive sampling. All male children with ipsilateral inguinal hernia (confirmed clinically i.e. reducible and cannot get above the swelling), aged between 3 months to 10 years were included. Patients with obstructed hernia, undescended testes, recurrent hernia (previously managed surgically) and hernia in syndromic patients were excluded. Before recruitment written informed consent was taken from parents/guardians. Pre-designed performa was used to collect data. Demographic information (name, age and weight) was recorded. Patients were divided in to two equal groups using lottery method; Group A and B. Patients in Group A have single port needle assisted laparoscopic repair and Group B patients had open repair. To minimize selection bias, allocation concealment was ensured by having independent individual conduct the lottery draw. All procedures were performed by same surgical team expert in relevant filed for minimum 5 years. Patients were assessed after 24 hours to see scrotal hematoma (collection of blood inside the scrotum on clinical examination and USG) and regular follow up for 3 months to see the recurrence (re-appearance of inguino-scrotal swelling within 3 months after surgery assesses clinically). To analyze data, SPSS version 26.0 was used. While frequency and percentage were used to summarize qualitative data, mean and standard deviation were computed for quantitative variables. Independent sample t-test and chi-square test were used for continuous and categorical data among groups, with a p-value ≤0.05 considered significant. Normality of continuous data was assessed before applying parametric tests, and if violated, an appropriate non-parametric test was used.

RESULTS

As shown in table 1, mean age of the patients calculated was 6.3 ± 2.99 and 6.6 ± 2.78 years in group A, and B, respectively. Mean weight calculated was 7.62 ± 3.23 kg and 8.21 ± 2.29 kg, respectively.

Table 1: Comparison of Demographic Characteristics (n=254)

Age (Year)	Group A Frequency (%)/(Mean ± SD)	Group B Frequency (%)/(Mean ± SD)	p-Value
1 to 5 Years	62 (48.8%)	55 (43.3%)	0.378
>5 to 10 Years	65 (51.2%)	72 (56.7%)	
Age	6.3 ± 2.99 Years	6.6 ± 2.78 Years	0.400
Weight	7.62 ± 3.23 kg	8.21 ± 2.29 kg	0.090

As showed in table 2, postoperative scrotal hematoma formation was found only in 2 patients (1.6%) of Group A 95% CI: 0% to 3.74% versus 13 patients (10.2%) of Group B 95% CI: 4.96% to 15.51%, (p=0.003).

Table 2: Comparison of Postoperative Hematoma Formation (n=254)

Postoperative Hematoma Formation	Group A Frequency (%)	Group B Frequency (%)	p-Value
Yes	2 (1.6%)	13 (10.2%)	0.003
No	125 (98.4%)	114 (89.8%)	

Postoperative recurrence between two groups was comparable and statistically insignificant Group A 6.3% (95% CI: 2.07% to 10.52%) vs Group B 4.0% (95% CI: 0.55% to 7.32%), p=0.393)(Table 3).

Table 3: Comparison of Postoperative Recurrence (n=254)

Postoperative Recurrence	Group A Frequency (%)	Group B Frequency (%)	p-Value
Yes	8 (6.3%)	5 (4.0%)	0.393
No	119 (93.7%)	122 (96.0%)	

DISCUSSION

Inguinal hernia repair is common practice, in pediatrics, and choice of technique can significantly impact patient outcomes. In this study, we have compared single-port laparoscopic inguinal hernia repair (Group A) with open herniotomy (Group B), specifically evaluating recurrence rates and the incidence of postoperative scrotal hematoma. According to results of our study, postoperative scrotal hematoma formation was found significantly less in Group-A versus 10.2% in Group-B, and recurrence rate was 6.3% and 4%, respectively. However, this variance in recurrence rate was not significant statistically. Similar to current findings, in a study by Zhang *et al.*, in 2023 scrotal hematoma was reported in none

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following laparoscopic repair, versus 3.7% in open repair [12]. In contrast to current observations, in study by Pillai and Nair, recurrence was observed only in single patient who underwent open repair, whereas no recurrence was noted in laparoscopic repair. Additionally, minor complications, including hematoma formation, were noted more among laparoscopic repairs (19%), and compared to those who had open repair (14.7%) [13]. Further supporting our results, in another study, the recurrence rate noted was higher (1.5%) with the laparoscopic approach versus 0.4% with the open approach [14]. However, other studies have indicated that the recurrence risk varies, ranging from 0% to 6% in open repair and 0% to 15.5% in laparoscopic repair [15]. Compared to open herniorrhaphy, laparoscopic repair resulted in fewer testicular complications without raising the risk of ipsilateral hernia recurrence. Therefore, it was found to be a viable and less invasive option for inguinal hernia repair in boys [16]. A review of 13 RCTs revealed several advantages of laparoscopic repair compared to open repair, among them shorter operative time for bilateral hernia repairs, lower complication rate, and reduced wound complications. However, similar to our results, no significant differences were observed between the two techniques for recurrence rates [17]. Recurrence in inguinal hernia repair can arise due to insufficient ligation of the internal ring, damage to the inguinal canal, a weak hernia sac, or hematoma formation. In laparoscopic repair, it may result from incomplete closure of the patent processus vaginalis or the use of absorbable sutures [3, 18]. Open herniorrhaphy can be challenging in children due to the thin hernia sac, which may tear during dissection. In contrast, laparoscopic repair avoids the need for extensive dissection of the inguinal canal, leading to shorter operating times and potentially lower recurrence rates due to its simpler approach [19, 20]. Consistent with other studies, laparoscopic repair showed fewer complications and is considered a less invasive and viable option for paediatric inguinal hernia repair. Limitations of this study were that patients were not followed for late recurrence and not have been compared for the duration of surgery between single-port laparoscopic repair and open herniotomy. Surgical time was important factor that can influence patient outcomes, including anesthesia duration and recovery time. Future studies should incorporate this variable to provide more comprehensive assessment of benefits and drawbacks of each technique.

CONCLUSIONS

In conclusion, laparoscopic-assisted hernia repair and open herniotomy demonstrate comparable recurrence rates. However, laparoscopic-assisted repair is associated with significantly lower incidence of postoperative hematoma. These findings indicated that laparoscopic repair may be a safer option with fewer postoperative complications, making it a favorable choice for pediatric inguinal hernia surgery.

Authors Contribution

Conceptualization: HUR, QD, BC
Methodology: HUR, QD, MN, MS, BC, MN
Formal analysis: HUR, QD, MN, MS, BC, MN
Writing, review and editing: MN, MS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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Original Article

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Association of Possible Developmental Delays with Emotional and Behavioral Disorders, and Risk Factors in Children Under Six in Karachi, Pakistan: A Cross-sectional Study

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ABSTRACT

Developmental delays refer to a child not reaching expected milestones. They are linked to various factors and, if unaddressed in early childhood, can lead to long-term consequences in adulthood. **Objectives:** To determine the association of developmental delays with emotional and behavioural disorders and other risk factors in children less than six years of age. **Methods:** This cross-sectional study was conducted at a primary healthcare center in a Karachi slum from October 2020 to July 2021. Using non-probability consecutive sampling, 425 participants (parents of children aged 1-5½ years) were selected. Data were collected using the validated Survey of Well-being of Young Children tool and analyzed in SPSS version 23.0. Logistic regression assessed associations between outcomes and risk factors. **Results:** Of 425 participants, 161 (37.9%) had possible developmental delays. No association was found with emotional/behavioural disorders (p=0.30). Binary logistic regression linked delays to male gender, uneducated parents, unemployed mothers, low income, domestic violence, and tobacco/drug exposure at home (p<0.05). After adjustment, significant associations remained with the mother's education (aOR=1.785, CI: 1.040-3.065, p=0.036), income (aOR=3.361, CI: 1.197-9.434, p=0.021), and domestic violence (aOR=2.603, CI: 1.055-6.423, p=0.027). **Conclusions:** It was concluded that the prevalence of developmental delays in slum-dwelling children is high. No association was found with emotional/behavioural disorders. Socioeconomic factors, such as the mother's education.

INTRODUCTION

Developmental delays refer to the lag in the progression of speech and language skills, motor abilities, social-emotional growth, and cognitive development [1]. Such delays occur when a child does not achieve developmental milestones at the anticipated age across any areas of functioning [2]. The increased prevalence of such delays is linked to factors such as poverty, health issues, violence, malnutrition, inadequate care and stimulation, and limited growth opportunities [3]. Around 25% of the children are suffering from developmental delays globally. The prevalence of suspected developmental delay varies from 10% in Europe and Central Asia to 42% in West and Central Africa [4]. A study conducted at primary health care in South Africa found that the prevalence of possible developmental delays in children living in slums is around 35% [5]. A multicenter study carried out in Pakistan found that 61.1% of children less than five years' old who are suffering from malnutrition have delayed global

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development [6]. Another study conducted in a developed urban area of Pakistan reported a prevalence of developmental delays in 29.1% of the participants [7]. Unfortunately, despite such high prevalence, Pakistani parents exhibit a significantly limited understanding of developmental milestones [8]. Earlier detection of developmental delay in children through a validated, parent-completed questionnaire and identification of risk factors is critical for primary health care where their growth and development can be monitored regularly [1]. Timely referral to rehabilitation services may help improve children's quality of life and it is essential for promoting children's well-being [9]. There remains a lack of data on the neurodevelopment of children living in slums in Pakistan. Additionally, the factors contributing to developmental delays and their interrelationships have been rarely explored.

This study aims to evaluate the prevalence of possible developmental delays and their predictors in children under six. This study aims to fill the gap in knowledge regarding developmental delays in children in Pakistan.

METHODS

This cross-sectional study was conducted at the Primary Health Care (PHC) Centre in Gulshan e Sikandrabad in Karachi, Pakistan, from October 2020 to July 2021. Before commencing the fieldwork, ethics clearance was obtained from the Ethical Review Committee, Ziauddin University, Karachi (Reference code: 2270620SSCHS). Before the data collection process, informed consent was obtained from each participant through a signature or thumbprint. Participants were provided with a detailed explanation of the study's purpose, procedures, potential risks, and benefits, as well as their rights to confidentiality and voluntary participation. They were also informed that they could withdraw from the study at any point without any consequences. Non-probability consecutive sampling technique was used to recruit participants. Children of one year to less than six years of age with or without any ailment (e.g. infectious diseases like diarrhea, respiratory tract infections, skin diseases, etc.) visiting PHC with their parents were included in the study. Those with any known mental health issues or gross motor disability were excluded from the study. The sample size was calculated through the software open epi (version 3) with a 95% confidence level, 10% margin of error, and an anticipated frequency of 61.6% [6]. A total of 425 participants were enrolled in the study. Direct one-to-one interviews were conducted with the parents of the recruited participants. Before the interview, parents were briefed about the study, and their written consent was obtained before proceeding. Data were collected through a validated questionnaire, freely available online, called the Survey of Wellbeing of Young Children (SWYC) available in the English language. This tool is specifically designed for administration in Primary Health Centers (PHCs). It consists of four components: (1) SWYC milestones for assessing possible developmental delays, (2) the Baby Pediatric Symptoms Checklist (BPSC) and the Preschool Pediatric Symptoms Checklist (PPSC) for evaluating the risk of emotional and behavioural disorders (EBDs), (3) Parent's Observation of Social Interaction (POSI) for screening of autism and (4) family-related questions. Developmental milestones were assessed using a 10-item scale with a 3-point Likert system: "Not Yet" (0), "Somewhat" (1), and "Very Much" (2). The total score was calculated by summing all items and interpreted based on age-specific cutoffs provided in the questionnaire manual. Children were categorized as either "Needs Review," indicating possible developmental delays, or "Appears to Meet Age Expectations." Emotional and behavioural disorders (EBDs) were evaluated through the Baby Pediatric Symptoms Checklist (BPSC) for children aged 12–15 months. This included three subscales with four items each, scored on a 3-point Likert scale: "Not at All" (0), "Somewhat" (1), and "Very Much" (2). A score of 3 or higher on any subscale indicated a risk of EBDs, necessitating expert evaluation. For children aged 16–66 months, the Preschool Pediatric Symptoms Checklist (PPSC) was used, which consisted of 18 items across three subscales. A score of 9 or higher on any subscale suggests a risk of EBDs. Substance use disorder was screened using three questions, with "Yes" scored as 1 and "No" as 0. A score of 1 or higher indicated substance abuse among family members. Food insecurity was assessed by scoring "never" as 0, "sometimes" as 1, and "often" as 2. A score of 1 or 2 indicated food insecurity. Maternal depression was evaluated through two questions on a 4-point Likert scale, with a total score of 3 or higher suggesting depression. Domestic violence was screened using the Woman Abuse Screening Tool (WAST), where a score of 1 or higher indicated its presence. This study included questions related to developmental delays, emotional and behavioural disorders and family questions. The scoring of questions to assess the risk of developmental delays, emotional and behavioural disorders, and other risk factors was conducted according to the guidelines provided by the author on the website [10]. Data were entered and analyzed using SPSS version 23.0. For demographic variables, frequencies and percentages were calculated. Univariable binary logistic regression was computed to assess the association of predictor variables with the risk of developmental delays. Multivariable logistic regression was performed to see the combined effect of the predictor variables on the outcome. A p-value<0.05 was considered significant.

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RESULTS

In total, 425 children were recruited. The same number of children (i.e., 85) were included in each age bracket. Among the participants, 226 (53.2%) were male, and 199 (46.8%) were female. Regarding family structure, 173 (40.7%) children belonged to nuclear families, while the remaining 252 (59.3%) lived in joint or extended families. Among fathers, 116 (27.3%) were uneducated, while the remaining had at least primary education. Compared to fathers, more mothers were uneducated, 189 (44.5%). The majority of the fathers worked as daily wage laborers (201 (47.3%)), while the majority of the mothers were homemakers (323 (76%)). Among all the children, 161 (37.9%) screened positive for possible developmental delay. Other demographic factors are shown in Table 1.

Table 1: Socio-Demographic Characteristics of the Study Group

Variables	Categories	n (%)
Age	1 To 2 Years	85 (20%)
	2 To 3 Years	85 (20%)
	3 To 4 Years	85 (20%)
	4 To 5 Years	85 (20%)
	5 To 5½ Years	85 (20%)
Gender	Male	226 (53.2%)
	Female	199 (46.8%)
Family Structure	Nuclear	173 (40.7%)
	Joint/Extended	252 (59.3%)
Marriage	Cousin	260 (61.2%)
	Non-cousin	165 (38.8%)
Father's Education	Uneducated	116 (27.3%)
	Primary	67 (15.8%%)
	Secondary	72 (16.9%)
	Matric	135 (31.8%)
	Intermediate	13 (3.1%)
	Graduate/Postgraduate	6 (1.4%)
	Madrassa	16 (3.8%)
Mother's Education	Uneducated	189 (44.5%)
	Primary	80 (18.8%)
	Secondary	39 (9.2%)
	Matric	54 (12.7%)
	Intermediate	5 (1.2%)
	Graduate/Postgraduate	3 (0.7%)
	Madrassa	55 (12.9%)
Father's Occupation	Daily Wager	201 (47.3%)
	Private Employment	149 (35.1%)
	Personnel Business	42 (9.9%)
	Government Employment	6 (1.4%)
	Jobless	23 (5.4%)
Mother's Occupation	Home Maker	323 (76.0%)
	House Maids	67 (15.8%)
	Private Employees	27 (6.4%)
	Personnel Business	3 (0.7%)
	Government Employee	1 (0.2%)
Monthly Income (PKR)	5,000-10,000	63 (14.8%)
	11, 000-15,000	188 (44.2%)
	16,000-20,000	135 (31.8)
	21,000-25,000	22 (5.2)
	26,000-30,000	8 (1.9%)
	≥31,000	9 (2.1%)
Tobacco/Smokers at Home	Yes	101 (23.8%)
	No	324 (76.2%)
Food Insecurity	Yes	345 (81.2%)
	No	80 (18.8%)
Drug Abuser at Home	Yes	72 (16.9%)
	No	352 (82.8%)
Domestic Violence at Home	Yes	210 (49.4%)
	No	215 (50.6%)
Parents' Concern for Child's Development	Yes	29 (6.8%)
	No	396 (93.2%)
No. of Siblings	3 or Less	215 (50.5%)
	4 or More	210 (49.5%)
First Child vs Other Order	First Child	69 (16.2%)
	Not First Child	356 (83.7%)
School Going Status	Yes	44 (10.3%)
	No	381 (89.6%)
Depression in Mother	Yes	99 (23.3%)
	No	326 (76.7%)
Developmental Delays	Yes	161 (37.9%)
	No	264 (62.1%)

Binary logistic regression was performed to examine the relationship between developmental delay and various socio-demographic factors. Male gender, an uneducated father, an uneducated mother, an unemployed mother, low family income, domestic violence, and the presence of tobacco smoke and drug abuse at home showed a significant association with developmental delay in children ($p<0.05$). Other risk factors, i.e., possible emotional and behavioural disorders in the child, type of family, father's occupation, cousin marriage, child's birth order, number of siblings, number of people living in the house, child's school-going status, food security, and maternal depression, were not found to be statistically significant ($p\geq0.05$). Results are shown in Table 2.

Table 2: Uni-Variable Binary Logistic Regression Analysis of Factors Associated with Developmental Delays

Variables	Odds Ratio (OR)	95% Confidence Interval of OR	p-Value
Gender			
Female	Ref	-	0.008
Male	1.723	1.156-2.567	
Type of Family			
Nuclear	Ref	-	0.356
Joint	0.828	0.554-1.236	
Father's Education			
Educated	Ref	-	0.045
Uneducated	3.962	1.033-15.188	

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Mother's Education			
Uneducated	Ref	-	0.003
Educated	1.660	0.894-3.082	
Father's Occupation			
Employed	Ref	-	0.948
Unemployed	1.512	0.209-10.957	
Mother's Occupation			
Employed	Ref	-	0.044
Unemployed	1.637	1.013-2.647	
Monthly Income (PKR)			
More than 15000	Ref	-	0.015
Up to 15000	3.065	1.240-7.574	
Cousin Marriage			
No	Ref	-	0.259
Yes	1.263	0.842-1.895	
Number of Siblings			
4 or More	Ref	-	0.084
Up to 3	1.638	1.042-2.349	
Order of Child			
Other than first	Ref	-	0.096
First	1.097	0.984-1.224	
School Going			
Yes	Ref	-	0.565
No	1.161	0.621-2.207	
No. of People in House			
Up to 10	Ref	-	0.059
More Than 10	1.835	1.180-2.931	
Parents' Concern			
Yes	Ref	-	0.062
No	0.291	0.145-0.621	
Tobacco Smokers in the House			
Yes	Ref	-	0.001
No	0.478	0.304-0.752	
Substance Abuse in the House			
Yes	Ref	-	0.039
No	0.514	0.309-0.858	
Food Security			
Yes	Ref	-	0.938
No	1.020	0.617-1.686	
Depression in Mother			
No	Ref	-	0.723
Yes	1.087	0.685-1.724	
Domestic Violence			
Yes	Ref	-	0.024
No	0.645	0.324-0.833	
Emotional and Behavioral Disorder			
No	Ref	-	0.301
Yes	0.811	0.545-1.207	

After adjusting for confounding factors, a significant association was found between possible developmental delays and the mother's education (aOR: 1.785, 95% CI: 1.040-3.065, p=0.036), monthly income (aOR: 3.361, 95% CI: 1.197-9.434, p=0.021), and domestic violence (aOR: 2.603, 95% CI: 1.055-6.423, p=0.027). The risk of developmental delays among children witnessing domestic violence is doubled. Children whose parents' income is less than Rs. 15,000 have a threefold risk of experiencing developmental delays. Only statistically significant values are shown in Table 3.

Table 3: Multivariable Analysis of Risk Factors for Developmental Delays

Variables	Adjusted Odd's Ratio (OR)	95% Confidence Interval of OR	p-Value
Mother Education			
Educated	Ref	-	0.036
Uneducated	1.785	1.040-3.065	
Monthly Income			
More Than 15000	Ref	-	0.021
Joint	3.361	1.197-9.434	
Domestic Violence			
Educated	Ref	-	0.027
Uneducated	2.603	1.055-6.423	

DISCUSSION

This study aimed to screen children living in slums for possible developmental delays and identify the associated factors. Current analysis revealed that around 37.9% of children under six years of age had possible developmental delays and required further assessment to confirm the diagnosis. This aligns with the findings of a meta-analysis, which found that between 38% and 49% of children experience developmental delays globally [11]. Developmental delays are more common among male as compared to female. Many national and international studies have found a statistically significant relationship between male gender and developmental delays. Males are found to have higher odds of developmental delays as compared to female ($p<0.05$) [12, 13]. Current study also found that male were more likely to have developmental delays. (OR: 1.723, 95% CI: 1.156-2.567, p=0.008). Socioeconomic status, measured by parental education, occupation, and family income, strongly predicts children's developmental outcomes [14]. The father's social status and education level also affect the development of children. Research studying the influence of a father's education level on child development found a positive association between the two factors ($\beta=0.93$, $t=3.12$, $p<0.01$)[15]. Present study found the same results showing that fathers of developmentally delayed children were less educated. (OR: 3.962, 95% CI: 1.033-15.188, p=0.045). A mother's education is also important to a child's early development. A study conducted to find the association of mothers' education on a child's development after controlling confounding factors found that children of less educated mothers had higher odds of developmental delays [16]. Another study showed that mothers of higher levels of education had lower levels of developmental delays in their children compared to the lower education

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groups [6]. Analysis of current study is consistent with these results. Even after adjusting for co-factors the association remained significant (OR: 1.660, 95% CI: 0.894-3.082, p=0.003) (aOR: 1.785, 95% CI: 1.040-3.065, p=0.036). A family's socioeconomic status and income directly affect the child's developmental outcome. Low socioeconomic status is associated with a delayed or different developmental pattern [14]. Several studies support the fact that lower household income leads to poor growth and development in children (p<0.05) [10, 13]. Current study found the same association, i.e. the children whose families earned less than Rs.15000 per month had higher odds of developmental delays. These odds remained high even after adjusting for other determinants (OR: 3.065, 95% CI: 1.240-7.574, p=0.015) (aOR: 3.361, 95% CI: 1.197-9.434, p=0.021). Parents in cousin marriages share a higher percentage of genes that carry risks, leading to a significantly higher chance of genetic disorders in their offspring compared to children of unrelated parents. Cousin marriage has been considered one of the biggest risk factors for the developmental delay of children (p<0.05) [17, 18]. However, present study does not support the results. There was no significant association between cousin marriage and children's developmental delay. (OR: 1.263, 95% CI: 0.842-1.895, p=0.259). This lack of association was also observed in a study conducted in Pakistan among children up to 5 years of age (X^2=0.14, p=0.71) [13]. Exposure to tobacco smoke affects mental health and neurodevelopment in children (p<0.001) [19]. Even secondhand smoke exposure increases the likelihood of delayed milestone achievement across various domains [20]. Present study also discovered a positive association between a child's developmental delay and the presence of tobacco smoke in the house. Children living in homes without tobacco smoke had lower odds of developmental delays (OR: 0.478, 95% CI: 0.304-0.752, p=0.001). A study conducted to find the association of depression in mothers during and after pregnancy on the mental development of their children up to five years of age found a positive relation between depression in mothers and lower developmental outcomes in their children (p=0.04) [21]. Another study found that depression in mothers affected the subareas of development in their children (p=0.037) [22]. However, Current analysis contradicts these results, as present study showed no such relationship (p=0.723). A meta-analysis revealed that domestic violence is a distressing event within a family that impacts all its members, including children. Children who are at a critical stage of development are particularly vulnerable to disruptions caused by stress and developmental challenges. Domestic violence can disrupt a child's development, leading to psychological, social, and academic challenges [23]. Maternal trauma due to exposure to violence may play a significant role in the development of disorders in children [24]. Present analyses found higher odds of developmental delay in children who witnessed violence in their homes. This association remained significant even after adjusting for the co-determinants. (aOR: 2.603, 95% CI: 1.055-6.423, p=0.027). Addressing trauma resulting from domestic violence should be a shared responsibility among parents, teachers, and healthcare professionals to implement interventions that prevent more severe consequences [23]. Children with neurodevelopmental delays are more likely to have emotional and behavioural disorders compared to neuro-typical children. A study conducted to find the association between developmental delays and emotional and behavioural disorders found that children having developmental delays exhibited more emotional and behavioural difficulties (p<0.01) [25]. However, current study found no significant association between these two factors. (p=0.301). Current study also found no association between developmental delay and type of family, father's employment status, number of siblings, child's order, school-going status, number of people in the house, parents' concern, and food security. (p≥0.05).

CONCLUSIONS

It was concluded that the prevalence of possible developmental delays in children living in the slums is high. There was no association between developmental delays and emotional and behavioural disorders in children.

Authors Contribution

Conceptualization: SS[1]
Methodology: SS[1], KM, NJ, GA, BF, SS[2]
Formal analysis: SS[1], KM, NJ, GA, BF, SS[2]
Writing review and editing: SS[1], KM, NJ, GA, BF, Ss[2]
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Lactate Dehydrogenase as a Prognostic Biomarker in Severe Sepsis in Intensive Care Unit

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ABSTRACT

Sepsis ranks as one of the principal death-causing conditions in present-day society. The medical community identifies lactate dehydrogenase (LDH) as a potential tool to assess sepsis severity. **Objectives:** To assess how LDH blood concentrations relate to severe sepsis progression. **Methods:** A retrospective examination took place within the intensive care unit (ICU) at Shahida Islam Medical Complex. Data of patients of both genders, aged between 18-75 years, and who were admitted to the intensive care unit with sepsis. Biochemical data, including necessary laboratory investigations, infection areas, and comorbidities, were documented. The study subjects were analyzed concerning LDH ≤230 U/L (n=41) and LDH >230 U/L (n=55). Univariate Cox regression analysis for 21-day mortality was also carried out. **Results:** The records of 96 patients as per inclusion and exclusion criteria were considered for this study. There were 61 (63.5%) patients who were male. The overall mean age was 54.2 ± 12.6 years. LDH ≥230 U/L was found to have a significant association with findings that included significantly higher CRP (p=0.0001) and LDH levels (p=0.0001) in patients with LDH ≥230 U/L compared to LDH <230 U/L. A significant association high SOFA score (p=0.002), and APACHE-II score (p=0.001) was found with LDH≥230 U/L. Strong associations of the biochemical levels, which included LDH levels (HR=1.006, p=0.010), lactate levels (HR=1.498, p=0.002), and creatinine levels (HR=1.483, p=0.005) were seen with mortality. **Conclusions:** It was concluded that elevated LDH levels were associated with increased disease severity and adverse clinical outcomes, including higher mortality rates, in severe sepsis patients.

INTRODUCTION

The human body develops sepsis when it responds poorly to infections [1]. The medical condition displays complex inflammatory mechanisms coupled with immune-organism dysfunction that produces declining organ functions [2]. Sepsis remains the world's top contributor to mortality and among the United States population sepsis causes death in 57 male per 100,000 persons alongside 45.1 female per 100,000 persons [3]. The worldwide medical impression of the disease is concerning since medical records indicate 50 million annual cases. Sepsis became responsible for 11 million fatalities in 2020 thus representing 19.7% of total global fatalities [4]. Sepsis prevalence remains poorly documented in Pakistan though its high rates of infectious diseases indicate a large impact which is made worse by the scarcity of both diagnostic tools and advanced critical care resources. Sepsis prevalence shows differences based on three key elements: socio-economic status as well as healthcare system structure and underlying health conditions incidence [5]. Research evidence indicates that bacterial infections lead to sepsis rates between 14.7% in Pakistan [6]. The intensive care unit (ICU) admission prevalence rate of sepsis patients reached 35% according to research conducted at a Karachi tertiary care hospital [7]. The physiological response of sepsis originates from unregulated immunity and metabolic disruptions that

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modify blood glucose metabolism and create elevated serum lactate. Lactate dehydrogenase (LDH) functions as an enzyme to transform both lactate and pyruvate into one another thereby being essential for metabolic reprogramming. Tissue hypoxia frequently emerges during septic shock to increase LDH enzymatic activity that leads to enhanced lactate production and subsequent damage throughout affected organs [8, 9]. The levels of LDH in blood establish connections to severe sepsis and unsatisfactory results in patients. The tools used most commonly for sepsis risk assessment such as Sequential Organ Failure Assessment (SOFA) score and Systemic Inflammatory Response Syndrome (SIRS) criteria assess clinical variables as their primary elements. These tools may not fully account for metabolic abnormalities. Recent evidence suggests that integrating biomarkers like LDH into prognostic models could enhance the accuracy of sepsis severity assessments [10, 11]. This research targets the present understanding deficit about LDH prognostic value for severe sepsis patients across Pakistan. Researchers have emphasized the particular biomarker in this study because it demonstrates both metabolic dysfunction characteristics and shows direct relationships to ICU patient disease severity and treatment results. This research subject was chosen because Pakistan requires region-relevant information and economical biomarkers to improve sepsis treatment management. Sepsis patients benefit from LDH as a reliable diagnostic marker since this tool enables a simple assessment of patient outcomes even when limited diagnostic options exist. This research investigation increases worldwide understanding of sepsis biomarkers while at the same time, addressing essential research gaps leading to better outcomes in low and middle-income countries(LMICs).

This study aims to investigate the relationship between sepsis seriousness and LDH measurements for evidence-based routine clinical practice that would enhance resource-limited patient risk assessment and healthcare management.

METHODS

This retrospective study was carried out at the ICU of Shahida Islam Medical Complex, Lodhran, Pakistan, from October 2023 to April 2024. Approval from the ethical committee of the institution was obtained (Letter number: SIMC/H.R./7337/23). Non-probability, consecutive sampling techniques were used for sample selection. Data were extracted for 119 patients from electronic medical records, the record of 22 patients didn't fit the inclusion criteria. The data analyzed patients of both genders, aged between 18 and 75 years, and who were admitted to the ICU with sepsis. All included patients were diagnosed with sepsis during their ICU stay with complete medical records available for data extraction. Patients with incomplete medical records who died within 24 hours of ICU admission, pregnant, immunocompromised (including but not limited to human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), malignancy, receiving immunosuppressive therapy) and patients with chronic liver disease were excluded from the study. The SOFA score and APACHE II score were calculated for all patients. Acute physiology and chronic health evaluation (APACHE) II scores (0-71 inclusive) determined sepsis severity risk because they used 12 physiological variables from first ICU admission day measurements (temperature, MAP, heart rate, respiratory rate, PaO2 with A-a gradient if FiO2 ≥0.5 or PaO2 if FiO2 <0.5, pH, sodium, potassium, creatinine, hematocrit, white blood cell count, Glasgow coma score (GCS)) along with age and chronic healthcare conditions. Daily SOFA scores (range 0-24, higher scores indicating higher mortality risk) assessed dysfunction across six systems including respiration (PaO2/FiO2: >400=0, ≤400=1, ≤300 with ventilation=2, ≤200 with ventilation=3, ≤100 with ventilation=4), coagulation (platelets: ≥150=0, <150=1, <100=2, <50=3, <20=4), liver (bilirubin: <1.2=0, 1.2-1.9=1, 2.0-5.9=2, 6.0-11.9=3, >12.0=4), cardiovascular (Mean arterial pressure (MAP)/vasopressors: MAP ≥70=0, MAP <70=1, Dopamine ≤5 or dobutamine=2, Dopamine >5 or epinephrine/norepinephrine ≤0.1=3, Dopamine >15 or epinephrine/norepinephrine >0.1=4), CNS (GCS: 15=0, 13-14=1, 10-12=2, 6-9=3, <6=4), and renal (creatinine/urine: <1.2=0, 1.2-1.9=1, 2.0-3.4=2, 3.5-4.9 or <500 mL/24h=3, >5.0 or <200 mL/24h=4). The study subjects were analyzed concerning LDH ≤230 U/L (n=41) and LDH >230 U/L (n=55) [12]. Survivors and non-survivors were compared concerning their characteristics for this study. Organ dysfunction and the treatment regimens that were employed in the treatment within the ICU were assessed. All the required information was recorded on a specifically predesigned proforma.Data analysis was done using IBM-SPSS Statistics, version 26.0. The quantitative variables like gender, infection area, and history of comorbidities were expressed in the form of frequency and percentage. For the qualitative data, such as age, SOFA score, APACHE II score, and biochemical assessments, means and standard deviations were computed. Comparisons of the groups were made using an independent t-test and a chi-square test with p-values less than 0.05, signifying the importance of the differences observed. To further evaluate LDH about its predictive validity for 21-day mortality, Cox regression was applied.

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RESULTS

The records of 96 patients as per inclusion and exclusion criteria were considered for this study. There were 61 (63.5%) patients who were male. The overall mean age was 54.2 ± 12.6 years. There were 55 (57.3%) patients who had LDH levels ≥ 230 U/L. Male and female contributions for patients with LDH levels < 230 U/L were 26 (63.4%) and 15 (36.6%), respectively. The mean age of the patients with LDH <230 U/L was recorded as 54.1±13.1 years, and for those who had LDH ≥230 U/L, it was 54.4 ± 11.9 years. LDH ≥230 U/L was found to have a significant association with findings that included significantly higher CRP (p=0.0001) and LDH levels (p=0.0001) in patients with LDH ≥230 U/L compared to LDH <230 U/L. A significant association high SOFA score (p=0.002), and APACHE-II score (p=0.001) was found with LDH ≥230 U/L. Infection areas or comorbidities were not found to have any significant association with LDH levels (p>0.05). Most of the abnormal biochemical data revealed a statistically significant association with raised LDH levels (p<0.05) and the details are shown in Table 1.

Table 1: Characteristics of Patient Based on LDH Levels (n=96)

Parameters		LDH Levels		Total (n=96)	p-value
		LDH <230 U/L (n=41)	LDH ≥ 230 U/L (n=55)		
Gender	Male	26 (63.4%)	35 (63.6%)	96	0.982*
	Female	15 (36.6%)	20 (36 .4%)		
Age in Years (mean ± SD)		54.1 ± 13.1	54.4 ±11.9		0.532♦
SOFA Score (mean ± SD)		10.04 ± 1.52	11.25 ± 2.07		0.002♦
APACHE II score (mean±SD)		18.90 ± 5.14	23.01 ± 5.99		0.001♦
Biochemical Data (mean ± SD)	WBC (x10^3/mm^3)	14.86 ± 6.28	16.6 ± 6.98		0.211♦
	CRP (mg/L)	42.01 ± 18.99	56.99 ± 23.01		0.001♦
	D-dimer (mg/L)	1.31 ± 0.81	1.51 ± 1.14		0.341♦
	Serum albumin (g/dL)	29.99 ± 4.60	30.01 ± 5.01		0.984♦
	Serum creatinine (mg/dL)	4.19 ± 1.08	4.79 ± 1.30		0.018♦
	Pa-O_2/Fi-O_2 (mmHg)	339.72 ± 74.02	304.03 ± 76.99		0.025♦
	B-type natriuretic peptide (pg/ml)	424.09 ± 432.14	410.09 ± 351.98		0.025♦
	Serum lactate (mmol/L)	2.41 ± 1.29	3.19 ± 1.79		0.020
	Interleukin-1b (pg/mL)	91.81 ± 18.01	105.01 ± 20.97		0.002♦
Infection Area	Lung	17 (41.5%)	20 (36.5%)		0.612*
	Abdomen	13 (31.7%)	19 (34.5%)		0.770*
	Urinary Tract	2 (4.9%)	6 (10.9%)		0.290*
	Circulation	7 (17.1%)	8 (14.5%)		0.736*
	Cranial Cavity	2 (4.9%)	2 (3.6%)		0.763*
Comorbidities	Hypertension	7 (9.8%)	9 (13.9%)		0.926*
	Arrhythmia	4 (5.6%)	4 (6.2%)		0.663*
	Diabetes	8 (11.2%)	9 (13.9%)		0.689*
	Cerebral Infarction	13 (18.3%)	17 (26.3%)		0.933*
	COPD	6 (8.4%)	5 (7.7%)		0.399*

*Chi-Square Test, ♦Independent t-test

The analysis showed survival in 65 patients (67.7%) with 31 patients (32.3%) experiencing mortality during the study period. ANOVA tests confirmed the APACHE II score (p<0.001), SOFA score (p<0.001), LDH and CRP levels (p<0.001), Pa-O2/Fi-O2 measurements (p<0.001) as well as serum creatinine and interleukin-1 b (p<0.001) values between survivors and non-survivors, as in Table 2.

Table 2: Characteristics of Patient Based on LDH Levels (n=96)

Characteristics	Survived (n=65)	Not-Survived (n=31)	p-value
Age (Years)	61.9 ± 13.0	62.9 ± 13.1	0.699*
SOFA Score	9.78 ± 1.49	12.59 ± 1.31	<0.001*
APACHE II Score	18.97 ± 5.77	26.02 ± 3.59	<0.001*
WBC (x10^3/mm^3)	15.42 ± 6.66	16.91 ± 7.01	0.316*
C-Reactive Protein (mg/L)	51.89 ± 24.24	45.78 ± 21.94	<0.001*
D-Dimer (mg/L)	1.29 ± 1.09	1.41 ± 1.07	0.613*
Pa-O_2/Fi-O_2 (mmHg)	341.21 ± 80.80	290.14 ± 66.34	<0.001*
Serum Albumin (g/dL)	29.81 ± 4.89	30.01 ± 5.02	0.853*
Serum Lactate (mmol/L)	2.04 ± 0.81	4.31 ± 1.51	<0.001*
LDH (U/L)	199.95 ± 107.08	330.41 ± 114.53	<0.001*
Serum Creatinine (mg/dL)	4.02 ± 1.24	5.29 ± 1.03	<0.001*
Interleukin-1b (pg/mL)	93.21 ± 18.01	112.95 ± 21.00	<0.001*
B-type Natriuretic Peptide (pg/ml)	419.09 ± 418.05	394.78 ± 339.51	0.772*

*Independent t-test

Strong associations of the biochemical levels, which included LDH levels (HR=1.006, p=0.010), lactate levels (HR=1.498, p=0.002), and creatinine levels (HR=1.483,

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p=0.005) were seen with mortality. The univariate Cox regression analysis for 21-day mortality concerning age and biochemical evaluations is expressed in Table 3.

Table 3: Univariate Analysis for 21-day Mortality (n=31)

Parameters	Hazard Ratio	Confidence Interval	p-value
Age	1.001	0.980-1.019	0.878
LDH	1.006	1.000-1.005	0.010
White Blood Cells	1.000	0.950-1.040	0.941
C-Reactive Protein	0.016	0.969-1.002	0.002
Interleukin-1b	1.003	0.990-1.020	0.761
Serum Lactate	1.498	1.290-1.800	0.002
Serum Albumin	1.030	0.959-1.200	0.439
Serum Creatinine	1.483	1.130-1.920	0.005
Pa-02/Fi-02	1.001	0.986-1.001	0.083
B-Type Natriuretic Peptide	0.989	0.996-1.002	0.399
D-Dimer Score	1.001	0.969-1.002	0.980

An increased incidence of ARDS (p=0.041), AKI (p=0.040), and septic shock (p=0.013) in patients with LDH ≥230 U/L compared to LDH <230 U/L was observed. A large proportion of patients with LDH ≥230 U/L received ventilation (p=0.050), CRRT (p=0.039), and vasopressors (p=0.007) in contrast to those with LDH <230 U/L. The prevalence of organ dysfunctions, which included acute respiratory distress syndrome (ARDS), Acute kidney injury (AKI), acute heart failure (AHF), acute lung injury (ALI), coagulopathy, and septic shock, along with the treatments offered like ventilation, Continuous renal replacement therapy (CRRT), and vasopressors, about LDH, is demonstrated in Table 4.

Table 4: Prevalence of Organ Dysfunction and Treatment of LDH (n=96)

Parameters		LDH <230 U/L (n=41)	LDH <230 U/L (n=55)	p-value
Organ Dysfunction	ARDS	6 (5.9%)	16 (29.1%)	0.041
	AKI	11 (26.8%)	25 (45.5%)	0.040
	AHF	2 (4.8%)	4 (7.3%)	1.021
	ALI	2 (4.8%)	3 (5.5%)	1.010
	Coagulopathy	8 (19.5%)	7 (12.7%)	0.998
	Septic Shock	13 (31.7%)	30 (54.5%)	0.013
ICU Treatment	Ventilation	4 (9.8%)	13 (23.6%)	0.050
	CRRT	11 (29.3%)	21 (38.2%)	0.039
	Vasopressor	11 (29.3%)	30 (54.5%)	0.007

LDH has a hazard ratio of 1.006 and 95% Confidence Interval=1.000-1.005, Serum Lactate (1.498, 1.297-1.800) and Serum Creatinine (1.483, 1.166-1.902). Multivariate Cox Regression for 21 Day Mortality are shown in Table 5.

Table 5: Multivariate Cox Regression for 21 Day Mortality

Parameters	Hazard Ratio	95% Confidence Interval	p-value
LDH	1.006	1.000-1.005	0.009
CRP	0.016	0.969-1.002	0.002
Serum Lactate	1.498	1.297-1.800	0.001
Serum Creatinine	1.483	1.166-1.902	0.003

DISCUSSION

The study demonstrates that patients who have an LDH level ≥230 U/L show higher values for both APACHE II and SOFA scores than those with lower LDH levels. The blood tests CRP, creatinine and lactate showed clear differences in patients who had higher LDH levels. Medical research by Zhang *et al.*, showed that higher levels of LDH in septic patients increased their chances of dying. In their study OR=1.83, 95% CI (1.68-1.98), p<0.001. The research data matches our results because LDH levels showed a strong connection to death with a p<0.001 value [13, 14]. Research indicates more mortal patients had higher lactate levels and this matches findings from Shetty *et al.*, and Algebaly *et al.*, earlier study. Research shows septic patients who have more advanced blood lactate levels face a greater risk of dying. A blood test showing lactate levels above 4 mmol/L proves a greater chance of dying. They found higher lactate levels led to higher mortality rates and our data back these results [15, 16]. A study by Algebaly confirmed that higher levels of LDH match worse sepsis cases which validates our present study findings [16]. The research links more severe sepsis disease with higher blood creatinine values in patients. The study connects with research published by Jaurila *et al.*, which showed creatinine levels above baseline increase the risk of poor outcomes in septic patients [17]. The results of a study done by Flannery *et al.*, also report similar findings [18]. Higher chances of death and severe health problems are directly associated with higher LDH measures and worsen patient results. The results show LDH serves as a useful sepsis monitoring tool and past research from Deng *et al.*, Jeon *et al.*, and Mohammad *et al.*, confirms these findings [19-21]. In addition to sepsis, LDH shows important changes in severe pneumonia and strokes [22, 23]. The diagnostic significance of LDH in septic assessments drives its important role in choosing the best care approaches for these patients.

CONCLUSIONS

It was concluded that the LDH levels that increase above average levels appeared linked to serious sepsis symptoms and raised the chances of dying. The current research demonstrates that LDH measurements offer helpful medical insights to help doctors evaluate septic patients and tailor their treatment options.

Authors Contribution

Conceptualization: AB
Methodology: AB, MRH
Formal analysis: SB, AZ
Writing review and editing: NN, SK

All authors have read and agreed to the published version of the manuscript

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Conflicts of Interest

All the authors declare no conflict of interest.

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Assessment of Predictors for Placental Weight and Birth Weight Ratios from Deliveries Conducted in Pakistani Tertiary Care Hospitals

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ABSTRACT

Anomalous placental morphology is associated with obstetric complications. To date, published data is not available regarding placental weights from Pakistan. The aim of the study was to obtain a reference value for placental weights in the Pakistani population and examined the predictors of birth weight to placental weight ratio an indicator of placental efficiency. **Objective:** To assess the predictors for placental weight and birth weight ratios in singleton pregnancies delivered at a tertiary care hospital in Pakistan. **Methods:** Data were collected prospectively for the study cohort at a tertiary care hospital unit in Islamabad, Pakistan. Placental and birth weight obtained and documented immediately post-delivery. Information about maternal factors was obtained from medical records. A linear regression model was employed to predict the effects of various risk factors on BW:PW. **Results:** Fetal weight varied from 2 to 4.5 kg with a mean of 3.016 ± 0.445 kg whereas mean placental weight was 0.667 kg (SD = 0.175). Fetal placental weight ratio (FPWR) existed in the range of 2.54 to 7.91 (mean = 4.732 ± 1.082). Anemia, $p < 0.001$ and pregnancy-induced hypertension p=0.001, can influence the weight of the placenta. **Conclusion:** The average placental weight reference values obtained represented the diverse multi-ethnic population residing in Islamabad, Pakistan. The correlation between placental weight and the birth weight to placental weight ratio offered valuable insights into how the placenta adapted to the various challenges posed by the various stages of pregnancy.

INTRODUCTION

The placenta experiences dynamic morphological transformations during the course of gestation as influenced by a multitude of factors. These changes are essential for the placenta to effectively adapt to the ever-evolving conditions it encounters within the maternal-fetal environment. The intricate nature of its function necessitates a high degree of specialization to meet the demands placed upon it. Ensuring the proper growth and operation of the placenta is crucial for the successful progression of a pregnancy characterized by optimal maternal and fetal health. Placental abnormalities can cause miscarriages in early pregnancy as well as other pregnancy-related complications in later gestation [1]. Five days following fertilization, placenta formation begins with the trophoblastic layer co-existing with the embryonic layer. Syncytiotrophoblast invades the endometrium, leading to the generation of primary villi. Rapid enlargement of the villous tree leads to the formation of secondary followed by tertiary villi, hence placental formation is mostly complete by the end of first trimester

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[2]. Disruptions anywhere during this process alter the placental morphology making the basis of several pregnancies related complications, for instance, early-onset preeclampsia has been shown to be associated with disordered villous development i.e., distal villous hypoplasia along with placental undergrowth (lower placental weight) [3]. It can be hypothesized that subnormal placental weight might be indicative of ongoing pathology. chronic hypertension and preeclampsia were also associated with low placental weight whereas diabetes, anemia, chorioamnionitis, chorangioma, circumvallate placenta, and marginal cord insertion are risk factors of higher weight of placenta [4]. Since placental weight correlates with the birth weight, birth weight to placental weight ratio (BW:PW) can serve as a more useful tool predicting aberrance in placental weight [5]. A large population based study illustrated a strong positive correlation between placental weight and birth weight as well as a consistent increase in placental weight until 41st week of pregnancy [6]. Placental weight and the BW:PW are frequently reduced in cases of fetal growth restriction (FGR) which may be a sign that the placenta has not been able to adapt its nutrient transfer capability according to its size [7]. Previous study demonstrated higher risk of cardiovascular morbidity later in life in neonates with lower BW:PW and relatively larger placentas [8]. Several studies showed maternal body mass index gestational age, lower socioeconomic status, maternal anemia, gestational diabetes, and smoking to be significantly associated with BW:PW. Pre-eclampsia, risk of induced labour, preterm delivery, low birth weight, and stillbirth were all significantly ($p<0.001$) related to lower placental weight [9-12]. On the other hand, higher placental weight significantly ($p<0.001$) correlated to an increased risk of caesarean section, post-term delivery, and large for gestational age birth. Apart from these pathological factors discussed above, BW:PW is also influenced by the gender of the baby. Richardson *et al.*, observed that BW:PW was lower in females which indicates reduced placental efficiency, similarly lower oxygen saturation of umbilical artery was seen, representing reduced systemic oxygenation [13]. Fetal oxygenation is thought to play the basic role behind altered morphogenesis of placenta. Hence the factors that influence fetal oxygenation bring changes in weight of placenta. For example, higher the maternal age, lesser the vascular compliance, and greater is the placental weight [14]. Risk of Small for Gestational Age (SGA) fetus correlated well with the lower placental weight and as placental weight crosses 50th centile, SGA risk becomes negligible [15]. Gestational Diabetes Mellitus (GDM), which produced a state of fetal hypoxia, is associated with larger placentas and lower BW:PW [16].

The aim of the study was to obtain a reference value for placental weights in the Pakistani population and examined the predictors of birth weight to placental weight ratio (BW:PW), an indicator of placental efficiency. To date, published data is not available regarding placental weights from Pakistan. It can be used as reference for population specific weight of placenta to measure pregnancy outcome and predict lifelong health of fetus.

METHODS

This prospective cohort study was conducted in Maternity Child Center Islamabad, a tertiary care maternity unit from December 2021 to November 2022. Sample size was calculated taking the population size of 1200 (100 patients delivered per month in the study settings) and confidence limit of 5% in Epi calculator and turned out to be 339 for a confidence level of 97%. Weights of 363 freshly delivered untrimmed placentas, as well as the fetal weight, were determined using electronic balance in the labor room and operating rooms of the study setting immediately after the delivery and recorded in the form of a hand-written document. All patients with singleton pregnancies delivering either vaginally or by Cesarean section were included. Multiple pregnancies, extremely preterm delivery at less than 24 weeks' gestation, and pregnancies with known fetal anomalies were excluded from the study. Fetal anomalies can impact placental development and fetal growth in ways that are not representative of the general population. These cases were excluded to avoid potential confounding factors and ensure the study's focus on typical pregnancy outcomes. For diagnosis of pregnancy and labor related complications e.g., preeclampsia, GDM, preterm labor, polyhydramnios, oligohydramnios, obstetric cholestasis, pre-labor rupture of membranes, intrauterine growth restriction (IUGR), postpartum hemorrhage (PPH) etc.,RCOG and NICE guidelines definitions of the respective complications were used. Maternal anemia was defined as hemoglobin concentration of less than 9g/dL in maternal blood sampled during labor. At least 3 antenatal visits were the prerequisites for 'appropriate antenatal care'.Sample size calculated from the Epi calculator was 339 taking sampling population of 1200, at 97% confidence interval and design effect of 1. Data were collected using consecutive sampling technique. Data were stored and analyzed in statistical package for social sciences (SPSS) version 26.0. Descriptive statistics were used to represent baseline characteristics of the study population. Continuous numerical data was expressed in mean ± standard deviation form whereas categorical data as percentage and frequencies.Multivariate regression analysis predicted the effects of various risk factors on weight of placenta as well as BW:PW. Pearson correlation was used to determine individual correlation of maternal weight and gestational age with placental weight. The ethical approval was taken from IRB (Ref No, FGPC.1/12/2021/Ethical Committee).

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RESULTS

Mean age of the participants was 28.09 ± 4.902 (range = 18-41 years). Most of the patients had parity of 2 or 3 (cumulative percentage of 71.1%). Gestational age at which patients presented were between 33^{+1} to 42 weeks (mean= 38^{+6}). Mean maternal BMI was 26.21 ± 4.71kg/m^2. Frequencies of various risk factors are given in the table 1.

Table 1: Frequencies of Risk Factors

Risk Factors	Frequency (%)	Risk Factors	Frequency (%)
Anemia	82 (22.6%)	Preeclampsia	4 (1.1%)
Rh-negative	19 (5.2%)	History of LSCS	21 (5.8%)
Pre-PROM	8 (2.2%)	IUD	2 (0.6%)
Lack of regular ANC	3 (0.8%)	GDM	13 (3.6%)
Oligohydramnios	2 (0.6%)	Obstetric cholestasis	3 (0.8%)
Polyhydramnios	5 (1.4%)	Preterm labor	21 (5.8%)
PIH	15 (4.1%)	PROM	4 (1.1%)
PPH	4 (1.1%)	IUD	2 (0.6%)
MSL	6 (1.7%)	IUGR	2 (0.6%)
Hydrocephalus	1 (0.3%)	DM type II	1 (0.3%)
Breech	5 (1.7%)	Antithrombotics use	1 (0.3%)
CPD	2 (0.6%)	Shoulder dystocia	1 (0.3%)
Post-dated	60 (16.5%)	Malpresentation	1 (0.3%)
Cord prolapse	2 (0.6%)	-	-

Pre-PROM (Preterm Prelabor Rupture of Membranes); ANC (Antenatal Care); LSCS (Lower Segment Cesarean Section); IUD (Intrauterine Death); GDM (Gestational Diabetes Mellitus); PIH (Pregnancy-Induced Hypertension); PROM (Prelabor Rupture of Membranes); PPH (Postpartum Hemorrhage); MSL (Meconium-Stained Liquor); IUGR (Intrauterine Growth Restriction); CPD (Cephalopelvic Disproportion)

Out of 344 newborns, 177 were male and 167 were females. Females have generally less birth weights and their placenta were also lighter than males (Figure 1).

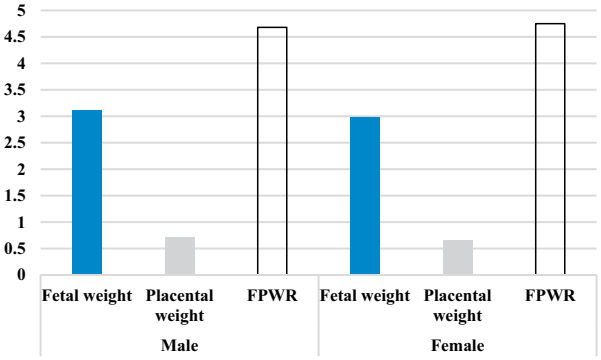

Figure 1: Comparison of Male and Female Placental Metrics

Fetal weight varied from 2 to 4.5 kg with a mean of 3.016 ± 0.445 kilograms whereas mean placental weight was 0.667 kg (SD = 0.175). Fetal placental weight ratio (FPWR) calculated from proportion of weight in kilograms of fetus to placenta, existed in the range of 2.54 to 7.91 (mean = 4.732 ± 1.082). Pearson 'r' of 0.209 showed weak positive correlation of gestational age and placental weight (Table 2).

Table 2: Correlation of Gender, Placental Weight, FPWR and Fetal Weight

Gender	N	Placental Weight Mean ± SD	FPWR Mean ± SD	Fetal Weight Mean ± SD
Male	177	0.70 ± 0.19	4.68 ± 1.13	3.11 ± 0.42
Female	167	0.65 ± 0.15	4.75 ± 1.01	2.97 ± 0.43

Increasing gestational age showed an increasing trend of placental weight but fetal placental weight ratio (FPWR) remained greatly unchanged with advancing gestational age (Figure 2).

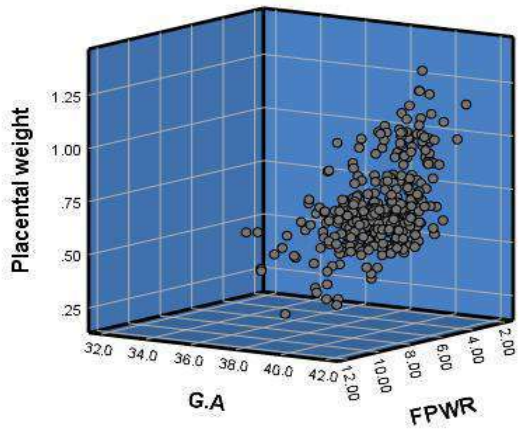

Figure 2: Correlation of Gestational Age Versus Placental Weight Fetal Placental Weight Ratio

Women with lowest BMI 16.40 kg/m2 delivered a 3.3 kg baby with fetoplacental weight ratio of 6.23g while Women with highest BMI 42.4 kg/m2 delivered a 3.6 kg baby with fetoplacental weight ratio of 5.29g (table 3). Maternal BMI exhibited a positive correlation with both birth weight and placental weight (p = 0.04 and 0.11 respectively). Placental weight was found positively correlated with oligohydramnios, PPH, obstetric cholestasis, and post-dated pregnancy and it had a negative correlation with PPROM, GDM and IUGR (p =0.13, p= 0.47, p=0.25). It suggested that PPROM itself may not directly influence these specific outcomes in the studied population. However, values were statistically insignificant with a mean placental weight of 674.90 ± 173.93g. The average ratio of birth weight to placental weight was 4.72 ± 1.07 g. There was no significant correlation between GDM and placental weight or birth weight ratios, it could suggest that GDM's impact on fetal growth might not be directly reflected in these ratios. hile IUGR affects birth weight, its impact on placental development or the ratio of placental to fetal weight is not straightforward (Table 3).

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Table 3: Association of Birth Weight, Placental Weight And Maternal BMI

Variables	BMI	Maternal Age	Fetal Weight	Placental Weight
Mean	26.214	28.07	3.043	0.674
Median	26.000	28.00	3.000	0.630
Standard Deviation	4.717	4.858	0.430	0.173
Minimum	16.40	19	2.0	0.28
Maximum	42.40	41	4.5	1.31

Table 4 cross-tabulated these variables to show the distribution of participants across different age and BMI groups, as well as their FPWR, and presents data on maternal age, Body Mass Index (BMI), and Fetoplacental Weight Ratio (FPWR) for a total of 344 participants. The majority of participants were in the 26-30 years' age group (139 participants), followed by 21-25 years (97 participants). Most participants fall in the 25.1-29 BMI group (105 participants), followed by the 18-23 BMI group (85 participants). The most participants have an FPWR of 4.1-5 (126 participants), followed by 5.1-6 (103 participants). Multivariate regression analysis was preceded by confirmation of homoscedasticity of data. Multivariate analysis predicted the higher placental weight in association with maternal anemia (standardized coefficient = 0.234, CI = 0.055 - 0.140, $p < 0.001$) while lower placental weights with pregnancy-induced hypertension [standardized coefficient = -0.180, CI = (-0.250) – (-0.065), $p = 0.001$). In multiple regression analysis using FPWR as the dependent variable, maternal anemia presented to be the sole highly significant predictor of placental weight [standardized coefficient = -0.277, CI = (-0.986) – (-0.448), $p < 0.001$], whereas PIH revealed no significance in predictability of placental weight ($p = 0.13$).

Table 4: Maternal Age, BMI and FPWR Cross-Tabulation

Variables	Categories (Years)	BMI Groups					Total
		<18.1	18-23	23-25	25.1-29	>29	
Maternal Age	<21	3	4	3	3	4	17
	21-25	1	25	19	35	17	97
	26-30	5	36	21	39	38	139
	31-35	0	17	7	16	22	62
	>35	1	3	6	12	7	29
Fetoplacental Weight Ratio	<3	1	5	2	0	2	10
	3.1-4	0	24	13	22	22	81
	4.1-5	7	32	19	36	32	126
	5.1-6	1	22	21	36	23	103
	>6	1	2	1	11	9	24
Total		10	85	56	105	88	344

DISCUSSION

Placental weights in this study exhibited a strong correlation with a limited number of risk factors, notably maternal anemia and pregnancy-induced hypertension. Among the 14 patients included in this research, there were cases of diabetes present, with 13 individuals diagnosed with gestational diabetes (GDM) and one with diabetes mellitus type 2. Analysis revealed that the average placental weights of diabetic patients compared to non-diabetic patients did not show a statistically significant variance, registering at 0.63 and 0.67 respectively ($p = 0.443$) within the study environment. These findings are compatible with the previous study reported that birth weight, birth weight/placental weight ratio (BPW) were higher in the diabetic group whereas placental weight and volume did not differ significantly in the two groups [17].These results can be projected to the study as the majority of the diabetics who participated had good glycemic control indicated by them in-hospital blood sugar monitoring. Maternal anemia, as operationalized within the parameters of the research, was characterized by a maternal hemoglobin level falling below 10 g/dL over the course of a trimester during pregnancy. The prevalence of anemia within the population under study stood at 22.6%, a finding that demonstrated a strong correlation with increased placental sizes when subjected to multivariate analysis. This observation aligns closely with the conclusions drawn in the investigation conducted by Godfrey and colleagues, thus reinforcing the consistency and reliability of study's results [18]. Several large-scale studies have shown a clear negative correlation between maternal hemoglobin levels and placental size. IDA and maternal nutrition may influence placental weight at birth [19]. However, patients with β-thalassemia minor and erythroblastosis had smaller placentas as well, indicating the possibility of placental insufficiencies arising in such cases. A large Japanese birth cohort study has also revealed that mean placental weight and placental weight to birth weight ratio was higher among smokers compared to non-smoking women [6]. This, again, can be an adaptive response of the placenta to meet the increased oxygen demand in a hypoxic in utero environment. Chronic fetal hypoxia caused by diminished placental blood flow results in a transformation of placental structure. Emerging indicators of placental performance, such as sFLIT1: PlGF (representing antiangiogenic soluble FMS-like tyrosine kinase-1 and placental growth factor), are presently being investigated. The examination of these markers, in addition to reduced ACGV (abdominal circumference growth velocity), can potentially function as prognostic tools for fetal growth restriction. The assessment of these parameters may aid in the early detection and management of FGR, thereby improving clinical outcomes for both the mother and the developing fetus [20]. Parameters investigated in placental morphometry through the use of ultrasonography and MRI studies consist of placental diameter, placental volume, placental quotient (which is the volume of the placenta divided by

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gestational age), and the placental thickness/volume ratio (PT/PV). A case-control research endeavor delving into the correlation between placental weight and surface area with fetal growth restriction found that a reduction of 10 units in placental weight and surface area resulted in a 21% increase (OR = 1.21, 95% CI, 1.08-1.44) and a 19% increase (OR = 1.19, 95% CI, 1.06-1.41) in the likelihood of FGR occurrence, respectively. This study underscores the significance of examining various morphometric parameters of the placenta and their impact on fetal growth and development, providing valuable insights into the intricate relationship between placental characteristics and adverse pregnancy outcomes such as fetal growth restriction [21]. In this study, increasing gestational age showed an increasing trend of placental weight but fetal placental weight ratio (FPWR) remained greatly unchanged with advancing gestational age whereas Richardson et al. revealed birth/placental weight ratio values increased with progressing gestational age [22]. Placental histopathology in cases with higher FPWR than anticipated in given gestational age revealed maternal vascular stromal lesions and villitis of unknown etiology. Another study conducted by Adeniran et al. showed that placental weight and birth weight increases with gestational age while placental to birth weight ratio (PBWR) increased till 36th week, declined from 37th to 42nd week with a rise from 43rd week [23]. This study demonstrated a positive correlation between maternal BMI and both placental weight and birth weight. Similar findings were observed by Sathasivum et al., Placental weight was positively correlated with birth weight and maternal BMI, but not with newborn sex [24]. However, unexpectedly in the study, mother with lowest BMI i.e. 16.40 kg/m2 delivered a 3.3 kg baby with fetoplacental weight ratio of 6.23g. Two cases of intrauterine fetal deaths were reported in the study where mean gestational age happened to be less than those with healthy pregnancies (38.913 versus 36.7; p = 0.039) but no relationship could be established between IUFD and FPWR or placental weight. However,previous study indicated that higher placental weight relative to birth weight was associated with an increased risk of neonatal death in preterm infants (aOR, 1.94; 95% CI, 1.40-2.70). For infants born at term, placental weight was not associated with neonatal death. Higher placental weight relative to birth weight was associated with an increased risk of neonatal mortality in term infants with congenital malformations (aOR, 1.82; 95% CI, 1.37-2.41)[25]. An economic history review in Barcelona concluded that even if placenta undergoes adaptive mechanisms to make up for the given conditions, it does less in neutralizing the effect of pathology behind it which explains why both higher and lower placental weights are associated with adverse early neonatal as well as later life outcomes despite the fact that they underwent adaptive morphological changes [26]. A retrospective crossectional study analysis of placental histopathological features and autopsies obtained from intrauterine fetal deaths revealed pathological characteristics in histopathology of 27% of placentas and usually existed with smaller placental sizes [27]. All parameters under study i.e. placental weight (PW), fetal weight (FW), and PW/FW were lower in pregnancies complicated by FGR owing to preeclampsia (PE) compared to FGR without PE or PE without FGR. Placental growth was slower in cases of oligohydramnios. PE in this analysis caused a significant decrease in placental weight. Similarly, the study found pregnancy-induced hypertension to significantly reduce placental weight and as a result decreases PW:BW [28]. In a prospective cohort study conducted at a tertiary care hospital, 430 untrimmed placentas from singleton pregnancies were collected and weighed. This study provided the values of placental weights in centiles at the given gestational ages in the population of Ireland. Although overall placental weight increases with gestational age, proportionately increasing birth weight causes BW:PW ratio to increase as well. Centile distribution presented in this study can be used to categorize placental weights and assess them accordingly. Another study conducted in Nepal shows that the ratio of placental weight to birth weight was 1:6.6 for 158 deliveries and calculated percentiles for birth weights in various placental weight groups [29]. The study is limited to a specific population from a tertiary care hospital in Pakistan, which may not be representative of broader or different populations. Further research is needed to validate the findings across diverse demographic and geographic settings. Expanding the research to include diverse populations from different regions and healthcare settings would enhance the generalizability of the findings. It is imperative for future investigators to ought to center on the examination of antenatal placental morphometry, delving deeper into this aspect to uncover valuable insights. Moreover, delve into the correlation between umbilical and uterine artery Doppler assessments and the BW/PW ratio, shedding light on potential associations. By pursuing these avenues of investigation, a more comprehensive understanding of the intricate dynamics at play in placental development and function can be achieved, leading to advancements in the field of maternal-fetal health. It is crucial for researchers to consider these recommendations to enhance the depth and breadth of knowledge in this critical area of study.

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CONCLUSIONS

Current study has revealed the average weight of placenta in Pakistani population and the result of adaptive changes in placenta in response to maternal medical conditions in pregnancy. The positive association between maternal anemia and higher placental weight suggests that anemia management during pregnancy is crucial. The negative association between pregnancy-induced hypertension and lower placental weights highlights the importance of closely monitoring and managing hypertension during pregnancy. The study's insights into the fetoplacental weight ratio (FPWR) can inform clinical practices related to assessing placental efficiency. Researchers were encouraged to conduct further studies pertaining to anatomical and functional modification in placenta in relation to complications of pregnancy

Authors Contribution

Conceptualization: MM, NF
Methodology: LK, SC, SA
Formal analysis: NWS, HUR
Writing, review and editing: MM, NWS, HUR, NF, LK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Prevalence of Awareness in Total Intravenous Anesthesia: A Cross-Sectional Study

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ABSTRACT

Intravenous anesthesia is a multifaceted condition characterized by hypnosis, forgetfulness, suppression of the stress reaction to stimuli, and the establishment of a tranquil surgical environment. **Objective:** To determine the prevalence of total intravenous anesthesia (TIVA) among patients in a tertiary care hospital. **Methods:** The research was a descriptive cross-sectional study. Total intravenous anesthesia was performed on 217 male and female patients aged 18-60 year. The patient's history in the first two post-operative days revealed intraoperative consciousness. Data were gathered, from 17th June, to November 30th, 2022. Statistical analysis was performed using SPSS version 23.0. **Results:** The study found that the prevalence of awareness during total intravenous anesthesia (TIVA) was 15.7%, with a higher occurrence in patients with metabolic equivalent test scores ≤4 (45.4%, $p < 0.001$) and those with a previous history of awareness (80.0%, $p < 0.001$). Gender (16.4% in males vs. 14.1% in females, $p = 0.654$), age (15.2% in ≤45 vs. 16.0% in >45 years, $p = 0.865$), BMI (17.2% in ≤23.0 vs. 13.9% in >23.0 kg/m^2, $p = 0.494$), diabetes (13.3% in diabetics vs. 16.6% in non-diabetics, $p = 0.558$), alcoholism (25.0% in alcoholics vs. 15.1% in non-alcoholics, $p = 0.360$), and ejection fraction (20.0% in ≤40% vs. 14.7% in >40%, $p = 0.403$) did not show statistically significant associations with awareness prevalence. **Conclusions:** Metabolic equivalent scores and a prior history of awareness were significant predictors of intraoperative awareness during TIVA, highlighting the importance of tailored preoperative evaluations.

INTRODUCTION

A form of general anesthesia known as Total Intravenous Anesthesia (TIVA) is one that only uses intravenous anesthetics [1, 2]. Traditionally, volatile agent-based anesthesia has predominated in general anesthetic treatment. Since the discovery of propofol in the 1970s, there has been a heightened interest in intravenous anesthesia [3]. TIVA can be provided using numerous techniques, including as intermittent bolus dose, manual syringe-type infusion pumps, and Target-Controlled Infusion (TCI) devices. Propofol, an intravenous anesthetic produced from alkylphenol, is the most efficacious medication for Total Intravenous Anesthesia (TIVA) [4]. Dr. Oliver Wendell Holmes reintroduced anesthesia, a reversible condition of insanity created for surgical and medicinal purposes, from the old Greek word [5]. General anesthesia uses breathed gases and intravenous medications to induce amnesia, trance, and immobilization. Benzodiazepines, opioids, and neuromuscular blockers are also used for anxiolysis, analgesia, and surgical accuracy. General anesthetics are unique in their capacity to produce unconsciousness, a key aim for surgical patient comfort and safety [6, 7]. Both volatile anesthesia and TIVA aid in preventing intraoperative consciousness, but volatile anesthesia provides superior control by continuously delivering agents into the airways. To maintain the proper depth of anesthesia, however, TIVA necessitates precise dosage changes. While BIS monitoring is not required for every

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patient, it is advised in high-risk situations, such as those undergoing complicated procedures or having a history of awareness. To lower the danger of awareness, a BIS value of less than 60 is often recommended [3]. Propofol (1.5-4.5 mg/kg/hr) is the primary agent, often used in combination with the opioid analgesic remifentanil (0.5-1 mcg/kg/hr), delivered at titrated doses and specified flow rates according on patient and procedural requirements [8]. Sevoflurane anesthesia is associated with common postoperative problems. As many as 80% of children undergoing surgeries with sevoflurane may have developing delirium [9]. Intraoperative awareness unintended consciousness under anesthesia is a serious psychological and medical issue. Rare, occurring in 1 in 750 general anesthetics, it is generally connected to neuromuscular blockade and poor dosage. Such occurrences emphasize the need for patient-specific anesthetic monitoring and dosage titration [10, 11]. Manage and Avoid Accidental Awareness (AWR), one of the rarest consequences of general anesthesia, whether with CIIA or TIVA. The patient self-reports this AWR after surgery due to poor anesthetic depth [12]. Depth of Anesthesia (DOA) monitoring or Conscious state monitoring with Cerebral Function Monitoring or Bi-spectral Index (BIS) can be used to monitor such incidence intraoperatively and advise therapy. A postoperative interview or questionnaire can measure forgetfulness, analgesia, and awareness at the time of surgery. That might happen 24–72 hours after surgery [13]. TIVA use may not increase despite advances. Lack of faith in its administration, insufficient training, and inaccessibility of key equipment, intraoperative awareness problems, and perceived greater cost are some factors [14, 15]. TIVA requires a longer duration to achieve adequate anesthetic levels compared to volatile agent-based anesthesia. The familiarity with volatile agent-based anesthetic may be a contributing factor to the reluctance of most anesthetists to utilize TIVA [16]. Intraoperative consciousness is rare but stressful, causing patients mental anguish and anesthesiologists professional, personal, and financial consequences. Total Intravenous Anesthesia (TIVA) awareness is important despite anesthetic advances reducing its frequency. Data on TIVA training and practices among Pakistani anesthetists were not discovered despite a thorough search of published literature utilizing databases including PubMed, Google Scholar, and regional medical publications. The Hayatabad Medical Complex, a tertiary care teaching hospital, was chosen for this study because of its large patient volume, sophisticated anesthetic facilities, and skilled anesthetists with TIVA administration experience.

The study concentrated on the modern comprehension of the pharmacological and molecular principles of general anesthetics, highlighting their mechanisms of action, clinical classification, and implications for anesthetic treatment at the Department of Anesthesiology, Hayatabad medical complex-MTI Peshawar.

METHODS

This descriptive cross-sectional was conducted in the operating theaters of Hayatabad medical complex-MTI Peshawar from 17th June to November 30, 2022. A total of 217 participants were included, determined using the WHO Sample Size Calculator, with a 17.5% incidence rate of consciousness under complete intravenous anesthetic, a 95% confidence interval, and a 5% margin of error [17]. Non-probability sequential sampling was employed. The study received ethical approval from the Hospital's Ethical Committee (Ref no. 748/HEC/BandPSC/2022) and the REU Department of CPSP Karachi. Written informed consent was obtained from all participants. Routine monitoring, including noninvasive blood pressure, electrocardiography (lead II), pulse oximetry, and end-tidal carbon dioxide monitoring, was established. Anesthesia induction was performed using propofol (1–2 mg/kg) with suxamethonium (100 mg) for rapid sequence induction, alongside pyrolate (0.2 mg), fentanyl (2 µg/kg) or nalbuphine (0.1–0.25 mg/kg), and ondansetron (4 mg) for antiemetic effects. Target-Controlled Infusion (TCI) with propofol (50–200 µg/kg/min) was used for maintenance, supplemented with muscle relaxants (rocuronium or cisatracurium) and incremental doses of fentanyl. BIS monitoring was utilized in high-risk surgical patients, including individuals with hypotension, elevated propofol demands, excessive BMI, decreased functional capacity, or at the patient's desire. Midazolam (2.5–5 mg) was used to reduce intraoperative consciousness when propofol dosages surpassed 6 µg/Kg. Ventilation was modified to sustain end-tidal CO_2 levels between 35 and 45 mmHg, while keeping airway pressures under 30 cm H_2O. The postoperative evaluation was performed within two days to test for intraoperative inadvertent awareness using structured interviews and standardized questionnaires. Data were evaluated utilizing SPSS version 23.0. Numerical data, including age, BMI, and operation time, were presented as means and standard deviations. Stratification was conducted to evaluate the correlation with intraoperative consciousness, followed by chi-square testing, with a significant threshold of $P < 0.05$. Results were displayed in graphical and tabular form.

RESULTS

A total 217 individuals were included in the study with an average participant age of 50 to 60 years and a standard deviation of 7.55 years, indicated a highly uniform age distribution. The mean weight was 75.14 ± 5.87 kg, and the average height was 172.89 ± 6.49 cm, indicated that the participants possess an average height relative to the

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general population. The computed Body Mass Index (BMI) was 25.20 ± 2.30 kg/m^2, categorized the average participant as overweight based on established BMI categories as shown in table 1.

Table 1: Mean of Patients According to Age, Weight, Height and BMI of Individual

Demographics and Baseline Characteristics	Mean ± S.D
Age (Years)	50.60 ± 7.548
Weight (Kg)	75.14 ± 5.874
Height (cm)	172.89 ± 6.493
BMI (Kg/m2)	25.20 ± 2.299

The study included 217 individuals, with 67.3% reporting as male and 32.7% as female. The age distribution was about comparable, with 48.4% of those aged 45 years or younger and 51.6% aged over 45 years. Concerning BMI, 53.4% exhibited a BMI ≤23.0 kg/m^2, whilst 46.6% shown a BMI >23.0 kg/m^2. Diabetes history was documented in 27.6% of patients, whereas 72.4% were non-diabetic. Only 5.5% of individuals indicated a history of alcoholism, whereas the majority (94.5%) remained abstinent. Cardiac assessments revealed that 18.4% of participants had an ejection fraction ≤40%, while 81.6% had an ejection fraction >40%. The metabolic equivalent test showed that 10.1% scored ≤4, whereas 89.9% scored >4. Regarding intraoperative awareness, 4.6% had a history of awareness, and 15.7% experienced awareness during anesthesia in the study, while 84.3% reported no such event shown in the table 2.

Table 2: Demographic and Clinical Characteristics of Study Participants (n = 217)

S. No.	Variables	Category	Frequency (%)
01	Gender	Male	146 (67.3%)
		Female	71 (32.7%)
02	Age	≤45 Years	105 (48.4%)
		>45 Years	112 (51.6%)
03	BMI (Kg/m^2)	≤23.0	116 (53.4%)
		>23.0	101 (46.6%)
04	Diabetes	Yes	60 (27.6%)
		No	175 (72.4%)
05	Alcoholism	Yes	12 (5.5%)
		No	205 (94.5%)
06	Ejection Fraction	≤40	40 (18.4%)
		>40	167 (81.6%)
07	Metabolic Equivalent Test	≤4	22 (10.1%)
		>4	195 (89.9%)
08	History of Awareness	Yes	10 (4.6%)
		No	207 (95.4%)
09	Awareness	Yes	34 (15.7%)
		No	183 (84.3%)

The awareness rates for both males and females (16.4% and 14.1% reported being aware), and the p-value of 0.654 shows that there was no significant difference between the sexes. Awareness was reported by 15.2% of patients aged ≤45 years and 16.0% of those aged >45 years, with a p-value of 0.865, indicating no significant age-related variations in awareness. Concerning BMI, 17.2% of patients with a BMI ≤23.0 kg/m^2 and 13.9% of patients with a BMI >23.0 kg/m^2 expressed awareness, with a p-value of 0.494 signifying no significant correlation between BMI and awareness. The history of diabetes shown no significant correlation, with 13.3% of diabetic patients and 16.6% of non-diabetic patients being aware, as indicated by a p-value of 0.558. In cases of alcoholism, awareness was noted in 25.0% of individuals with a history of alcoholism, in contrast to 15.1% among those without such a history; nonetheless, the p-value of 0.360 indicates an absence of a meaningful correlation. Ejection fraction levels exhibited comparable tendencies, with 20.0% of patients with an ejection fraction ≤40% experiencing consciousness, in contrast to 14.7% with an ejection fraction >40%, and a p-value of 0.403 signifying no significant difference. Nonetheless, a prior history of consciousness shown a robust correlation, with 80.0% of patients with such a history reporting awareness, in contrast to just 12.6% of those without, yielding a p-value of <0.001, signifying statistical significance. Finally, metabolic equivalent tests demonstrated a notable correlation with consciousness, as 45.4% of those with a MET ≤4 reported awareness, in contrast to just 12.3% of those with MET >4, yielding a p-value of <0.001 as shown in the table 3.

Table 3: Stratification of Awareness across Demographic and Clinical Variables in Patients Undergoing Total Intravenous Anesthesia

Variables	Category	Awareness		Total Frequency (%)	p-Value
		Yes Frequency (%)	No Frequency (%)		
Patient Gender	Male	24 (16.4%)	122 (83.6%)	146 (100.0%)	0.654
	Female	10 (14.1%)	61 (85.9%)	71 (100.0%)	
Age (Years)	≤45	16 (15.2%)	89 (84.8%)	105 (100.0%)	0.865
	>45	18 (16.0%)	94 (84.0%)	112 (100.0%)	
BMI (kg/m^2)	≤23.0	20 (17.2%)	96 (82.8%)	116 (100.0%)	0.494
	>23.0	14 (13.9%)	87 (86.1%)	101 (100.0%)	
Diabetes	Yes	08 (13.3%)	52 (86.7%)	60 (100.0%)	0.558
	No	26 (16.6%)	131 (83.4%)	157 (100.0%)	
Alcoholism	Yes	03 (25.0%)	09 (75.0%)	12 (100.0%)	0.360
	No	31 (15.1%)	174 (84.9%)	205 (100.0%)	
Ejection Fraction	≤40%	08 (20.0%)	32 (80.0%)	40 (100.0%)	0.403
	>40%	26 (14.7%)	151 (85.3%)	177 (100.0%)	
Previous History of Awareness	Yes	08 (80.0%)	02 (20.0%)	10 (100.0%)	<0.001
	No	26 (12.6%)	181 (87.4%)	207 (100.0%)	
Metabolic Equivalent Tests	≤4	10 (45.4%)	12 (54.6%)	22 (100.0%)	<0.001
	>4	24 (12.3%)	171 (87.7%)	195 (100.0%)	

DISCUSSION

This study's findings offer significant insights into the variables affecting intraoperative consciousness,

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emphasizing numerous demographic and clinical features that may contribute to its incidence. The frequency of Total Intravenous Anesthesia (TIVA) in the study group was quite low, with only 15.7% of patients experiencing consciousness during the operation [18]. Another research indicated that 1.8% of individuals had consciousness under anesthesia with postoperative recall. Patients exhibiting potential consciousness will also be incorporated into the analysis, elevating the incidence of awareness under anesthesia to 0.78% [19-21]. Notably, despite the little prevalence of TIVA utilization, a significant majority of participants (88.9%) expressed a desire for increased application of TIVA, while 99.3% regarded it as a crucial competency to acquire. Comparable results were reiterated by Arevalo *et al.,* in 2016 [22]. Other domains in which TIVA was perceived as superior than volatile anesthesia encompassed: environmental pollution (89.5%), diminished Postoperative Nausea and Vomiting (PONV) (86.9%), and decreased emerging delirium (75.2%). This suggested that the theoretical understanding of the indications and advantages of TIVA is adequate in the department [2, 23]. All patients were anesthetized with the Sleep-Awake-Sleep method (SAS). Dexmedetomidine was primarily utilized for conscious sedation. The Bispectral Index monitor (BIS) was employed to assess sedation depth, maintaining levels between 70 and 85 during the sedative period. All patients had effective intraoperative neurological monitoring, stimulation, and electrode implantation. The total duration of anesthesia exhibited considerable variation among the participants. The maximum duration was 600 minutes. None of the patients experienced any intraoperative incidents associated with anesthetic treatment [24]. According to the study, TIVA made patients more conscious of the hospital during their procedure (95% CI: 1.8–3.4, $p < 0.001$) is compared parallel findings by Yu H and Wu D showed that patients serviced by CIIA had lower awareness rates than those who got TIVA [25]. Compared to the 8.8% rate reported in the Priyadharsini *et al.,* in 2023 studied that the patient group's overall rate of patient consciousness during surgery was 15.7% (95% CI: 12.1%–19.3%) [26]. The direct expenses of TIVA are typically regarded as superior to those of volatile agent-based anesthesia (27). Although the department operates under budget constraints in a poor nation, only 56.9% of participants in the research identified cost as a barrier [28]. Likewise, several further research indicated that cost was perceived as a minor impediment to usage relative to other considerations [29]. The rationale for this may be that the perceived advantages of TIVA, including decreased PONV and enhanced patient satisfaction, warrant its application despite the increased expenses [30]. This confirms that the study's findings may be applicable to daily life. Administering an amnestic drug before to surgery and closely monitoring stress reactions indicative of a lighter anesthetic level is essential for avoiding alertness. This study has some limitations. The awareness interview was conducted only once. Owing to logistical constraints, it was unable to follow up on patient's post-hospital release. Research indicates that doing numerous interviews at different time intervals enhances the detection rate of awareness. Certain individuals can recall consciousness soon post-surgery, but others may not recognize it until month's after.

CONCLUSIONS

The study's findings showed that the frequency of intraoperative consciousness when utilizing TIVA is determined by certain hazards related to patient profiles. According to research, people with restricted physical ability or prior consciousness experiences need special attention when receiving expert anesthetic treatment. Although TIVA does not allow for direct anesthetic depth monitoring, individual medication dosage strategies in conjunction with depth-of-anesthesia monitoring techniques should lessen the likelihood that patients may become conscious throughout the treatment. Future studies should concentrate on this subject in order to determine long-term impacts and the most effective TIVA treatments that improve patient safety.

Authors Contribution

Conceptualization: MT
Methodology: MT, K
Formal analysis: BZ, MAK, K, FAQ
Writing, review and editing: BZ, MAK, SR, K, FAQ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

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Impact of Antioxidants in Preventing Dental Caries and Erosion

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ABSTRACT

Dental erosion and caries are common oral health problems with serious consequences. Due to the increased intake of acidic foods and beverages, dental erosion is becoming more widely acknowledged as a serious oral health concern. **Objectives:** To assess the anti-oxidant (green tea extract, vitamin C, and vitamin E) efficaciousness in reducing dental caries and erosion. To look for changes in the scores for the DMFT (Decayed, Missing, and Filled teeth) and BEWE (Basic Erosive Wear Examination). **Methods:** A quasi-experimental study with groups (using green tea extract, vitamin C, and vitamin E, respectively) were formed from the 120 participants. BEWE, DMFT, and baseline demographics were noted. Salivary samples were examined for oxidative stress markers and antioxidant levels, and patients receiving certain treatments were assessed for changes in scores. A paired t-test was used to assess significance statistically. **Results:** All therapy groups showed significant declines in BEWE. DMFT scores slightly increased in all therapy groups as compared to the control group. The DMFT for Group A (vitamin C) increased from 4.2 ± 1.3 to 4.3 ± 1.1, Group B from 4.0 ± 1.4 to 4.0 ± 1.2, and Group C from 4.1 ± 1.2 to 4.2 ± 1.0, all with p-values of <0.001. The treatment groups saw almost similar BEWE scores as compared to the control group. **Conclusion:** It was concluded that antioxidants are helpful in the prevention of dental caries and erosion.

INTRODUCTION

Globally both dental caries and erosion are serious problems that lead to significant health issues. Multiple factors are thought to play a role in dental caries such as loss of tooth enamel by acids that are produced upon fermentation of carbohydrates by bacteria present in the mouth and leading to cavities if left untreated [1]. Conversely, dental erosion refers to the gradual loss of tooth structure brought on by the chemical breakdown of non-bacterial acids, such as those found in food or gastric reflux. If treatment is not received for either problem, serious side effects such as infection, discomfort, and tooth loss may occur [2, 3]. Dental caries is one of the most common chronic illnesses in the world; according to WHO estimates, 2.3 billion adults and 530 million children will at some point in their lives suffer from it [4]. Due to the increased intake of acidic foods and beverages, dental erosion is becoming more widely acknowledged as a serious oral health concern, while being less prevalent. Young adults and kids are the group most frequently afflicted [5]. Caries can lead to feelings of worthlessness, impair nutritional status, cause an enormous financial strain because of the considerable cost of therapy, and disrupt interpersonal social interactions [6]. Investigators have been trying to figure out how oxidative stress-induced damage causes dental problems such as dental caries and eroding [7]. These dental issues are aggravated as a consequence of oxidative damage, which is an imbalance between the synthesis and eradication of reactive oxygen

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species (ROS) [8, 9]. The damage caused by free radicals can be addressed through a class of molecules that includes enzymatic antioxidants such as catalase and superoxide dismutase and non-enzymatic antioxidants such as vitamins and flavonoids [10]. Several studies have looked into the significance of antioxidants that serve in halting dental caries and erosion. They are important in maintaining the health of dental tissues. Among the effects are the prevention of cell membrane damage by vitamin E and the creation of collagen by vitamin C. Gum and periodontal ligament health are preserved partially by these actions [11, 12]. The constituents present in green tea include catechin which also leads to improving dental health by reducing cariogenic bacteria [13]. Although the exact processes behind these advantages are currently undetermined numerous in vitro and animal studies have studied the use of antioxidants in the avoidance of dental decay and erosion. High-quality clinical trials are still required to investigate the safety and efficacy of antioxidants [14, 15].

This study aims to see the efficacy of antioxidants Vitamin C, Vitamin E and green tea extract against dental caries and erosion.

METHODS

This quasi-experimental study was conducted over 12 months from June 2023 to May 2024. Participants were recruited from dental clinics and college campuses. Ethical approval was obtained from the Institutional Review Board (IRB) of the Shahida Islam Medical Complex, Lodhran IRB no: SIMC/ET.C./10006/23. A total of 120 participants aged 18-35 years were enrolled in the study. Inclusion criteria included having all-natural teeth intact and good general health. The included participants were prescribed vitamin C (ascorbic acid) mouthwash, vitamin E (alpha-tocopherol) gel, green tea extract rinse or placebo mouthwash randomly for at least six months. Exclusion criteria were smoking, systemic diseases affecting dental health, and the use of medications influencing salivary flow. Participants were assigned into four groups depending upon the prescribed treatment, each receiving a different antioxidant treatment: Group A: Vitamin C (ascorbic acid) mouthwash twice a day for 1 minute, Group B: Vitamin E (alpha-tocopherol) gel twice a day, Group C: Green tea extract rinse twice a day for 1 minute and Control Group: Placebo mouthwash (with alcohol). After ethical approval and obtaining informed consent from each participant, baseline dental examinations were conducted, including assessments of dental caries and erosion using standardized indices of Decayed, Missing, and Filled Teeth (DMFT) and Basic Erosive Wear Examination (BEWE). Saliva samples were collected to measure antioxidant levels and oxidative stress markers. Since they were not part of the objectives, therefore they were not reported in the results. Participants were instructed to use their assigned treatment twice daily after brushing their teeth for six months. Follow-up assessments were conducted at three and six months, with final evaluations at the end of the study period. i.e. six months. Patients were given a checklist from day 1 to 6 months for filling the use of their designated treatment regimen. The checklist was reviewed on follow-up. For calculation of DFMT scores, each decayed, missing or filling of each tooth was given a score of 1. BEWE score determined the level of tooth wear and tear. The criteria for the BEWE score are as follows: No erosive tooth wear (ETW): 0 scores; Initial loss of surface texture: 1 score; Distinct defect; hard tissue loss involving <50% of the surface area: 2 scores; Hard tissue loss involving ≥50% of the surface area: 3 scores. They are summed to obtain a cumulative score which is as follows: No ETW: 0 to 2; Low ETW: 3-8; Medium ETW: 9-13; High ETW: ≥ 14. Primary outcomes included changes in DMFT and BEWE scores. Data were analyzed using SPSS version 23.0, with significance set at $p<0.05$ after applying paired t-test at baseline and 6 months after treatment.

RESULTS

A total of 120 participants were divided equally into four groups: Group A, Group B, Group C, and a control group, each comprising 30 individuals. The mean age of participants in Group A was 25.3 years ± 4.2, in Group B was 24.8 years ± 3.9, in Group C was 25.1 years ± 4 and in the control group was 24.7 years ± 4.0. The gender distribution was relatively balanced across all groups, with Group A consisting of 14 male and 16 female, Group B comprising 13 male and 17 female, Group C including 15 male and 15 female, and the control group having 14 male and 16 female. The baseline demographics of the participants included in the study are presented in table 1.

Table 1: Baseline Demographics of Participants Included in the Study (n=120)

Groups	Mean Age (Years ± SD)	Gender	
		Male	Female
Group A (n=30)	25.3 ± 4.2	14	16
Group B (n=30)	24.8 ± 3.9	13	17
Group C (n=30)	25.1 ± 4.1	15	15
Control Group (n=30)	24.7 ± 4.0	14	16

The BEWE scores at baseline were similar across the groups, with Group A at 7.1 ± 1.9, Group B at 7.0 ± 1.8, Group C at 7.2 ± 1.7, and the control group at 7.3 ± 1.8. After six months, BEWE scores stabilization were observed in the treatment groups: Group A scores were 7.2 ± 1.5, Group B scores were 7.2 ± 1.4, and Group C scores were 7.3 ± 1.6, all with insignificant p-values of 0.66, 0.08 and 0.32 respectively. In contrast, the control group showed a significant change from 7.3 ± 1.8 to 7.7 ± 1.6 with a $p<0.001$.

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Due to the anti-oxidant effects of the prescribed regimens such as vitamin C promoting collagen synthesis, aiding repair of enamel and dentin, vitamin E protecting oral tissues from oxidative damage by preserving integrity, coupled with green tea's anti-inflammatory properties, possibly behind the reasons why BEWE scores were found to be stable. The changes in BEWE and DMFT scores from baseline to six months for each group are shown in table 2.

Table 2: Changes in BEWE and DMFT Scores at Baseline vs 6 Months(n=120)

Groups	BEWE (Baseline) Mean ± SD	BEWE (6 Months) Mean ± SD	p-Value	DMFT (Baseline) Mean ± SD	DMFT (6 Months) Mean ± SD	p-Value
Group A (n=30)	7.1 ± 1.9	7.2 ± 1.5	0.66	4.2 ± 1.3	4.3 ± 1.1	<0.001
Group B (n=30)	7.0 ± 1.8	7.2± 1.4	0.08	4.0 ± 1.4	4.0 ± 1.2	<0.001
Group C (n=30)	7.2 ± 1.7	7.3± 1.6	0.32	4.1 ± 1.2	4.2 ± 1.0	<0.001
Control Group (n=30)	7.3 ± 1.8	7.7 ± 1.6	<0.001	4.3 ± 1.3	5.1 ± 1.2	0.07

The DMFT scores exhibited a slight increase in the treatment groups over the six months while in Group B remained the same. Group A DMFT score slightly increased from 4.2 ± 1.3 to 4.3 ± 1.1, Group B score remained the same from 4.0 ± 1.4 to 4.0 ± 1.0 and Group C increased from 4.1 ± 1.2 to 4.2 ± 1.0, all with p<0.001. The control group showed a greater increase as compared to treatment groups from 4.3 ± 1.3 to 5.1 ± 1.2, which was not statistically significant with a p-value of 0.07.

DISCUSSION

The results of this research show that antioxidants such as vitamin C, E and green tea extract substantially prevented dental caries and improved dental erosion in comparison to a placebo mouthwash. The study further demonstrated the potential role of these anti-oxidants in maintaining oral health. The role of anti-oxidants in reducing oxidative stress through neutralization of free radicals was highlighted. The findings are in line with other research which underscores the protective anti-oxidant effect in dental erosions and caries [16]. Anti-oxidants have been shown to reduce oxidative stress through inhibition of cariogenic oral bacterial growth and enhance dental health [17]. Research demonstrated anti-oxidants' anti-microbial properties, especially in inhibition of cariogenic bacteria [18]. Another study reported catechism in green tea to have strong anti-bacterial activity, especially towards S. mutants, which is known to be the primary pathogen involved in the occurrence of dental caries [19]. This is by this study where erosive scores were improved and dental caries were prevented. Likewise, a study showed inhibition of oral bacterial growth and reduction in plaque formation was observed after treatment with vitamin C [20]. This significantly reduced caries formation. similar to this study where BEWE scores were almost the same in treatment groups indicating erosion repair and constant DMFT score in the Vitamin C treatment group. For instance, studies have shown that vitamin E, a potent lipid-soluble antioxidant, can protect cell membranes from oxidative damage and reduce inflammation in gingival tissues. This is in line with the findings of a study that reported vitamin E supplementation decreased oxidative stress in patients with periodontal disease [21]. The stabilization of BEWE scores in Group B, which used a vitamin E gel, further confirms the efficacy of alpha-tocopherol in protecting dental tissues from erosion. When multiple antioxidants are combined, they exhibit synergism, which may boost their protective value. A study by Sardari showed vitamin C and E together revealed higher protection than if used independently, and BEWE scores decreased substantially. This indicates that combined use is better at providing advantages, though our study did not specifically assess combination strategies [22]. Based on the latest studies, there may be considerable therapeutic advantages arising from substantial reductions in tooth cavities and erosion. Mouthwashes, gels, and rinses that include antioxidants should be part of your daily oral hygiene routine. By lowering oxidative damage and suppressing the development of toxic cariogenic bacteria, they can provide enhanced defence [23]. Mouthwashes containing vitamin C can have beneficial effects for those who have illnesses or other eating habits that reduce salivation and create dry mouth [24]. Vitamin E gels may be useful for a few additional health conditions including gastroesophageal reflux disease (GERD), which exposes the teeth to acidic environments regularly [25]. Antioxidant-rich food and oral hygiene items should be promoted to the public considering that they can contribute to lowering the prevalence of dental caries and erosion. The public should get awareness about the beneficial effects of these items and initiatives should be undertaken in various public meetings, and talks about different products that contain antioxidants should be included. Green tea, fruits, and vegetables should be utilized because of their high antioxidant content.

CONCLUSIONS

It was concluded that by the consumption of oral medications and changes in diet, this study has shown how antioxidants are helpful in the prevention of dental caries and erosion. The results of this study offer a better evaluation of the many physiological and anatomical causes behind tooth caries. The results of the study might be useful to medical professionals, who can employ oral care products and antioxidants to prevent dental problems. Additional research is required to expand on

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these findings and examine the broader implications for dental practice and public health policy.

Authors Contribution

Conceptualization: SA
Methodology: SUH
Formal analysis: GP
Writing review and editing: RS, GP, SLA, AZ

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Original Article

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Prevalence of Skin Changes and Their Management After Bariatric Surgery: A Prospective Study at International Metabolic and Bariatric Center

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ABSTRACT

Numerous skin disorders, including ulcerated necrobiosis lipoidica diabeticorum, hidradenitis suppurativa, intertrigo, and psoriasis, have shown improvement post-bariatric surgery. On the other hand, there have been reports of the occurrence of unfavourable skin disorders, most of which are related to nutritional deficiencies, such as those of iron, folic acid, vitamins, and trace elements. **Objectives:** To determine the prevalence of skin changes and diseases following bariatric surgery at our centre and their management strategies. **Methods:** This longitudinal study was carried out from April 2021 to March 2023. Patients were eligible for inclusion if they were aged 18 years or older, and had undergone one of the following bariatric procedures: sleeve gastrectomy, Roux-en-Y gastric bypass, or mini gastric bypass. Baseline clinical and demographic information was documented, At frequent follow-up intervals postoperative data were collected to record any new onset or changes in skin problems. **Results:** A total of 1656 patients who had undergone bariatric surgery were included. During the 12-month follow-up period, 1292 (78%) of patients experienced skin changes. Excess skin was the most prevalent type of skin alteration, affecting 1026 (62%) of patients, especially in the arms 745 (45%) and abdomen 1159 (70%). **Conclusions:** It was concluded that significant dermatological challenges are faced by patients post bariatric surgery and a holistic and multidisciplinary approach should be incorporated in managing these issues. By addressing both aesthetic and functional concerns, healthcare providers can enhance patients' overall satisfaction and quality of life.

INTRODUCTION

The most effective and widely used treatment for morbid obesity is bariatric surgery, which significantly improves several comorbid illnesses linked to obesity [1]. The literature on the side effects of bariatric surgery is extensive. Among the often reported ones are nutritional deficiencies, haemorrhage, infections, stomach leaks, , gastrointestinal leaks, strictures, and wound hematomas [2]. The effects of obesity on the skin are well-known. It is linked to changes in the composition and structure of collagen, increased transepidermal water loss, a rise in skin infections, and inadequate wound healing. In addition, the majority of obese patients experience hirsutism, acne, and occasionally androgenetic alopecia as a result of increased androgen production brought on by elevated insulin levels [3]. Furthermore, there are advantages and disadvantages to bariatric surgery for the skin. Numerous skin disorders, including ulcerated necrobiosis lipoidica diabeticorum, hidradenitis suppurativa, intertrigo, and psoriasis [4], have shown improvement. On the other hand, there have been reports of the occurrence of unfavourable skin disorders, most of which are related to nutritional deficiencies, such as those of iron, folic acid, vitamins, and trace elements [5]. Moreover, severe weight reduction also causes skin laxity [6]. Due to the significant amount of superfluous skin, the majority of the patients are likely to exhibit adverse consequences after undergoing bariatric surgery and experiencing significant weight loss [7]. Due to the extra skin and tissue after weight loss, fungal infections, dermatitis, pruritus, excessive sweating, and hygiene problems are common post-bariatric surgery [8].

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Furthermore, anomalies in the extracellular matrix and skin of post-bariatric patients are common compared to normal skin tissue, the extracellular matrix in the patients' cases is loose. The tissue collected from striae and normal-appearing skin showed signs of elastin deterioration, collagen resorption, inflammation, and scarring [9]. Different skin conditions post-bariatric surgery also include Bowel-associated dermatosis–arthritis syndrome (BADAS), psoriasis, nutritional deficiency dermatoses and alopecia [10]. Prevention and management of these skin abnormalities are of paramount importance and need a multidisciplinary approach. An important factor in post-bariatric patients' care is nutrition. To identify any nutritional deficits, a thorough nutritional study should be carried out during the preoperative tests, and a suitable intervention should be planned. Additionally, patients undergoing significant weight reduction and body contouring should consider the possibility of "induced malnutrition," which can impact surgical recovery, scar quality, and the likelihood of complications [11]. All patients must have a clinical investigation for indications of nutritional inadequacies to prevent and/or manage the skin conditions associated with bariatric surgery [12]. Although alterations in the post-bariatric skin are acquiring attention worldwide, there is relatively little evidence from Pakistan regarding these changes and treatment. The different kinds and extents of skin issues following weight loss surgery may also vary with each region's special genetic susceptibility to these changes along with dietary and healthcare accessibility patterns., Most of the current research focuses on Western populations, which leaves a question of how well the results can be applied to patients in Pakistan.

This study aims to assess current management practices in a Pakistani tertiary care bariatric hospital and provide region-specific statistics on the prevalence of skin alterations.

METHODS

This longitudinal study was carried out at the International Metabolic and Bariatric Center in Peshawar, from April 2021 to March 2023. The Institutional Review Board (IRB) granted ethical approval (reference no 103/DME/AMC), and each subject provided informed consent. A total of 1656 patients who underwent bariatric surgery at the centre were included in the study utilizing non-probability convenience sampling calculated through open epi software. Patients were eligible for inclusion if they were aged 18 years or older, had undergone one of the following bariatric procedures: sleeve gastrectomy, Roux-en-Y gastric bypass, or mini gastric bypass, and were willing to participate in follow-up assessments for a minimum of 12 months post-surgery. Exclusion criteria included patients with pre-existing dermatological conditions, previous bariatric surgery, or any history of significant comorbidities that could affect skin integrity. Patient medical records, in-person physical examinations, and patient-reported results were all used to gather data. Baseline clinical and demographic information was documented, including age, sex, BMI, kind of bariatric surgery, and skin condition before surgery. Data were collected throughout the follow-up period of one year, postoperative data were collected to record any new onset or changes in skin problems, such as the appearance of striae, rashes, infections, or excess skin. At every follow-up visit, skilled medical personnel conducted physical examinations. The existence and severity of skin changes which were divided into groups including excess skin, striae distensae, intertriginous dermatitis, and surgical scars were evaluated using standardized methods. With the consent of the patient, photos were taken utilizing a standard setup to guarantee consistency and record any evident skin modifications. Patients presenting with skin changes were offered a variety of management options based on the severity and type of changes observed. Treatment modalities included topical applications, oral medications, lifestyle modifications, and, in some cases, referral for plastic or reconstructive surgery. The choice of treatment was determined collaboratively by the attending bariatric surgeon, a dermatologist, and the patient. All treatments and patient adherence were documented. The frequency of various skin alterations following bariatric surgery and the efficacy of the management techniques used were the main end measures. A validated patient satisfaction survey was used to measure the secondary outcomes, which included patient satisfaction with the appearance and functional results of their skin following surgery. Data analysis was performed using statistical software SPSS version 26. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. The prevalence of skin changes was calculated as a proportion of the total number of patients. Comparative analyses were conducted to evaluate differences in the occurrence of skin changes based on variables such as age, sex, BMI, and type of surgery. The effectiveness of different management strategies was assessed using appropriate statistical tests, with a p-value of <0.05 considered statistically significant.

RESULTS

In all, 1656 patients who had undergone bariatric surgery at the International Metabolic and Bariatric Center between April 2021 and March 2023 were included in this study. 530 (32%) of the patients were female and 1126 (68%) were male, with a mean age of 42 years (range: 18–65 years). The majority of patients 775 (47%) had mini gastric bypass followed by sleeve gastrectomy 529 (32%) and 352 (21%) Roux-en-Y gastric bypass (RYGB). The mean preoperative

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BMI was 42 kg/m^2 (range: 35–38 kg/m^2). At 12 months postoperatively, the average percentage of excess weight loss was 65% (Table 1).

Table 1: Demographic and Clinical Characteristics

Characteristics	Values
Total Patients	1656
Mean Age (Years)	42
Gender Distribution	
Female	530 (32%)
Male	1126 (968%)
Bariatric Procedures	
Mini Gastric Bypass	775 (47%)
Sleeve Gastrectomy	529 (32%)
RYGB	352 (21%)
BMI	
Mean Preoperative BMI	42 kg/m^2
Percentage of Weight Loss	65%

During the 12-month follow-up period, 1292 (78%) of patients experienced skin changes. Excessive skin was the most prevalent type of skin alteration, affecting 1026 (62%) of patients, especially in the arms 745 (45%) and abdomen 1159 (70%). In 662 (40%) of cases, there were striae distensae, and in 464 (28%) of cases, intertriginous dermatitis was observed, mostly in regions where skin folds were present. 911 (55%) of patients had surgical scars, which were a common postoperative observation. However, at one year, the majority of scars were reported to be small and well-healed. Alopecia was reported in 596(36%) of the patients. A total of 47% of patients suffering from psoriasis pre-surgery reported improvements in their symptoms (Table 2).

Table 2: Prevalence and Types of Skin Changes

Types of Skin Change	n (%)
Excess Skin	1026 (62%)
Striae Distensae	662 (40%)
Intertriginous Dermatitis	464 (28%)
Surgical Scars	911 (55%)
Alopecia	596 (36%)

794 (48%) of the patients who presented with alterations in their skin were treated non-surgically using topical lotions and lifestyle changes. In 662(40%) instances, topical therapies were utilized, mostly for the management of striae and intertriginous dermatitis. These treatments included moisturizers and anti-inflammatory creams. 199 (12%) of patients received prescriptions for oral drugs, primarily for the management of infections in cases of dermatitis. A referral for plastic or reconstructive surgery was necessary for 323 (25%) of the patients, and in 129 (10%) of those situations, operations like abdominoplasty were carried out. 1408 (85%) of patients reported regular topical application use and compliance with lifestyle modifications, indicating a high level of patient adherence to the prescribed therapy. Most patients said they were happy with how their treatments had worked out. According to the Body-Q questionnaire, 1159 (72%) of patients were happy with how their skin looked and worked after surgery, whereas 497 (28%) were not, mostly because of residual extra skin or the presence of scars (Table 3).

Table 3: Management of Skin Changes and Patient Satisfaction

Treatment Modality	n (%)
Topical Applications	662 (40%)
Oral Medications	199 (12%)
Plastic/Reconstructive Surgery	129 (10%)
Patient Satisfaction	1159 (72%)
Dissatisfied	497 (28%)

A comparative analysis showed that individuals with a higher preoperative BMI had a considerably greater prevalence of extra skin (p=0.01), whereas younger patients had a higher prevalence of striae distensae (p=0.03). The severity of skin problems was successfully reduced by non-surgical treatments, especially topical applications; after six months of treatment, 994 (60%) of patients reported improvement (p=0.04). A large percentage of patients 1411 (85%) expressed satisfaction with the results of surgical procedures for extra skin (p=0.01)(Table 4).

Table4: Association among Different Variables

Findings	Subgroups	Prevalence n (%)	Statistical Significance (p-value)
Prevalence of Excess Skin by BMI	Higher Preoperative BMI	1026 (62%)	p=0.01
Prevalence of Striae Distensae by Age	Younger Patients	662 940%)	p=0.03
Effectiveness of Non-Surgical Treatments	Improvement After 6 Months	994 (60%)	p=0.04
Satisfaction with Surgical Interventions	Post-Surgery Satisfaction	1411 (85%)	p=0.01

DISCUSSION

This study investigated the prevalence and types of skin changes in patients following bariatric surgery at the International Metabolic and Bariatric Center, along with various management strategies and their effectiveness. Literature has reported that skin changes after bariatric surgery are mainly due to rapid weight loss, which can exceed the skin's ability to retract, resulting in loose or sagging skin, especially on the abdomen, arms, and thighs. Nutritional deficiencies in protein, vitamin C, and zinc, common post-surgery, further weaken skin structure and delay healing, contributing to stretch marks and dermatitis. These factors highlight the need for ongoing skin and nutrition management to support patient recovery and satisfaction [13]. Our findings reveal that 78% of patients experienced skin-related issues within 12 months

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post-surgery, with excess skin (62%), striae distensae (40%), and intertriginous dermatitis (28%), alopecia 298 (18%) being the most common. Additionally, 55% reported postoperative scars, underscoring the impact of rapid weight loss on skin health and patient satisfaction. The findings of our study are consistent with another study which highlights the high prevalence of excess skin, particularly in areas like the arms and abdomen, following rapid weight loss. This excess skin, more common in patients with higher preoperative BMIs (p=0.01), can create functional issues in hygiene and cause discomfort. The study also reported that patients achieving at least 50% excess body weight loss (EBWL) showed improved skin conditions, with a reduced prevalence of acanthosis nigricans, keratosis pilaris (aOR=0.21, p=0.02), and pebble fingers (aOR=0.09, p=0.04). However, a higher incidence of alopecia was noted, suggesting post-surgical nutritional challenges [6]. The findings of our study showed that striae distensae 662 (40%) and intertriginous dermatitis 464 (28%) were also common post-surgery, with a higher prevalence of striae in younger patients (p=0.03). These findings are from a study which reported the increased prevalence of acquired perforating dermatosis [14]. Another study supported our findings and showed an even greater prevalence of stria in 30 (97%) of the patients along with acanthosis nigricans in 29 (93%) patients [15]. Alopecia was reported in 596(36%) of the patients in our study. The literature has reported the rates of alopecia post-bariatric surgery as between 12 to 93%. Reports of telogen effluvium linked to iron and zinc nutritional deficiencies typically start six months following surgery [16]. These skin issues can impact patients' quality of life, emphasizing the need for regular dermatological monitoring after bariatric surgery. In comparison Razvigor at, el. Showed that Striae distensae (stretch marks) and intertriginous dermatitis are prevalent concerns in obese patients, exacerbated by rapid weight fluctuations and the unique skin physiology associated with obesity. Striae arise due to the mechanical stretching of the dermal layer, leading to collagen disruption and subsequent scar tissue formation, commonly seen in areas like the abdomen, thighs, and arms. Intertriginous dermatitis, frequently observed in skin fold areas (e.g., underarms and groin), results from friction, moisture accumulation, and poor ventilation, which create an environment conducive to bacterial or fungal growth. These skin conditions, typical in the post-bariatric population, significantly impact the patient's quality of life, emphasizing the necessity for dermatological monitoring and preventive care in weight management programs [17]. Different pre-existing skin conditions have shown improvements following bariatric surgery including Hidradenitis suppurativa and Psoriasis. The results of a retrospective analysis showed that 35 patients with HS symptoms underwent bariatric surgery out of which 24 patients (69%) showed improvements, 7 patients (20%) showed no change, and 4 individuals (11%) saw their HS symptoms increase [18]. Similarly in another retrospective survey, following bariatric surgery, 62% of respondents reported improvements in their psoriasis, 26% reported no change, and 12% reported deterioration [19]. However, in our study, the data of only psoriasis patients pre-surgery was collected according to which 47% of the patients showed improvements post bariatric surgery. We found that management strategies for skin changes including non-surgical treatments like topical applications and lifestyle adjustments, benefited many patients. For severe excess skin, surgical interventions, such as abdominoplasty, were performed in 129 (10%) of cases, with 85% of these patients reporting satisfaction (p=0.01). These findings suggest that non-surgical options suit milder cases, while surgical intervention is vital for more severe skin issues [20]. Another study which examined the strategies for bariatric patients experiencing skin-related changes showed that multidisciplinary approaches are an essential part of management. Their findings showed that approximately 30% of patients benefited from dietary adjustments and targeted supplementation, with significant improvement in vitamin levels over six months (p=0.05). For cases with severe skin complications, surgical interventions, such as abdominoplasty and other reconstructive procedures, were undertaken for 20% of patients as compared to 10% in our study, resulting in an 80% satisfaction rate reported postoperatively (p=0.02). These findings highlight that while non-surgical measures can adequately support mild cases, surgical options are often critical for managing more extensive skin-related challenges in post-bariatric surgery patients [21]. Another study was findings of the high prevalence of excess skin following bariatric surgery and its associated impacts. Findings indicated that in comparison to the reference group (1.5 ± 3.5), excessive skin scores were significantly higher for obese adults (10.5 ± 8.5) and even higher for adults and adolescents (12.3 ± 8.1 versus 14.4 ± 7.7) following obesity surgery [22]. Another study reported that redundant skin following significant weight loss is a common occurrence affecting up to 96% of patients who undergo bariatric surgery [23].

CONCLUSIONS

It was concluded that significant dermatological challenges are faced by patients post bariatric surgery and a holistic and multidisciplinary approach should be incorporated in managing these issues. By addressing both aesthetic and functional concerns, healthcare providers can enhance patients' overall satisfaction and quality of life. Further research is encouraged to explore long-term

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outcomes and to develop optimized treatment plans that cater to the specific dermatological needs of post-bariatric patients.

Authors Contribution

Conceptualization: MA[1]
Methodology: MA[1], MA[2], WA
Formal analysis: MA[2], WA
Writing review and editing: MA[1], MNDK, AHS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Weight Changes in Mandibular Fracture Patients After Maxillomandibular Fixation

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ABSTRACT

Maxillofacial injuries, frequently caused by accidents or violence, often result in mandibular fractures. Treatment options include open and closed reduction, the latter utilising maxillomandibular fixation. Although maxillomandibular fixation is a cost-effective method, it may restrict normal dietary intake, leading to weight loss and potential malnutrition that can negatively impact recovery. **Objective:** To assess weight changes in mandibular fracture patients following maxillomandibular fixation. **Methods:** A comparative cross-sectional study was conducted at the Pakistan Institute of Medical Sciences from November 2023 to April 2024, enrolling 75 adult patients (ages 18-50) undergoing maxillomandibular fixation for mandibular fractures. Weight measurements were recorded preoperatively and at one and four weeks postoperatively. Statistical analysis was performed using SPSS Version 27.0. **Results:** The mean age of participants was 26.4 years, with 92% being male. The average preoperative weight was 63.08 kg, decreasing significantly to 58.57 kg after one week and 57.57 kg after four weeks ($p<0.001$). This weight loss was attributed to dietary restrictions and discomfort from jaw immobilisation. **Conclusions:** It was concluded that this study reveals significant weight loss post-maxillomandibular fixation, indicating a need for targeted nutritional support during recovery. These findings emphasize the importance of developing effective intraoperative and postoperative care protocols to meet nutritional needs, potentially enhancing recovery outcomes and quality of life for patients. Future research should explore the long-term effects of weight changes and interventions to mitigate weight loss during recovery.

INTRODUCTION

Maxillofacial injuries are commonly caused by car accidents, falls, physical assaults, and sports activities [1]. Mandible fractures are prevalent in maxillofacial injuries and are typically treated in two ways. The first possibility is open reduction, in which intraoral or extraoral incisions are used, allowing visualisation, reduction, and fixation of the fractured segments with screws, plates, and wires. The other option is a closed reduction using maxillomandibular fixation (MMF) that immobilises the fractured segments by securing the upper and lower jaws adjacent to each other to promote healing [2]. This closed reduction technique limits normal food intake, particularly solid and semisolid foods, often resulting in weight loss and malnutrition, which in turn can affect recovery [3, 4]. Despite the risk of malunion, non-union, malnutrition, and periodontal inflammation, MMF is widely used. The duration of MMF varies based on the type and location of the fracture, the patient's age and health, and other factors, but generally lasts 3 to 6 weeks [5]. Many studies show a direct link between nutrition and the body's healing process, suggesting that MMF could affect recovery. MMF has the advantages of being inexpensive and non-technique

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sensitive. However, MMF is not without risk, and its effect on nutrition intake emphasizes the need for appropriate care and monitoring during treatment [6, 7]. According to a study conducted by Kayani *et al.*, they enrolled 30 patients with a mean age of 36.67 ± 9.743 years. Out of these patients, 90% were male and 10% were female. The participants had a pre-operative weight of 80.57 ± 9.995 kilograms, and by the fourth week after the surgery, their weight decreased to 76.47 ± 10.244 kilograms.The study found that patients experienced a weight loss of 6 kilograms by the end of the first week after the surgery, and this weight loss was maintained at 5 kilograms by the fourth week. The authors concluded that significant weight loss was observed among all patients in the first week following operation [8]. In a study conducted by Yazadani *et al.*, a total of sixty patients were enrolled. Their initial weights ranged from 49 to 98 kilograms, with an average weight of 69.45 ± 1.6 kilograms before undergoing inter-maxillary fixation (IMF). After 4 weeks, the mean weight showed a decrease of approximately 2.64 kilograms, reaching around 66.81 ± 1.4 kilograms (p=0.025). The study also observed the highest weight loss of 5 kilograms in one patient. The study suggests that while severe and acute malnutrition was not observed among patients, IMF did lead to mild to moderate malnutrition in some cases [9]. In the study conducted by Lone *et al.*, 300 patients were selected, out of which only 6 experienced mild malnutrition. 68.87 ± 11.250 kilograms was recorded as the average weight of participants preoperatively, which decreased to 65.25 ± 11.286 in the 5th week following surgery.The results of this study were found to be statistically significant (p<0.001)[6].

This study aims to assess the weight changes in patients with mandibular fractures following maxillomandibular fixation. Through examining the rate of weight reduction, this study provided valuable insights that could enhance patient care and deepen our comprehension of MMF's influence on general health.

METHODS

A comparative cross-sectional study was carried out in the Department of Oral and Maxillofacial Surgery at the Pakistan Institute of Medical Sciences in Islamabad between November 2023 and April 2024. Ethical Approval was given by the ethical review board of Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad (no. F. 1-1/2015/ERB/SZABMU/1065). Using the WHO sample size calculator and assuming a postoperative mean weight of 66.8 ±11.4), a 95% confidence level, and an absolute precision of 0.35 [9], the sample size was determined to be 75 participants. Using a non-probability purposive sampling technique, the study enabled researchers to choose volunteers who fudelfilled particular requirements pertinent to the study's goals. Participants were chosen according to present inclusion criteria, which included being between the ages of 18 and 50 years, irrespective of gender, presenting with a history of maxillofacial trauma with isolated mandibular fracture and receiving maxillomandibular fixation (MMF) without concurrent open reduction and internal fixation. These patients reported a history of maxillofacial trauma further classified based on etiology of trauma such as a history of falls from a minimum height of 6 to 7 feet, Road Traffic accidents, Physical Assault and sports injuries. Patients with poly-trauma, diabetes, cardiovascular or renal diseases, chronic obstructive pulmonary disease (COPD), altered consciousness from head injuries, pregnant women, and those with bi-maxillary or complex facial fractures were among the exclusion criteria created to guarantee the study's safety and applicability. Informed written consent was obtained from all participants. Demographic data were meticulously recorded, including participants' names, ages, genders, causes of trauma, and the duration of MMF before treatment. Participants were categorized into three distinct age groups to facilitate analysis of age-related effects. Group A included participants aged 18-28, Group B included those aged 29-39, and Group C included participants aged 40-50. Eligible patients underwent a standardized four-week maxilla-mandibular fixation using stainless steel wires. To address dietary constraints brought on by the surgical process, participants were given a liquid diet supplemented with nutritional supplements during this time. Weight measurements were meticulously taken at three-time points: immediately before surgery, one week postoperatively, and at the end of the four-week fixation. Upon completion of the four weeks, the MMF was removed from all participants. Data were systematically entered and analyzed using SPSS Version 27.0. Frequencies and percentages were used to represent categorical factors, such as gender and trauma cause. The averages and standard deviations of numerical variables, including age and preoperative and postoperative weights, were displayed. A paired sample t-test was used to compare preoperative and postoperative weights, and the data were further stratified by age, gender, and trauma origin to enable a more in-depth examination of the findings. Additionally, differences within particular subgroups were examined using post-stratified paired t-tests. A p-value of less than 0.05 was deemed statistically significant, indicating meaningful differences in weight changes throughout the study. This thorough methodological approach was designed to ensure the reliability and validity of the findings.

RESULTS

Results indicates a mean age of 26.40 ± 9.262, with a male predominance, making up 92% of the cohort. Most participants belonged to the younger age range, as 64% were in Group A. The demographic characteristics of the participants are summarized in Table 1.

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Table 1: Demographic Details of the Study Population

Variables	Frequency (%)
Gender	
Male	69 (92.0%)
Female	6 (8.0%)
Age of Participants	
Group A	48 (64.0%)
Group B	18 (24.0%)
Group C	9 (12.0%)
Etiology of Trauma	
RTA	59 (78.7%)
Fall	10 (13.3%)
Physical Assault	5 (6.7%)
Sport Injury	1 (1.3%)
Total	75 (100%)

The mean preoperative weight of the patients was recorded as 63.0833 ± 14.88503. Notably, the mean weights observed at subsequent intervals were 58.5707 ± 14.34538) after the first week post-surgery and 57.5687 ± 14.18959 after the fourth week, showing a gradual weight decline following the procedure. Weight measurements at various intervals are presented in Table 2.

Table 2: Descriptive Statistics of Participant Demographics and Weight Measurements

Variables	No. of Participants	Minimum	Maximum	Mean ± SD
Age of Participants	75	18	50	26.40 ± 9.262
Weight –Preoperative	75	38.70	110.00	63.0833 ± 14.88503
Weight-First Week Postoperatively	75	34.00	102.00	58.5707 ± 14.34538
Weight-Fourth Week Postoperatively	75	33.00	102.60	57.5687 ± 14.18959

The paired sample t-tests significant interaction between genders, with male showing greater weight loss across all time points compared to female. The results highlight a consistent trend of postoperative weight reduction, particularly in male participants. The weight changes of participants (preoperatively, one week postoperatively, and four weeks postoperatively) stratified by male and female are presented in Table 3.

Table 3: Postoperative Weight Changes After Stratification with Gender

Gender of the Participant		Mean ± SD	p-value
Male	Pair 1-Weight of the Participants-Weight of the Patient First Postoperatively	4.53406 ± 2.07677	0.000
	Pair 2-Weight of the Participants-Weight of the Patient's Fourth Postoperatively	5.53188 ± 3.14059	0.000
Female	Pair 1- Weight of the Participants of the Patient First Postoperatively	4.26667 ± 2.24470	0.006
	Pair 2-Weight of the Participants-Weight of the Patient's Fourth Postoperatively	5.31667 ± 3.36477	0.012

Furthermore, the study highlights the statistically significant differences in mean weight changes, with p-values of 0.000 for both the preoperative to the first week and preoperative to fourth-week comparisons and 0.002 for the first week to the fourth-week comparison. This table also explores the weight change across different age groups, with significant p-values mostly at 0.000. Notably, the first-week-to-fourth-week comparison was not statistically significant in Group A (p=0.054) and Group C (p=0.159). This analysis highlights the varied impact of age on postoperative weight changes, as shown in Table 4.

Table 4: Postoperative Weight Changes After Stratification by Age Group

Variables	Mean ± SD	p-value
Preoperative Weight-Postoperative Weight After First Week	4.51267 ± 2.07583	0
Preoperative Weight-Postoperative Weight After Fourth Week	5.51467 ± 3.136	0
Postoperative Weight After First Week-Postoperative Weight After Fourth Week	1.0020 ± 2.691	0.002
Age Group A		
Preoperative Weight-Postoperative Weight After First Week	3.98437 ± 2.106	0
Preoperative Weight-Postoperative Weight After Fourth Week	4.71875 ± 2.964	0
Postoperative Weight After First Week-Postoperative Weight After Fourth Week	0.73438 ± 2.575	0.054
Age Group B		
Preoperative Weight-Postoperative Weight After First Week	5.68889 ± 1.819	0
Preoperative Weight-Postoperative Weight after Fourth Week	7.18333 ± 3.264	0
Postoperative Weight After First Wee-Postoperative Weight After Fourth Week	1.49444 ± 2.997	0.049
Age Group C		
Preoperative Weight-Postoperative Weight After First Week	4.97778 ± 1.316	0
Preoperative Weight-Postoperative Weight After Fourth Week	6.42222 ± 2.387	0
Postoperative Weight After First Week-Postoperative Weight After Fourth Week	1.44444 ± 2.787	0.159

Analysis shows the mean weight changes of patients after four weeks postoperatively, stratified by the etiology of trauma, with a total of 75 patients. The Chi-Square test results indicate no significant differences in weight changes among the different trauma groups, with a p-value of 0.292, as shown in Table 5.

Table 5: Fourth Week Postoperative Weight Changes After Stratification by Etiology of Trauma

Etiology of Trauma	No of Patients	Maximum	p-value
RTA (59)	59	57.86 ± 13.69	0.292
Fall (10)	10	51.60 ± 11.89	

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Assault	5	66.44 ± 22.32	
Sport Injury	1	56.00 ± 1.0	
Total	75	57.5687 ± 14.19	

DISCUSSION

The classic technique of immobilizing the jaws for the treatment of maxillofacial fractures is called maxillomandibular fixation (MMF). For minimally displaced fractures, MMF is an alternate option that may be able to avoid open surgery and its associated problems, even though open reduction and internal fixation (ORIF) offer an early recovery. In terms of lower treatment expenses, shorter hospital stays, and avoiding the postoperative complications of open surgery, it produces better results.[3] Important insights into demographic traits, weight variance, and the overall impact of MMF on recovery were uncovered by analyzing the data gathered from 75 participants. In our study, most patients undergoing maxillomandibular fixation (MMF) were young adults, with a mean age of 25.4 years, consistent with the findings of Derebaşınlıoğlu *et al.*, who reported that road traffic accidents, interpersonal violence, and sports-related injuries are common causes of maxillofacial trauma in this age group [10]. Additionally, 92% of the patients in our study were male, confirming the male predominance observed in the literature by Khan *et al.*, Kanala *et al.*, and Bicsák *et al.*, which highlights a higher incidence of facial fractures in men compared to women [11-13]. This is further stratified with gender through a paired sample t-test, which demonstrated a statistically significant relationship between gender, and weight changes. Due to the higher percentage of male patients with a small number of female patients, these statistics cannot be applied to the general population.It also emphasizes the importance of implementing targeted prevention strategies for high-risk groups, particularly young male [14]. The mean weight of the participants decreased from preoperative measurements (63.0833 kg) to the first week postoperatively (58.5707 kg), and this trend continued to the fourth week (57.5687 kg). This substantial weight loss can be caused by several factors related to MMF: likely restrictive diet intake, pain, and difficulty eating due to jaw immobilization.The p-values for the comparison of preoperative weight to the weight taken at the first and fourth weeks postoperatively were statistically significant at 0.000 and for the first week to the fourth week at 0.002. This suggests that weight loss is a direct result of this intervention rather than an incidental finding. Similar results were reported by Homaid *et al.*, Inaba *et al.*, and Pillai *et al.*, [15-17]. Moreover, it is important to study the relationship between age and weight variation, because younger participants may respond to the surgery differently metabolically than the older population. Weight loss not only affects physical health but also has potential implications for psychological well-being and recovery. The fact that weight loss may result in diminished strength, decreased energy, and a longer recovery period highlights the significance of controlling nutrition following surgery [18, 19]. In our study, the analysis of weight changes following maxillomandibular fixation (MMF) revealed non-significant postoperative weight loss, with a mean weight of 57.86 kg for patients with road traffic accidents and 51.60 kg for those who experienced falls, yielding a p-value of 0.292. This finding is consistent with recent research by Zaidi *et al.*, which reported an average weight loss of 2.57 kg after MMF with a significant p-value, emphasizing the impact of surgical intervention on patient weight and the necessity for nutritional management during recovery to mitigate potential complications [20]. The results of this study demonstrate the need to provide patients undergoing MMF with thorough postoperative care that includes counselling and nutritional support [21]. Healthcare professionals must put systems in place to guarantee patients obtain enough nutrition during their recuperation, given the possibility of weight loss. High-calorie, easily digested foods and additional nutritional drinks that aid in weight maintenance may fall under this category [22, 23]. By showing a significant decrease in mean weight following maxillomandibular stabilization in individuals with maxillofacial fractures, this study accomplishes its objective.The results emphasize the need for more studies to develop efficient postoperative care guidelines that address these patients' dietary needs, thereby enhancing their quality of life and recovery results. Future research should examine potential strategies to lessen the impact of weight loss during recovery after MMF, as well as the long-term impacts of weight alterations.

CONCLUSIONS

It was concluded that the significant weight loss that patients with maxillofacial fractures have following maxillomandibular fixation (MMF) is highlighted in this study,underscoring the critical need for targeted nutritional support after surgery.The findings highlight how crucial it is that medical professionals put plans in place to satisfy these patients' nutritional needs to aid in their rehabilitation and enhance their quality of life.The long-term impacts of weight fluctuations should be investigated further, as should possible countermeasures. Putting a high priority on comprehensive postoperative care will eventually improve results for patients having MMF

Authors Contribution

Conceptualization: RA
Methodology: RA, BP, HUM MKS
Formal analysis: MUF
Writing review and editing: RAB

All authors have read and agreed to the published version of the manuscript

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Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Efficacy of Intravenous Ferric Carboxymaltose Versus Iron Sucrose in the Treatment of Iron Deficiency Anemia of Pregnancy

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ABSTRACT

Iron deficiency anemia (IDA) during pregnancy is a widespread disease associated with adverse effects on both the mother and fetus. **Objectives:** To determine the effectiveness of intravenous ferric carboxymaltose (FCM) versus iron sucrose (IS) for improving hematological parameters in pregnancy-related iron deficiency anemia. **Methods:** This Quais experimental study was conducted over six months from January 2024 to June 2024 at Rai Medical College Sargodha. A total number of participants was n=120 pregnant IDA women (Hb<10.5 g/dL), gestational age (GA) 16 to 34 weeks), were seen and randomly assigned to either group A or group B. Iron sucrose was given as 200 mg intravenously in 200 ml of normal saline over 15-20 minutes on alternate days, with a maximum dose of 1000 mg per week. Ferric Carboxymaltose was given in a single dose, diluted in normal saline over 15-20 minutes, with a maximum of 1000 mg per day or per week. Assessment of Serum Ferritin and Hemoglobin levels at Baseline, 4th Weeks, and 8th Weeks Post-treatment, and adverse events. **Results:** There was a significant difference in mean Hb values between Group 1 and Group 2 in 4th week ($p<0.05$). Serum ferritin also improved significantly in the FCM group. When comparing FCM with IS, FCM was safer, with fewer adverse events. Patients in the FCM group also had higher rates of satisfaction and adherence and had fewer missed doses. **Conclusions:** It was concluded that FCM has quickly restored iron levels in pregnant women, significantly increasing Hb and ferritin levels over the 8th week with minor side effects.

INTRODUCTION

According to estimates from the World Health Organization (WHO), almost two billion individuals, or 25% of the global population are anemic with around half of them having iron deficiency anemia (IDA). Additionally, there is at least one patient with iron deficiency who does not have anemia for every IDA patient. Thus, iron deficiency with or without anemia affects over two billion people worldwide, the majority of whom live in nations with limited resources. Iron deficiency anemia (IDA) during pregnancy is a critical public health problem. Intravenous (IV) iron therapies, including ferric carboxymaltose (FCM) and iron sucrose (IS), are often used by pregnant women with IDA [1, 2]. Both mothers and their children may experience negative health consequences from anemia and IDA, including infections, early membrane rupture, fetal development restriction, fetal hypoxia, early birth, low birth weight, and fetal death. Maternal anemia is responsible for 18% of perinatal deaths, 19% of preterm deliveries, and 12% of low birth weights in low- and middle-income nations [3]. In general, IV iron therapy is preferred, after some wide practice showing its

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better repletion of iron stores quicker and more efficiently in cases of severe anemia or low response to oral therapy [4]. Intravenous iron therapy has a notable benefit over oral iron supplements for treating moderate-to-severe iron deficiency anemia (IDA), most importantly when prompt iron level correction is needed or when oral therapy has failed because of gastrointestinal (GI) side effects, non-compliance, or mal-absorption issues [5, 6]. Intravenous iron bypasses the digestive system, because of which rendered effective and direct, increasing the rate of hemoglobin restoration and the rate of iron storage restoration [5]. Among the various IV iron formulations available, iron sucrose (IS) and ferric carboxymaltose (FCM) are the most widely studied. FCM allows to administer substantially larger doses via a single infusion to decrease the follow-up visits and improve patient and convenience [7, 8]. It is also associated with a lower risk of adverse infusion-related events [9]. In contrast, IS is administered in smaller doses over multiple sessions, and it often takes 5–10 infusions to achieve the same total FCM dose [10]. While FCM and IS are both effective treatments for IDA, the choice is often dependent on patient preference, clinical circumstances and elements of the healthcare system [6, 11]. Ferric carboxymaltose and iron sucrose differ in pharmacokinetics, effect on patient adherence and dosing schedule, suggesting that both treatments could be compared. As indicated earlier that IS requires multiple small doses within several sessions, which has medical adherence implications, FCM allows high, single-session, rapid administration with the convenience advantages of shortening treatment duration. Limited studies are conducted in Pakistan regarding the alleviation of anemia among pregnant women using FCM and IS in dose-dependent manner.

This study aims to determine the effectiveness of intravenous ferric carboxymaltose (FCM) versus iron sucrose (IS) for improving hematological parameters in pregnancy-related iron deficiency anemia in hospitals.

METHODS

This Quasi experimental study was conducted over six months from January 2024 to June 2024 at Rai Medical College Sargodha. The study was approved by the Institutional Review Board number (RMCS/ERC/26/23), ensuring adherence to ethical standards. Informed consent was obtained from all participants before their involvement in the research. Inclusion criteria were pregnant women with (IDA) and Hb <10.5 g/dl, aged between 16 and 34 weeks of gestation were included in the study. Exclusion criteria included hypersensitivity to IV iron, causes of anemia other than IDA, and renal or hepatic impairment. The sample size formula was calculated by expected mean improvement in hB in ferric carboxymaltose11.6 ± 0.77 g/dl and iron sucrose 10.60 ± 0.87g/dl) by taking 80% power of test and 95% confidence interval as 22 which is too small to perform god statistical test with good efficiency so we increase sample size upto 120 (60 in each group) [12]. The sample size was calculated based on 80% power and at a significance level of 5% to detect a significant difference in hemoglobin (Hb) between the two groups, targeting 60 participants per group [13]. Participants were equally distributed in two groups, using block randomization. Iron sucrose was given as 200 mg intravenously in 200 ml of normal saline over 15-20 minutes on alternate days, with a maximum dose of 1000 mg per week. Ferric Carboxymaltose was given in a single dose, diluted in normal saline over 15-20 minutes, with a maximum of 1000 mg per day or per week. All patients were monitored for adverse reactions during and for 1-hour post-infusion in the ward. Patients were discharged from the ward after completion of the regimen, and each of them was followed up in the 4th week and 8th week after completion, to assess the increase in peripheral hemoglobin, serum ferritin and smear. Data were analyzed by SPSS version 22.0 and involved both descriptive and comparative analyses. Paired samples t-test for comparison of pre-treatment with post-treatment values (4th and 8th week) within each group (FCM and IS). Independent samples t-test for comparison between FCM and IS groups at 8th week post-treatment. The chi-square test was applied for the comparison of categorical data (side effects) between groups. A p-value<0.05 was considered statistically significant.

RESULTS

In our study, the number of subjects in the study was 120 (60 per group, FCM and IS). Demography including age, gestational age, BMI, parity and gravidity was similar between groups (p>0.05 for all). There was no significant difference in spans or means between pregnancies. For continuous variables presented as mean ± SD including age, gestational age, and inter-pregnancy interval, we used the independent t-test. For ordinal variables presented as medians with interquartile ranges which include parity and gravidity, the Mann-Whitney U test was applied. Categorical variables, including pre-treatment anemia type, iron supplementation use, and inter-pregnancy interval categories, were analyzed using the chi-square test. Additionally, Fisher's exact test was used when the expected frequencies in any cell were less than five (Table 1).

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Table 1: Demographic Characteristics of Participants

Characteristics	FCM Group (n=60)	IS Group (n=60)	p-Value
Age (Years) Mean ± SD	28.5 ± 4.8	29.3 ± 5.1	0.45
Gestational Age (Weeks) Mean ± SD	26.2 ± 3.6	25.8 ± 3.4	0.62
Parity	Median=2 (IQR: 1-3)	Median=2 (IQR: 1-3)	0.73
Gravidity	Median=3 (IQR: 2-4)	Median=3 (IQR: 2-4)	0.68
Pre-treatment Anemia Type (% Age)			
Microcytic Hypochromic	35%	36%	0.55
Normocytic Normochromic	40%	38%	0.55
Normocytic Hypochromic	25%	26%	0.55
Inter-Pregnancy Interval (Years)			
<1 Year	20 (33.3%)	25 (41.7%)	0.42
1-2 Years	25 (41.7%)	22 (36.7%)	0.42
>2 Years	15 (25.0%)	13 (21.6%)	0.42
Mean ± SD	1.8 ± 0.9	1.7 ± 0.8	0.56

The study compared changes in blood levels between Ferric Carboxymaltose (FCM) and Iron Sucrose (IS) from before treatment to the 4th and 8th weeks. In the FCM group, hemoglobin, serum ferritin, and iron levels, all increased significantly, with hemoglobin rising from 9.2 to 11.9 g/dL and ferritin from 20 to 85ng/mL by the 8th week. In the IS group, the improvements in these levels were smaller and not statistically significant. This shows that FCM works better than IS for improving iron levels and related blood markers (Table 2).

Table 2: Comparison of Hematological Changes Pre-Treatment (4th Week And 8th Week) Between FCM and IS Groups. p-value is Calculated Using an Independent T-Test

Parameters	Time Point	FCM (mean ± SD)	IS (mean ± SD)	p-Value
Hemoglobin (g/dL)	Pre-Treatment	9.2 ± 1.1	9.3 ± 1.2	<0.001
	4th Week	11.2 ± 1.0	11.1 ± 1.0	
	8th Week	11.9 ± 1.0	11.3 ± 1.1	
Serum Ferritin (ng/mL)	Pre-Treatment	20.0 ± 6.5	18.0 ± 5.9	<0.001
	4th Week	80.0 ± 8.3	70.0 ± 7.2	
	8th Week	85.0 ± 8.0	75.0 ± 7.5	
Iron (µg/dL)	Pre-Treatment	30 ± 8	28 ± 9	<0.001
	4th Week	90 ± 12	88 ± 11	
	8th Week	95 ± 11	92 ± 10	

The percentage of microcytic hypo-chromic, normocytic normochromic and normocytic hypo-chromic cells throughout the various time points was not different between the two treatments. p-value is Calculated Using the Chi-Square Test (Table 3).

Table 3: Comparison of Peripheral Blood Smear Pre vs Post-Treatment (4th Week and 8th Week) Between FCM and IS Groups Shown as Count and % Age

Anemia Type	Time Point	FCM Count (% Age)	IS Count (% Age)	p-Value
Microcytic Hypo-chromic	Pre-Treatment	21 (35.0%)	22 (36.7%)	0.771
	Post-Treatment (4th Week)	10 (16.7%)	13 (21.7%)	0.671
	Post-Treatment (8th Week)	5 (8.3%)	7 (11.7%)	0.770
Normocytic Normochromic	Pre-Treatment	24 (40.0%)	23 (38.3%)	0.221
	Post-Treatment (4th Week)	35 (58.3%)	32 (53.3%)	0.221
	Post-Treatment (8th Week)	45 (75.0%)	42 (70.0%)	0.667
Normocytic Hypo-chromic	Pre-Treatment	15 (25.0%)	15 (25.0%)	0.687
	Post-Treatment (4th Week)	15 (25.0%)	15 (25.0%)	0.687
	Post-Treatment (8th Week)	10 (16.7%)	11 (18.3%)	0.117

There were no significant differences in the incidences of GI issues, headache, dizziness, local pain, allergy, or fatigue between both groups based on FCM versus other IS groups by using Chi-square tests, p>0.005. P-values are calculated using Chi-square tests (Table 4).

Table 4: Adverse Effect in FCM vs IS Groups

Adverse Effect	FCM (mean ± SD)	IS (mean ± SD)	p-Value
Gastrointestinal Issues	25%	30%	0.541
Headache	15%	12%	0.617
Dizziness	18%	20%	0.792
Injection Site Pain	10%	8%	0.752
Allergic Reactions	5%	3%	0.651
Fatigue	20%	18%	0.812

Adverse effects of gastrointestinal issues, headache, dizziness, local pain, allergy, or fatigue between both groups based on FCM versus other IS group were analyzed (Figure 1).

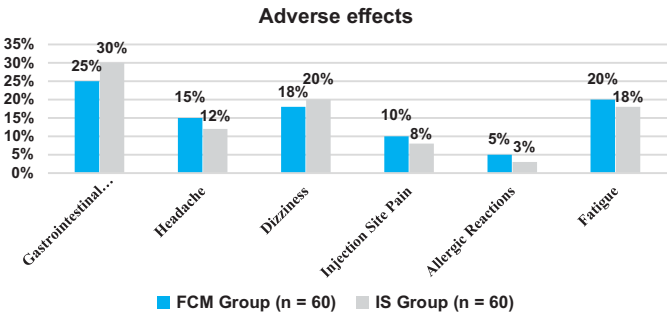

Figure 1: Bar Graph Represent the Comparison of Adverse Effects Between FCM and IS Groups

DISCUSSION

Iron supplements are commonly given for iron deficiency anemia, particularly during pregnancy because it is associated with low birth weight, preterm birth, and maternal morbidity [14]. Several studies have been

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conducted which have used FSM to treat iron deficiency and evaluated the efficacy of FCM during pregnancy. One such study has shown that FSM was safe and effective within 6 weeks of pregnancy, based on the Hb, RBC and serum ferritin levels [15]. Another study has evaluated the effectiveness and Safety of FCM in comparison to IS for treating iron deficiency anemia during pregnancy. They have found that FCM helped better in replenishing iron among pregnant women in comparison to IS [16]. One study reported that in FCM treated group, hemoglobin level was 9.87 ± 0.77 in iron sucrose group it was 9.39 ± 0.72 (p=0.001), 3 week post treatment, Whereas hemoglobin level in the FCM group was 11.51 ± 0.76 and in iron sucrose group it was 10.78 ± 0.61 (p=0.001), 6 week post treatment, which suggested that change in hemoglobin level was higher among patients of FCM compared to Iron sucrose group [17]. The results of the current study revealed that in the FCM group, overall (from baseline to 8th week) increase in hematological was significant 9.2 ± 1.1 to 11.9 ± 1.0 along with serum ferritin rising from 20 ± 6.5 ng/mL to 85 ± 8.0 ng/mL and serum iron levels from 30 ± 8 µg/dL to 95 ± 11 µg/dL while the IS group showed less pronounced increases, hemoglobin levels 9.3 ± 1.2 g/dL to 11.3 ± 1.1 g/dL, ferritin levels rising from 18 ± 5.9 ng/mL to 75 ± 7.5 ng/mL and serum iron level from 28 ± 9 µg/dL to 92 ± 10 µg/dL Hence this study advocates the high efficacy of FCM over IS (with p value<0.001 for all the three iron deficiency markers) in replenishing iron stores and thus treating iron deficiency. One study has reported 2.9 ± 0.2 g/dl Increase in Hb in the treated group versus 1.4 g/dl in IS treated group during 4 weeks, with a significant p-value of 0.004. They have also reported an increase of 63.1 ng/mL ferritin in the treated group versus 26.1 in the IS-treated group, with a significant p-value of 0.001 [18], which is more pronounced than our study. Although, in the reported study, change has been seen in both groups, however, FCM group has shown more robust changes [18]. Such results are in line with others that have demonstrated a higher effect of FCM compared to IS on the immediate increase of Hb and ferritin. Bharadwaj et al., suggested that FCM turns out to be better than IS due to a higher rise of hemoglobin and ferritin levels with lesser side effects [19]. Another study reports a randomized controlled trial for pregnancy-related IDA, comparing a single IV infusion of 1000mg of FCM over 15 minutes, a single IV infusion of 1000mg of IPM, over 2 hours and 325mg daily oral ferrous sulphate until delivery. They have found that usage of IV FCM during pregnancy was safe and showed better efficacy than IV IPM or oral iron [20]. This indeed correlates well with our data showing the superior effect of FCM on serum ferritin levels. In our study, we did not see any significant difference between the two groups regarding microcytic hypochromic, normocytic normochromic and normocytic hypochromic cells checked at the 4th and 8th week after implantation. These findings imply that both treatment modalities have a comparable impact on peripheral blood smear, even though there appeared to be greater improvements in iron status with FCM. Additionally, we did not find significant adverse effects in both groups, which indicates that FCM and IS have not caused any harm to the treatment groups. Moreover, the existing data coming from observational studies [18, 7] as well as in randomized controlled trials [10], suggests that intravenous iron carboxymaltose administration in pregnancy is likely to be safe and effective. IS has been proven but requires multiple doses while FCM is advantageous as higher doses can be given in a single sitting which reduces hospital visits. To optimize both maternal and fetal outcomes, comparative effectiveness, Safety, and adherence studies are needed.

CONCLUSIONS

It was concluded that FCM was an effective treatment for pregnant women suffering from iron-deficient anemia. While therapeutic effects were comparable for both FCM and IS, FCM achieved much faster serum ferritin increases, even improving it up to the normal range, though hematological parameters improved with both FCM and IS.

Authors Contribution

Conceptualization: KA
Methodology: SJ, RA[1], RA[2]
Formal analysis: SJ, AM
Writing review and editing: RA[2], AM, MAUR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Knowledge Attitude and Practice of Nutritional Management of Acute Pancreatitis among General Surgery Residents of Tertiary Care Hospital

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ABSTRACT

Nutritional management is a critical component in the treatment of acute pancreatitis, yet its integration into clinical practice among surgical residents remains suboptimal. **Objectives:** To evaluate the knowledge, attitude, and practice of general surgery residents regarding nutritional management in a tertiary care hospital. **Methods:** A descriptive, cross-sectional study was conducted among 106 general surgery residents at the District Headquarters Teaching Hospital, Narowal. Residents with a minimum of six months of clinical experience who provided informed consent were included. Data were collected using a structured, validated questionnaire comprising three sections: knowledge (multiple-choice questions assessing evidence-based nutritional practices), attitude (Likert scale responses on perceptions and confidence in nutritional management), and practice (self-reported adherence to guidelines and barriers faced). Descriptive statistics summarized participant characteristics, while inferential analysis assessed correlations, with $p<0.05$ considered statistically significant. **Results:** The mean knowledge, attitude, and practice scores were 72.3% ± 12.4%, 80.7% ± 10.2%, and 68.5% ± 15.3%, respectively. While most residents acknowledged the importance of early enteral nutrition (84.9%), only 36.8% adhered to evidence-based guidelines in practice. Significant barriers included resource limitations (64.2%) and inadequate training (52.8%). A positive correlation was observed between knowledge and attitude scores ($r=0.48$, $p<0.01$). **Conclusions:** It was concluded that this study highlights discrepancies between knowledge, attitude, and practice in the nutritional management of acute pancreatitis. Despite healthcare providers demonstrating positive attitudes, adherence to evidence-based guidelines remain suboptimal due to resource limitations and insufficient training. Implementing targeted education and structured training programs can enhance compliance with best practices and improve patient outcomes.

INTRODUCTION

Common in the digestive system, acute pancreatitis (AP) can present itself in many different ways, from a minor ailment self-limiting to major issues fatal to the individual [1]. AP is still a main source of disease and death even if its occurrence varies greatly worldwide; this is particularly true in tertiary care environments where severe cases are transferred. AP management has evolved greatly, and nutritional treatment has grown in significance in improving patient conditions [2, 3]. Controlling the inflammatory response, reducing the risk of infection, and accelerating the healing process generally depends on starting the proper dietary assistance early on [4]. AP patients' diet was traditionally largely controlled by bowel rest and complete parenteral nutrition (TPN). New studies, meantime, point to early enteral nutrition (EN) as a preferable choice. Better outcomes including fewer infections, shorter hospital stays, and lower death rates depend on EN [5]. This generally helps to maintain the stomach intact and stops the movement of germs. Following the best dietary recommendations is still challenging even with these advances, particularly in cases with limited resources or when healthcare professionals are ignorant of the most recent evidence-based recommendations [6, 7]. In the treatment of patients with

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AP, surgical fellows—especially those nearing the end of their training are rather crucial. The way patients are cared for depends much on what first-line caregivers know, feel, and do (KAP) regarding nutritional management [8]. In tertiary care facilities, where severe AP is more common, it is quite crucial to ensure that staff members follow effective dietary guidelines and are well-informed. Studies have revealed, however, that healthcare professionals vary in practice and produce less-than-ideal results depending on whether they follow these criteria or not [9, 10]. Not much is known about the knowledge, attitudes, and behaviours of surgical residents in Pakistan, even though there is increasing evidence that dietary control influences AP. Most research done thus far has concentrated on clinical results or patient-handling techniques. Few have examined the level of knowledge and readiness of the caregivers personally. Finding solutions and means of improving training and exercise depends on closing this disparity.

This study aims to ascertain the knowledge, opinions, and practices of general surgery trainees in a tertiary care hospital about nutritional management of acute pancreatitis. The findings will provide us with knowledge about present practices, highlight areas where education is required, and enable us to develop particular strategies to enhance treatment for acute pancreatitis.

METHODS

This cross-sectional study examined general surgery residents at the District Headquarters (DHQ) Teaching Hospital Narowal, to assess the knowledge, attitude, and practices regarding properly managing their acute pancreatitis. From January 16 to March 21, 2024, there were three months of study effort. Participating in the study were all DHQ hospital general surgery residents. These residents were selected as the target group since they have advanced field experience caring for patients with acute pancreatitis and a lot of experience overall. The sample size was calculated using the formula for single proportions, assuming an estimated proportion (p) of 0.5, asn=Z^2.p.(1-p)/ d^2.Where: Z is the standard normal variate corresponding to a 95% confidence level (1.96), p is the estimated proportion of residents with adequate knowledge of nutritional management (0.5) and d is the margin of error, set at 10% (0.1). To account for potential non-response, the sample size was increased by 10%, resulting in a final sample size of 106 residents. A convenience sampling technique was used to include all eligible residents available during the study period. General surgery residents both male and female aged 25 to 35 years actively involved in patient care at DHQ Teaching Hospital, Narowal, during the study period were included. Residents who were on leave, unavailable for participation, or outside the specified age range were excluded. Using a standardized questionnaire already tested [10], with an eye on three primary categories, information was gathered. To follow evidence-based standards, the knowledge component examined how well residents recognized when, what kind, and how to provide nutritional support to individuals with acute pancreatitis. Participants in the attitude piece were asked what they believed to be the value of nutritional management and how confident they were in their abilities to manage these types of situations. Finally, the practice domain gathered data on individuals' stated degree of adherence to clinical nutritional management guidelines. Participants received the questionnaire in person, and their responses were gathered anonymously to respect their privacy and inspire honesty. The acquired data were examined using version 26 of the Statistical Package for the Social Sciences (SPSS). Descriptive statistics was applied to compile the findings. There were found frequencies and percentages for binary variables. Means and standard deviations emerged for continuous variables. By aggregating the significant questions in every area, one may determine the knowledge, attitude, and practice scores. Those who obtained more than 75% in an area were judged to have "adequate" knowledge, a "positive" attitude, or "good" behaviour. Comparisons between residents with adequate and inadequate scores were made using the chi-square test for categorical variables and an independent t-test for continuous variables. Participation in the study was voluntary, and informed consent was obtained from all participants. The questionnaire was anonymized, and no identifying information was collected to ensure participant confidentiality.

RESULTS

A total of 106 general surgery residents participated in the study, achieving a response rate of 100%. The mean age of the participants was 29.4 ± 2.1 years. Of these, 73 participants (68.9%) were male, and 33 (31.1%) were female. The mean residency experience was 3.8 ± 0.5 years. Additionally, 21 participants (19.8%) had attended workshops or seminars on nutritional management within the past year as shown in Table 1.

Table 1: Demographic Characteristics of Study Participants

Characteristics	Frequency (%)
Total Participants	106
Age (Years) Mean ± SD	29.4 ± 2.1
Gender	
Male	73 (68.9%)
Female	33 (31.1%)
Residency Experience (Years) Mean ± SD	3.8 ± 0.5
Attended Nutritional Workshops	21 (19.8%)

The mean knowledge score among the participants was 72.3% ± 12.4%. A total of 49 residents (46.2%) were

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categorized as having adequate knowledge, scoring above 75%. Among the domains assessed, 90 participants (84.9%) correctly identified the benefits of early enteral nutrition in reducing complications of acute pancreatitis, and 83 (78.3%) recognized the risks associated with parenteral nutrition. However, only 42 participants (39.6%) correctly estimated daily caloric needs and 34 (32.1%) identified protein requirements accurately. Residents who had attended workshops demonstrated significantly higher knowledge scores than those who had not ($p<0.01$) (Figure 1).

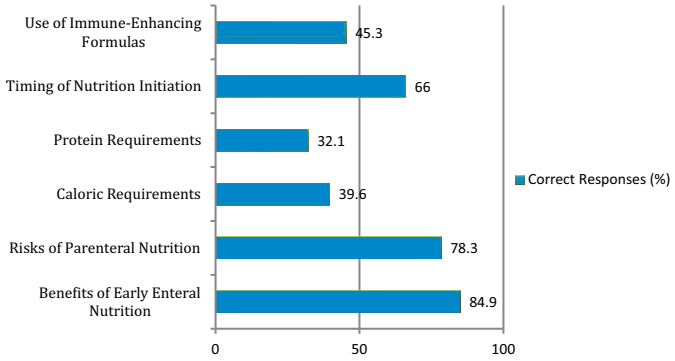

Figure 1: Knowledge Scores by Domains

The mean attitude score was 80.7% ± 10.2%. Out of the participants, 71 (67%) demonstrated a positive attitude toward nutritional management. A total of 94 participants (88.7%) agreed that early nutritional intervention improves patient outcomes, while 81 (76.4%) expressed confidence in discussing nutritional strategies with colleagues. However, only 44 participants (41.5%) felt confident in independently managing nutritional therapy for severe cases. Residents with higher knowledge scores were more likely to exhibit positive attitudes ($p<0.05$) (Table 2).

Table 2: Attitude Responses by Domains

Attitude Statements	Agree (%)	Neutral (%)	Disagree (%)
Early Nutrition Improves Patient Outcomes	88.7%	7.5%	3.8%
Confidence in Discussing Nutritional Strategies	76.4%	15.1%	8.5%
Confidence in Independently Managing Nutrition	41.5%	34.0%	24.5%
Importance of Nutritional Education in Residency	82.1%	11.3%	6.6%

The mean practice score was 68.5% ± 15.3%. Only 39 residents (36.8%) adhered to evidence-based guidelines in practice. A total of 60 participants (56.6%) reported recommending enteral nutrition as the first-line therapy frequently, whereas 33 (31.1%) occasionally relied on parenteral nutrition due to logistical challenges. Furthermore, 68 participants (64.2%) identified resource limitations as a major barrier, while 56 (52.8%) cited insufficient training as another significant obstacle (Table 3).

Table 3: Practice Scores by Domains

Practice Parameters	Frequently (%)	Occasionally (%)	Rarely/ Never (%)
Use of Enteral Nutrition	56.6%	31.1%	12.3%
Reliance on Parenteral Nutrition	31.1%	42.5%	26.4%
Use of Evidence-Based Guidelines	36.8%	41.5%	21.7%
Barriers (Lack of Resources)	64.2%	-	35.8%
Barriers (Inadequate Training)	52.8%	-	47.2%

Correlation analysis revealed a significant positive correlation between knowledge and attitude scores ($r=0.48$, $p<0.01$). A moderate correlation was observed between attitude and practice scores ($r=0.39$, $p<0.05$), while the correlation between knowledge and practice scores was weak ($r=0.26$, $p=0.08$) (Table 4).

Table 4: Correlation between Knowledge, Attitude, and Practice Scores

Variables Correlated	Correlation Coefficient (r)	Significance (p)
Knowledge and Attitude	0.48	<0.01
Attitude and Practice	0.39	<0.05
Knowledge and Practice	0.26	0.08

DISCUSSION

This study assessed the knowledge, attitude, and practice of general surgery residents regarding the nutritional management of acute pancreatitis. The findings revealed adequate knowledge and positive attitudes among the participants, but significant gaps in the practical application of evidence-based guidelines. While the majority recognized the importance of early enteral nutrition, fewer participants were confident in estimating caloric and protein requirements or independently managing nutritional therapy, highlighting areas requiring improvement. Residents who had attended workshops demonstrated significantly better knowledge and attitudes, emphasizing the role of targeted educational interventions. Despite positive attitudes, less than 40% of the residents adhered to evidence-based guidelines, citing resource limitations and insufficient training as primary barriers. The weak correlation between knowledge and practice further underscores the disconnection between theoretical understanding and clinical implementation. The average knowledge level seen matches what other research conducted in tertiary care environments has discovered [11, 12]. Those investigations revealed that individuals lacked sufficient knowledge about some topics, including protein and calorie estimation. Early enteral feeding was generally regarded to be beneficial, which conforms to global guidelines for treating acute pancreatitis [13-15]. But the lack of confidence in managing nutritional therapy on one's own is reminiscent of what has been observed elsewhere where surgical residency programs provide little official nutritional instruction.

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Attitude scores in this study were greater than in several international investigations, in which fewer participants felt that a nutritional intervention would help to improve results. This variation could be due to people's increasing awareness of the significance of nutrition in their field of work, which could result from new guidelines stressing multidisciplinary approaches [16, 17]. Practice scores matched those observed in similar environments, where adhering to evidence-based guidelines proved less than ideal. About one-third of the participants required parenteral nutrition, which is comparable to issues people throughout the world deal with such as lack of finances or means of procurement [18, 19]. Furthermore, the significant role resources play as a barrier corresponds with what studies in areas with inadequate resources reveal. This emphasizes how difficult it is, on a systemic level, to follow dietary guidelines [20].

CONCLUSIONS

It was concluded that while general surgery residents in a tertiary care hospital possess adequate knowledge and positive attitudes toward the nutritional management of acute pancreatitis, their clinical practices remain suboptimal due to training gaps and institutional barriers. Strengthening institutional support and implementing targeted educational initiatives can enhance adherence to evidence-based nutritional management strategies, ultimately improving patient care.

Authors Contribution

Conceptualization: MZM
Methodology: MBB
Formal analysis: US, ZAC
Writing review and editing: MZM, RH, ZM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Knowledge and Practices of Nurses Regarding Prevention of Surgical Site Infections in Tertiary Care Hospitals Peshawar

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ABSTRACT

Surgical procedures have many complications of which the leading one is post-surgical site infection (SSI), which can be prevented by following appropriate guidelines. SSI may lead to loss of body parts, septicemia and increase hospital bed occupancy. **Objective:** To assess nurses' knowledge and practices regarding the prevention of surgical site infections in tertiary care hospitals in Peshawar. **Methods:** Descriptive cross-sectional study was conducted among 172 nurses recruited through convenient sampling. Study settings were two tertiary care hospitals in Peshawar. Data was collected through an adopted, self-administered questionnaire and were analyzed by SPSS version 26.0. **Results:** Findings of the study revealed that the knowledge level of the nurses was poor about the prevention of SSI, while their practice levels were also average. A significant difference was found in the knowledge level of the study participants on the basis of their gender with a p value; 0.001, qualification with a p value; 0.000. Years of experience with a p value; 0.007, and attending infection control courses with a p value; 0.03. In addition, a significant difference was found among the practices of nurses regarding the prevention of SSI on the basis of their gender with a p value; 0.012. **Conclusion:** The study's findings revealed that nurses had a poor level of knowledge about SSI, while their practices were average according to arbitrary.

INTRODUCTION

In the healthcare setup, the Healthcare Workers [HCWs] are directly involved in the provision of patient care. They perform an important role in the prevention of SSI. Post-operative surgical wounds have a direct relation with surgical interventions and are one of the important preventable Healthcare-Associated Infections [HCAIs]. SSI hints at several consequences, which may include loss of body parts, septicemia, cost-effectiveness, and increased length of hospital duration. The mortality rate of patients who are suffering from SSIs is greater than that of those who have not developed SSIs [1, 2]. A Surgical Site Infection [SSI] can be defined as an infection following a surgical procedure that develops within thirty days without placement of any implant or one year later if an implant is placed. Despite being preventable, Surgical Site Infections [SSIs] account for up to 30%, of which 14% are due to Healthcare-Associated Infections [HAIs]. 11% of patients become infected due to surgical procedures, which leads to the risk of increased morbidity, mortality, and healthcare expenses. Among Healthcare-Associated Infections [HAIs], SSI is one of the most widely reported infections. It is a great concern for infection control team to control the increasing rate of infection fallowing surgical intervention [3, 4]. A wound infection that develops following surgical procedures can be considered a health problem. Worldwide, at least 312.9 million surgical procedures are

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carried out yearly. SSI is regarded as one of the major postoperative problems that can lead to unfavorable patient outcomes, despite advances in surgical techniques, hospital technology, environmental enhancements, and the use of preventative antibiotics. Critical care units and surgical wards are the main contributing areas to increase the incidence of healthcare-related infections [3, 5]. The global incidence rate of SSI varies from 7.8% in Singapore and Southeast Asia [pooled incidence] to 6.1% in countries of low middle income. Australia contributes 2.8% to the total, while in Italy the incidence rate is 2.6%. The Republic of Korea's rate was 2.1%, while the USA rate was very low and was 0.9% of the cumulative SSI rate. What absolutely stands out is the peak incidence rates in low- and middle-income countries and Southeast Asia, but in comparison, the Australia, USA, and Europe rates are very low. This finding indicates the requirement for SE Asians to find out the exact contributing factors that worsen the condition and plan operational infection prevention strategies, and these would be affordable for the local population [6, 7]. Surgical site infection can be prevented or decreased in a number of ways, such as hand washing, use of sterilized instruments, nutritional maintenance, preoperative cleaning, mechanical gut evacuation, oral antibiotic use, hair removal, and skin preparation of the operative site. All of these preventive measures can be easily adopted with just a basic understanding of medical protocol [8-10]. Literature revealed that some intrinsic factors such as old age, metabolic diseases, malnutrition, cigarette smoking, overweight, immune suppression, hypoxia, and the time of hospitalization contribute to SSIs [11-13]. Nursing staff working in Tertiary Care Hospital Peshawar are engaged with different surgically intervened patients, which include general surgery, thoracic surgery, urology surgery, neurosurgery, and Paediatrics surgery patients. Patients in old age are more susceptible to infections. The greater attachment of nursing staff with surgically wounded patients stresses the importance of nursing staff knowledge level regarding prevention of surgical site infection.

The aim of the study was to evaluate the knowledge and practice level of nurses about SSI. Though many studies highlight that the majority of nurses engaged in patient care are not equipped with proper education on the prevention of operated wound infections, numerous of these nurses did not provide care to patients as recommended by evidence-based practice guidelines [14].

METHODS

The current study was conducted among nurses employed by two tertiary care hospitals in Peshawar. The study population was 310 nurses providing care in different surgical units, including surgical ward, surgical ICU, emergency department, and Operation Theater (OT). The study design was descriptive cross-sectional. The sample size of the study participants was n = 172; the sample size was calculated by the Raosoft sample size calculator with alpha: 0.05 and response distribution: 50%, with a 10% attrition. The eligible nurses were recruited by convenience sampling technique. The data from study participants were collected between September 2023 and November 2023. The data were obtained from those nurses who matched the inclusion criteria, such as registered nurses with at least 1 year of working experience in surgical units, emergency rooms, SICUs, and OTs of the selected hospital; nurses who were available at the time of data collection; and nurses who were willing to participate voluntarily. Nurses were not involved in the direct care of patients (head nurses), and nurses who were on leave were excluded from the study. All the study participants responded timely. The response rate was 100% and there was 0% attrition. Before the data collection, approval from the IRB was obtained (KMU-INS/14-10/6230). Then informed written consent was obtained from each of the study participants, and data were collected through a validated and adopted questionnaire. The data were collected by Sickder et al., 2014 scale; CVI of the tool was 0.97, and Cronbach's Alpha of the scale was 0.92 [14]. The questionnaire has three major parts. Part A was the general part of the questionnaire, including information regarding demography, training sessions, and workplace experience. Part B was based on the knowledge section. Questions were related to testing the respondents' knowledge about the prevention of SSI. The knowledge part of the scale was divided into 25 items. In the first part, I (Knowledge part), there are 25 multiple-choice questions, each with three possible answers. The third option had the right response, while the other two were wrong. The right answer was assigned a "1" for each question, and the wrong answer was assigned a "0." Individuals who answered more than 14 correctly were considered as having "good knowledge." Part C section was related to practice questions regarding surgical site infection. There are 25 questions on a 5-point Likert scale (ranging from "never practice=1," "rarely practice=2," "sometimes practice=3," "often practice=4," and "always practice=5"). Participants who were familiar with practicing preventive activities, such as practicing more than 14 questions frequently and usually, were considered "Good Practice," while those who did not practice at all, seldom, or only occasionally, were classified as "Poor Practice" [14, 15]. The data were collected from all the participants matching the inclusion criteria. To analyze the data, SPSS version 26.0 was used. The findings were represented in the form of bar and pie charts as well as in

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detailed descriptions. In descriptive analysis, mean and standard deviation were calculated for numerical variables, while frequency and percentages were computed for categorical variables. Associations were assessed by using parametric tests such as independent samples t-test for dichotomous variables and one-way ANOVA.

RESULTS

Selected hospitals had a total strength of 310 nurses working in surgical wards, ICUs, ERs, and OTs, out of which 172 nurses participated in this study with a response rate of 100%. The following table showed the demographic data of the study participants. Both hospitals had proper infection control manuals or refresher courses, but a great proportion of nurses (66%) had not attended any infection control training as shown in (Table 1).

Table 1: Demographic Characteristics of The Participants

Variables	Category	Mean ± SD/ Frequency (%)
Age	Mean ± SD	26.9 ± 3.636
Gender	Male	72 (41.9%)
	Female	100 (58.1%)
Qualification	Diploma	74 (43.0%)
	BSN	96 (55.8%)
	MSN	2 (1.2%)
Total Professional Experience in Year	1-2 Year	38 (22.1%)
	3-4 Year	64 (37.2%)
	5-6 Years	40 (23.3%)
	More than 6 Years	30 (17.4%)
Department	General Surgical Ward	72 (41.9%)
	Critical Care Unit	38 (22.1%)
	ER	22 (12.8%)
	OT	40 (23.3%)
Training of Infection Control	Yes	58 (33.7%)
	No	114 (66.3%)

The study findings reported that 40.7% of the nurses had poor knowledge level, 10.4 % had average knowledge, 22 % had good knowledge and 26.74% of nurses had excellent knowledge regarding surgical site infection (Figure 1).

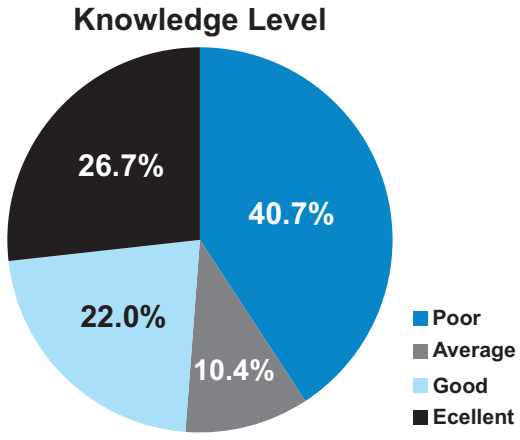

Figure 1: Knowledge Level of the Study Participant's

The current study revealed that the majority of the nurses, 65%, had an average level of practice scores, 14% had good practice scores, 14% had poor practice scores, and only 7% of the studied participants had excellent practice scores regarding surgical site infection. Therefore, it can be inferred that the majority of nurses have poor knowledge regarding SSI, and their practices regarding the prevention of SSI are also poor (Figure 2).

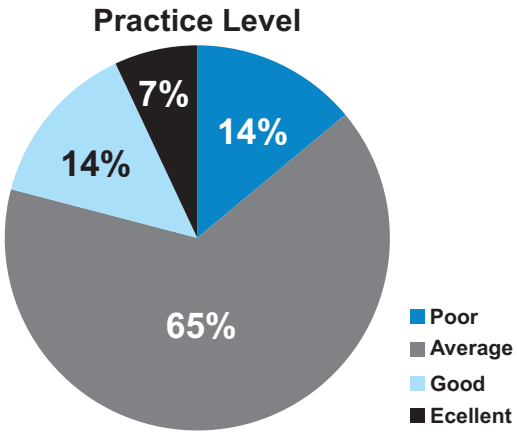

Figure 2: Practice Level of the Study Participant's

Table 2 showed the differences between the knowledge level and practice scores among the study participants on the basis of their demographic characteristics. It was discovered by the current study that males were more knowledgeable regarding SSI as compared to female nurses, with a p-value reported as 0.001. Similarly, there was a significant difference between the knowledge level of those nurses who had attended the infection control training and those who had not attended it, with the p-value reported as 0.03. Furthermore, a significant difference in the knowledge level was found among the study participants on the basis of their qualification with a p-value reported as 0.000, years of clinical experience with the p-value reported as 0.007, and department [unit of practice] with a p-value of 0.000. On the other hand, the study also discovered that there was a significant difference in practices regarding the prevention of SSI among nurses on the basis of their gender, with a p-value of 0.012. There was only significance found in the gender status of study participants, with a p-value reported as 0.012 (Table 2).

Table 2: Comparison between Demographic Variable and Knowledge and Practice Score

Variables	Status	Knowledge Significance	Practice Significance
Gender	Male	p = 0.001 t = -0.973	p = 0.012 t = 0.401
	Female		
Qualification	Diploma	p = 0.000 f = 117.934	p = 0.25 f = 0.646
	BSN		
	MSN		

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Total Professional Experience	1-2 Year	p = 0.007 f =4.146	p = 0.106 f =2.069
	3-4 Year		
	5-6 Years		
	More than 6 Years		
Department	General Surgical Ward	p = 0.000 f = 13.873	p = 0.699 f = 0.76
	Critical Care Unit		
	ER		
	OT		
Training of Infection Control	Yes	p = 0.003 t = 4.460	p = 0.424 t = -1.803
	No		

DISCUSSION

The purpose of this study was to assess the knowledge and practices of nurses regarding the prevention of Surgical Site Infection [SSI]. The current study revealed that the majority of nurses have poor knowledge and average practices scores regarding the prevention of SSI. These findings were in line with many other studies conducted across the world. Accordingly, a study conducted in Ethiopia reported that the majority of nurses had insufficient knowledge about the prevention of SSIs [16]. Similarly, another study conducted in Egypt reported a low level of knowledge among surgical unit nurses [17]. Moreover, a study conducted in Lahore, Pakistan, also reported a low level of knowledge among nurses regarding the prevention of SSI [18]. However, the findings of some studies were in contrast with the current study. In this regard, a study conducted in Lahore, Pakistan, reported that 75% of the study participants had an excellent level of knowledge regarding SSI. It was reported by the aforementioned study that most of the nurses had attended the refresher courses regarding infection control and prevention; that's why their knowledge level and practice scores were excellent [19]. In the current study, most of the nurses had not attended the training on infection control and prevention; therefore, their scores were poor. Similarly, a study conducted in Northwest Ethiopia reported that training in infection control has enhanced the knowledge level and practices of nurses regarding the prevention of SSI [20]. The findings of the present study reported that the majority of the nurses have an average level of practice scores regarding the prevention of SSI. These findings were aligned with research in the South West Region of Cameroon, which revealed that nurses in the surgical units had pitiable practices for the prevention of SSI [21]. Similarly, research conducted by Jaleta also reported average levels of practice among nurses in the prevention of surgical wound infection [22]. Moreover, a study conducted by Mengesha revealed that the practices of nurses were poor in the prevention of SSI.

CONCLUSIONS

The study findings showed that the knowledge level and practices of nurses regarding the prevention of SSI were inadequate. Based on these findings, the researcher recommends the arrangement of proper infection control training for clinical nurses regularly, as well as a focus on infection control courses in academia. In addition, the study highlighted that the most significant demographic factor for the prevention of surgical site infection is qualification, which signifies the role of high qualification in the prevention of surgical site infection.

Authors Contribution

Conceptualization: SM
Methodology: SM, SUH, MR
Formal analysis: SM, MNK
Writing, review and editing: SM, MNK, SUH, MR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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Original Article

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Reamed Versus Unreamed Intramedullary Interlocking Nail for Gustilo and Anderson Type II and IIIA in Open Fractures of Shaft of Tibia

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ABSTRACT

Open fractures of the tibial shaft, particularly Gustilo and Anderson Type II and IIIA fractures, present a unique and challenging scenario in orthopedic trauma care. **Objectives:** To compare the outcomes of reamed versus unreamed intramedullary nailing in the management of Gustilo and Anderson Type II and IIIA open tibial shaft fractures. **Methods:** This prospective cohort study study was conducted at Gajju Khan Medical College/ Bacha Khan Medical Complex, Swabi from May 2023 to December 2023. Data were collected from 129 patients. All surgeries were performed under general or spinal anesthesia by experienced orthopedic trauma surgeons. The standard anterolateral approach was used for tibial nailing. **Results:** 129 patients were enrolled in the study, with 64 patients in the reamed group and 65 patients in the unreamed group. The mean age of patients in the reamed group was 36.4 ± 9.2 years, and in the unreamed group, it was 37.2 ± 8.7 years. The mechanisms of injury were also comparable, with both groups experiencing similar proportions of motor vehicle accidents (58%), falls from height (34%), and industrial accidents (8%), with p-values all greater than 0.05, indicating no significant differences between the groups. The Reamed Group had significantly better outcomes compared to the Unreamed Group. **Conclusions:** It was concluded that reamed intramedullary nailing is superior to unreamed nailing in the treatment of Gustilo and Anderson Type II and IIIA open tibial shaft fractures. The reamed group demonstrated higher union rates, faster healing times, lower infection rates, and better functional outcomes.

INTRODUCTION

Open fractures of the tibial shaft, particularly Gustilo and Anderson Type II and IIIA fractures, present a unique and challenging scenario in orthopedic trauma care. These fractures often occur in association with high-energy precipitating factors, including road traffic accidents, and falls from tall structures or at workplaces. Due to the anatomic position and the subcutaneous nature of the tibia, open injuries of the bone are easily obtained with exposure and contamination of the bone [1]. The management of these injuries involves an understanding of the biomechanics by which fracture fixation and the biology of fracture healing occur. Interlocking nailing has become the gold standard for the management of tibial shaft fractures, making use of inherent advantages that include stability and early mobilization and maintenance of the anatomical alignment. But, the mode of nail installation

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either with reamed or unreamed still being the subject of controversy [2]. Both methods have advocates and supporters and different arguments are given on the impact on fracture healing, infection incidence, and functional outcome. There are two variants of intramedullary nailing; reamed and non-reamed intramedullary nailing; reamed intramedullary nailing entails the mechanical enlargement of the medullary canal to accommodate a bigger diameter nail. It is assumed that such an approach improves the stability of the implant resulting from the increased contact area between bone and nail and possible effective compression in the fracture zone [3]. Intramedullary nailing that has not been reamed, however, does not present these risks since the medullary blood flow is preserved and there is a least thermal shock and mechanical insult to the bone [4]. This technique utilizes smaller diameter nails that may prove to have minimal interference with the biology of the fracture site [5]. Even though unreamed nailing is thought to be less traumatic, following its use of arguments including the fact that infection rate is reduced, as well as local blood supply is not interfered with, which is highly important in open fractures with moderately to severely affected soft tissues [6]. Some of the negatives discussed by opponents of unreamed nailing include claims that, because the diameter of the nail is less than that of a reamed nail, it offers less mechanical support and stands a greater likelihood of failure in the middle of the fractured segments or when dealt with in segmental fractures [7]. Type II and IIIA of Gustilo and Anderson classification are a spectrum of open tibial fractures wherein the extent of soft tissue injury varies. Type II fractures have moderate contamination and soft tissue injury while Type IIIA shows severe soft tissue injury but adequate coverage of the bone [8]. Most studies regarding reamed and unreamed intramedullary nailing are concentrated in metropolitan regions where there are sophisticated surgical facilities, well-maintained sanitary conditions, and follow-up care is ensured. This method also neglects the rural portion of the study, which is impactful due to its lack of infrastructure, considerably lagged interventions, and limited access to specialized orthopedic care. There are gaping holes in the assumption that surgical procedures in highly equipped urban hospitals will have the same results and effectiveness in rural hospitals. Quite a few rural regions are plagued with delays in dealing with the first step of a fracture, poor control of infection, and insufficient resources during rehabilitation, which all aggravate already hard open tibial fractures [9].

This study aims to compare the outcomes of reamed versus unreamed intramedullary nailing in the management of Gustilo and Anderson Type II and IIIA open tibial shaft fractures.

METHODS

This prospective cohort study study was conducted at Gajju Khan Medical College/ Bacha Khan Medical Complex, Swabi. The duration of the study was May 2023 to December 2023. The institutional review board Gajju Khan Medical College / Bacha Khan Medical Complex, Swabi reference no 2259/Ethical Board /GKMC approved the study. A written informed consent was taken. Data were collected from 129 patients. The sample size was calculated using an Open-Epi calculator. These participants represent a diverse range of demographics, including both genders and spanning a specified age range. Data were collected through a purposive sampling technique. This approach was justified by the need to focus on a specific patient population most relevant to the study's objectives. Adults aged 18-60 years with Gustilo and Anderson Type II or IIIA open fractures of the tibial shaft and presenting within 72 hours of injury were included in the study. Patients with Gustilo and Anderson Type I or Type IIIB fractures, with poly-trauma or fractures in which fixation was contraindicated and with Open fractures with severe contamination or infected wounds requiring extensive debridement or flap coverage were excluded. Patients were randomly allocated to either the reamed or unreamed intramedullary nailing groups based on their treatment preferences or surgeon discretion. Group 1: Reamed Intramedullary Nailing (n=64) Group 2: Unreamed Intramedullary Nailing (n=65). In Group I, the medullary canal was reamed to an appropriate size to accommodate a larger diameter interlocking nail. Reaming was performed using standard reaming instruments, and the nail was inserted under fluoroscopic guidance. The fracture site was stabilized with interlocking screws at both the proximal and distal ends of the tibia. In Group II, an unreamed intramedullary nail was inserted without prior reaming of the medullary canal. The nail size was chosen to closely match the diameter of the canal, and interlocking screws were inserted as in the reamed group. All surgeries were performed under general or spinal anesthesia by experienced orthopedic trauma surgeons. The approach used was the standard anterolateral approach for tibial nailing. In both group's analyses, detailed wound debridement was performed, and any object or necrotic tissue was removed from the wound. For Type IIIA fractures where the periosteum was damaged but the soft tissue avulsion was severe, special consideration was paid to managing the soft tissues. Open lesions, which were infected or contaminated, were treated by infection control measures. In addition to the specific interventions, all patients were managed according to the overall postoperative plan, which consisted of antibiotic

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prophylaxis for 48 hours. Pain relief according to universal anesthesia standard operational procedures and early ambulation with the assistance of crutches or a walker depending on the amount of pain felt by the patient and the degree of comfort received. Data were analyzed using SPSS version 25.0 (IBM, Armonk, NY). Continuous variables such as age and time to union were expressed as mean ± standard deviation, and categorical variables, such as the incidence of infection and nonunion, were presented as proportions. A p-value <0.05 was considered statistically significant. Transcriptions of qualitative data were analyzed using both deductive and inductive coding methods. A predefined coding framework was applied to categorize infection rates, union time, soft tissue complications, and functional recovery, while an inductive approach was used to capture emerging themes from patient feedback and surgeon reports. To ensure coding reliability, two independent reviewers analyzed a subset of the data, and inter-coder agreement was measured using Cohen's Kappa statistic which was >0.80.

RESULTS

In total, 129 patients were enrolled in the study, with 64 patients in the reamed group and 65 patients in the unreamed group. The mean age of patients in the reamed group was 36.4 ± 9.2 years, and in the unreamed group, it was 37.2 ± 8.7 years. The mechanisms of injury were also comparable, with both groups experiencing similar proportions of motor vehicle accidents (58%), falls from height (34%), and industrial accidents (8%), with p-values all greater than 0.05, indicating no significant differences between the groups (Table 1).

Table 1: Patient Demographics and Mechanism of Injury

Parameters	Reamed Group (n=64)	Unreamed Group (n=65)	p-Value
Mean Age (Years)	36.4 ± 9.2	37.2 ± 8.7	0.58
Gender (Male : Female)	45:19	42:23	0.45
Mechanism of Injury			
Motor Vehicle Accident (%)	58%	58%	1.00
Fall from Height (%)	34%	34%	1.00
Industrial Accident (%)	8%	8%	1.00

The fracture types between the two groups were well-matched, with both groups having 75% of patients with Type II fractures and 25% with Type IIIA fractures. The distribution of fracture types was identical in both the Reamed and Unreamed groups (Type II: 48 Vs. 49 patients, Type IIIA: 16 Vs. 16 patients), with a p-value of 1.00, indicating no significant differences between the groups (Table 2).

Table 2: Fracture Classification (Gustilo and Anderson Type)

Fracture Type	Reamed Group (n=64)	Unreamed Group (n=65)	p-Value
Type II (%)	48 (75%)	49 (75%)	1.00
Type IIIA (%)	16 (25%)	16 (25%)	1.00

The Reamed Group had significantly better outcomes compared to the Unreamed Group. The union rate was higher in the Reamed Group (96.9% vs. 89.2%, p=0.04), and the time to union was shorter (18.3 ± 3.5 weeks vs. 21.5 ± 4.1 weeks, p=0.02). Infection rates were also lower in the Reamed Group, with fewer superficial infections (7.8% vs. 13.8%, p=0.03), deep infections (0% vs. 3.1%, p=0.04), and a lower total infection rate (7.8% vs. 17.7%, p=0.03) (Table 3).

Table 3: Union Rates, Time to Union and Infection Rates

Parameters	Reamed Group (n=64)	Unreamed Group (n=65)	p-Value
Union Rate (%)	96.9%	89.2%	0.04
Time to Union (Weeks)	18.3 ± 3.5	21.5 ± 4.1	0.02
Superficial Infection (%)	7.8%	13.8%	0.03
Deep Infection (%)	0%	3.1%	0.04
Total Infection Rate (%)	7.8%	17.7%	0.03

The American Orthopedic Foot and Ankle Society (AOFAS) scores at both 6 months (88.2 ± 5.3 vs. 84.3 ± 6.1, p=0.01) and 1 year (91.5 ± 4.2 vs. 87.1 ± 5.7, p=0.02) were significantly higher in the Reamed Group, indicating better functional recovery. Additionally, the VAS pain scores were lower in the Reamed Group at both 6 months (2.1 ± 1.4 vs. 3.2 ± 1.8, p=0.03) and 1 year (1.4 ± 1.2 vs. 2.6 ± 1.5, p=0.02), suggesting less pain. The Reamed Group also had a lower total complication rate (3.1% vs. 7.7%, p = 0.04), with fewer implant failures (3.1% vs. 7.7%, p=0.04) and no cases of malalignment (0% vs. 4.6%, p=0.01). The mean fracture angulation was also smaller in the Reamed Group (3.2 ± 2.1° vs. 5.3 ± 3.2°, p=0.01), indicating better alignment at union (Table 4).

Table 4: Functional Outcomes, Complication Rates and Radiological Findings

Parameters	Reamed Group (n=64)	Unreamed Group (n=65)	p-Value
AOFAS Score (6 Months)	88.2 ± 5.3	84.3 ± 6.1	0.01
AOFAS Score (1 Year)	91.5 ± 4.2	87.1 ± 5.7	0.02
VAS Pain Score (6 Months)	2.1 ± 1.4	3.2 ± 1.8	0.03
VAS Pain Score (1 Year)	1.4 ± 1.2	2.6 ± 1.5	0.02
Total Complications (%)	3.1%	7.7%	0.04
Implant Failure (%)	3.1%	7.7%	0.04
Malalignment (%)	0%	4.6%	0.01
Mean Fracture Angulation (°)	3.2 ± 2.1	5.3 ± 3.2	0.01

DISCUSSION

This study compares the outcomes of reamed versus unreamed intramedullary nailing for the treatment of open tibial shaft fractures classified as Gustilo and Anderson Type II and IIIA. The study shows that there are profound

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differences between the two groups of treatment that include, fracture union, infection, functional outcome, and complications. The work under consideration offers a promising understanding of the most effective treatment of open tibial fractures, which is a problematic issue because of infection, nonunion and poor function outcomes [10]. Consequently, one of the highlights of this study was the increased rate of union and the time it took for union among the reamed patients as compared to the unreamed patients. In the reamed group, 96.9% of the fractures united within the expected time and with a mean time to union of 18.3 weeks [11]. The literature shows that reaming hastens fracture healing through biological means. Reaming is known to enhance the flow of intramedullary blood and it is thought that this hence speeds up the osteogenesis process and union. The unreamed group on the other hand had a union rate of 89.2% and meant time to union of 21.5 weeks. These findings correlate with those of earlier studies, which have suggested that unreamed nails may lead to delayed union or nonunion in some instances, especially in severe or open fractures with substantial soft tissue involvement [12]. Even though reamed nails offer increased safety in situations with gross contamination or soft-tissue involvement, the postoperative healing results in the reamed group were superior in the present study [13]. The faster union observed in the reamed group may also be attributed to biomechanics which can be attributed to improved stability offered by the increased caliber of the reamed nail which essentially locks into the smooth, tightly fitting hole of the medullary canal designed to support the healing bone [14]. Infection is still one of the most feared complications in open fractures whereby Gustilo and Anderson Type II and IIIA fractures cause significant soft tissue injury [15]. The infection rate of the reamed group was lower than that of the unreamed group (7.8 % vs 17.7 %), and the number of deep infections was also less. This is in line with the hypothesis that reaming may not raise the risk of infection as postulated previously where the practice was held to risk the introduction of more debris or bacteria to the medullary space [16]. Surprisingly, though the superficial infection rate was significantly higher in the unreamed group (13.8% compared to 7.8% in the reamed group), deep infection and osteomyelitis rates were also higher in the former group (3.1 %compared to 0% in the latter group). Parmar Deep wound infections may need other operations, such as wound debridement or longer courses of antibiotics, and can greatly influence the outcome, leading to lengthened patient stays, impaired mobility, and increased costs [17]. The overall lower infection rate in the reamed group may therefore be a result of superior fracture stabilization and less manipulation of soft tissues. He also said that reamed nailing results in better and more stable versions of stability, which could lessen any micro-motion that occurs at the fractured area and decrease the odds of infection. Thus, improved soft tissue control during the surgery can also be attributed to the reasons of the lower infection rate in the reamed group [18]. In this study, functional results as measured by the AOFAS Ankle-Hind foot scale and VAS pain score were superior in the reamed group. The AOFAS score was greater in the reamed group than the unreamed group at both, 6 months of 88.2 and 1 year of 91.5 as compared with the unreamed group 84.3 at 6 months and 87.1 at 1 year [19]. Likewise, the pain scores on VAS were lower in the reamed group at both the follow-up points suggesting lesser pain and better functional status. The authors suggest that the improvement of the other indicators in the same group is explained by several reasons. First, the time to union in the reamed group in this study was faster, and patients were unlocked allowing early weight bearing and rehabilitation. Faster healing in turn reduces the length of time that the patient lays off the affected joint, hence reducing cases of joint stiffness, muscle waste and permanent disability [20]. Naseer *et al.*, studied the infection rates and fracture union of patients with open tibia fractures on reamed compared to unreamed interlocked IM nailing. It was a prospective comparative study. Group A's mean age was 378.3 and Group B's mean age was 368.49. In group A Vs B, fracture union occurred in 40 (40%) and 47 (47%) patients (p=0.037) and Supplemental Security Income (SSI) occurred in 2 (4%) and 5 (10%) patients (p=0.240), respectively. It was found that reamed IM interlocking nails were superior in terms of fracture union compared to unreamed nails and there was no significant difference in the frequency of SSI between both interventions [21]. Furthermore, the increased stability provided by the reamed intramedullary nail may have provided a stable environment for better alignment of the fracture promoting better functional recovery. To the best of the author's knowledge, this study fills the gap in the existing literature by comparing the outcomes of reamed and unreamed intramedullary nailing for open tibial fractures.

CONCLUSIONS

It was concluded that reamed intramedullary nailing is superior to unreamed nailing in the treatment of Gustilo and Anderson Type II and IIIA open tibial shaft fractures. The reamed group demonstrated higher union rates, faster healing times, lower infection rates, and better functional outcomes. Therefore, reamed nailing should be considered the preferred method of fixation in these cases, provided there is adequate soft tissue coverage and minimal contamination.

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Authors Contribution

Conceptualization: MS
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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Antibiotic Prescription Practices among Dentists After Extractions in Lahore

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ABSTRACT

Antibiotics, discovered by Sir Alexander Fleming in 1929, have significantly advanced medical therapeutics. However, the rising antibiotic resistance has been the result of its overuse in the past few decades. **Objective:** To evaluate the antibiotic prescribing practices after dental extractions of house officers in Lahore. **Methods:** A study was conducted with a sample size of 127 house officers/interns from March to June 2024, from various dental hospitals in Lahore. These participants were asked to complete an anonymous questionnaire that explored their knowledge, attitudes, and practices related to prescribing antibiotics following tooth extractions. The data collected were analyzed using SPSS version 25.0 to identify trends and gaps in their understanding. **Results:** The participants had an average age of 23.77 years, with slightly more females than males. A vast majority (92.1%) prescribed antibiotics when a patient had a periapical abscess with a fever, while fewer (18.9%) did so simply because a patient requested it after a routine extraction. A significant knowledge gap among house officers in classifying antibiotics, with 81.1% incorrectly identifying Azithromycin as a broad-spectrum antibiotic and 64.6% misclassifying narrow-spectrum antibiotics. **Conclusions:** This study highlighted that while there is a general awareness of antibiotic resistance among house officers, there is still a significant gap in their adherence to proper guidelines when prescribing antibiotics after tooth extractions. The findings suggested a need for multi-prog strategies and their application to ensure that antibiotics are used judiciously, thereby helping to combat the growing problem of antibiotic resistance.

INTRODUCTION

Antibiotics, defined by Britannica as chemical substances produced by living organisms to inhibit other microorganisms, were accidentally discovered by Sir Alexander Fleming in 1929. This breakthrough significantly revolutionized 20th-century therapeutics. Initially used for military purposes during World War II, antibiotics became widely available, reducing life-threatening illnesses [1]. Dentists frequently treat bacterial infections originating in the orofacial region, primarily originating in tooth pulp. Standard treatments include fillings, scaling, root planning, root canal therapy, extractions, and abscess [2]. When surgery is not suitable, antibiotics are prescribed for conditions like necrotizing ulcerative gingivitis, bacterial sialadenitis, certain periodontitis, pericoronitis, and facial cellulitis [3]. Tooth extraction is common in dental practice, though its frequency has declined over the years [4]. Caries and periodontal disease remain the main reasons for extractions, with impacted third molars often requiring removal due to inflammation or complications [5]. Post-extraction care aims to minimize discomfort and prevent complications like trismus, pain, trismus, edema, fever, and dry socket, which can disrupt daily life. These issues stem from inflammatory responses or postoperative infection, especially in cases of severe periodontitis, extensive caries, or aggressive extractions [6, 7]. Alveolar osteitis (dry socket) occurs when a blood clot dissolves due to bacterial invasion causing severe pain. Although rare, postoperative infections are more likely

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after complex facial surgeries, especially after roadside accidents or in patients with systemic conditions like SLE, HIV, diabetes, or cancer [8]. In such cases, prophylactic antibiotics are necessary. Common antibiotics include erythromycin, amoxicillin, penicillin, metronidazole, doxycycline, and clindamycin, administered orally or parenterally [9, 10]. A review of Canadian dentists' prescribing habits revealed a 62% increase in antibiotic use from 1996 to 2013. A Cochrane review found that antibiotics reduced the risk of infection, dry socket, and pain after third molar extraction but questioned their use in routine extractions due to the potential for antibiotic resistance [5]. Antibiotic resistance highlights the importance of evaluating prescribing patterns following post-tooth extraction. Inappropriate use not only contributes to resistance but also incurs significant healthcare costs. Studies have shown over 50% of antibiotics are inappropriately prescribed raising safety concerns [9]. Furthermore, antibiotics are not necessary after routine dental extractions supplementing the need to reduce its misuse [11, 12]. Addressing this issue requires continuous professional development and targeted educational program initiatives to improve antibiotic prescribing practices [13]. However, research indicates dentists do not always follow the guidelines, often prescribing antibiotics unnecessarily. Evidence indicates prophylactic antibiotics are frequently prescribed without assessing the patient's endocarditis risk status [14]. Despite improvements following interventions and audits, adherence to the latest guidelines from the American Heart Association and the American Association of Orthopaedic Surgeons remains inconsistent [15].

The study aimed to evaluate the antibiotic prescribing practices of house officers/interns at various dental hospitals in Lahore. This would help us assess their knowledge and awareness of rational antibiotic use post-tooth extraction.

METHODS

This cross-sectional study used anonymous self-administered questionnaires distributed via Google Forms using a convenience sampling technique. This was conducted at various dental hospitals in Lahore from March to June 2024. Ethical approval was obtained from the Ethical Review Board of the University College of Dentistry, Lahore (UCD/ERCA/24/205). A sample size of 127 participants was calculated using $n=\frac{Z^2_{1-\alpha/2}\ P\ (1-P)}{d^2}$ with a 90% confidence level, a 6.76% margin of error, and an expected 69% average knowledge score on antibiotics prescription [16]. House Officers were briefed on completing the questionnaire. Informed consent was obtained. Only recently graduated house officers (BDS) were included while dental students, post-graduate trainees, general dentists, and specialists were excluded. The questionnaire had three parts: (a) Fifteen questions assessing knowledge of antibiotic prescriptions [17, 18]; (b) Eight questions evaluating attitude towards antibiotic use after routine dental extractions. [2, 19]; and (c) Questions assessing knowledge of broad- and narrow-spectrum antibiotics for odontogenic. Data were analyzed using SPSS version 25.0. Quantitative variables were presented with mean +/- standard deviation. Qualitative variables were presented with frequency and percentages. An Independent sample t-test was applied and p-value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of the house officers surveyed was 23.77 years, with a standard deviation of 1.009 years. The sample consisted of 48% males and 52% females, resulting in a male to female ratio of 1:1.2. The survey explored the antibiotic prescription practices of house officers after routine tooth extraction under various conditions. It was found that 92.10% of house officers prescribed antibiotics for periapical abscesses with fever. For atraumatic single tooth extraction in immunocompromised patients, 74.00% of house officers prescribed antibiotics. Notably, only 18.90% of house officers prescribed antibiotics on patient's demand after simple tooth extraction. The detailed results are summarized in the following (Table 1).

Table 1: Knowledge of House Officers Towards Antibiotic Prescription Practices After Tooth Extraction

S.No.	Are Antibiotics Recommended For Use?	Yes Frequency (%)	No Frequency (%)	Don't Know Frequency (%)
1.	Asymptomatic chronic periapical pathology	63 (49.6%)	55 (43.3%)	9 (7.1%)
2.	Acute periapical abscess with no signs of fever or chills	70 (55.1%)	56 (44.1%)	1 (0.8%)
3.	Periapical abscess with fever	117 (92.1%)	6 (4.7%)	4 (3.1%)
4.	Periapical pathology progressed into cellulitis	111 (87.4%)	12 (9.4%)	4 (3.1%)
5.	3rd molar extraction with mild pericoronitis	71 (55.9%)	52 (40.9%)	4 (3.1%)
6.	3rd molar extraction with moderate pericoronitis	86 (66.9%)	35 (27.6%)	7 (5.5%)
7.	3rd molar extraction with severe pericoronitis	110 (86.6%)	13 (10.2%)	4 (3.1%)
8.	On patient's demand after simple tooth extraction	24 (18.9%)	100 (78.7%)	3 (2.4%)
9.	Trismus resulting from dental infection	77 (60.6%)	40 (31.5%)	10 (7.9%)
10.	Atraumatic single tooth extraction in immunocompetent patients	37 (29.1%)	83 (65.4%)	6 (4.7%)
11.	Atraumatic multiple tooth extraction in immunocompetent patients	51 (40.2%)	72 (56.7%)	4 (3.1%)

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12.	Atraumatic single tooth extraction in immunocompromised patient	94 (74%)	30 (23.6%)	3 (2.4%)
13.	Atraumatic multiple tooth extraction in immunocompromised patients	106 (83.5%)	16 (12.6%)	5 (3.9%)
14.	Severe pain not attributed to infection	36 (28.3%)	82 (64.6%)	9 (7.1%)
15.	Alveolar osteitis (Dry Socket)	32 (25.2%)	86 (67.7%)	9 (7.1%)

Males and females showed similar awareness of drug resistance and antibiotic guidelines with no significant gender-based differences. However, significantly more females (86.9%) believed self-medication contributes to antibiotic resistance than males (67.4%) (p=0.33). Additionally, males reported noticing adverse drug reactions more frequently (60.5%) compared to females (34.5%) (p=0.018). Other responses, such as dosage calculation and allergy inquiries did not show significant gender variation(Table 2).

Table 2: Attitude of House Officers Towards Antibiotic Prescription Practices After Tooth Extraction

Questions	Responses	Total	Males Frequency (%)	Females Frequency (%)	p-value
Have you heard about the word 'Drug Resistance'?	Yes	111	36 (83.7%)	75 (89.3%)	0.268
	No	16	7 (16.3%)	9 (10.7%)	
Are you aware of the latest antibiotic guidelines for prescribing antibiotics in patients after tooth extraction?	Yes	52	16 (37.2%)	36 (42.9%)	0.488
	No	75	27 (62.8%)	48 (57.1%)	
Do you follow the latest antibiotic guidelines for prescribing antibiotics in patients after tooth extraction?	Yes	54	18 (41.9%)	36 (42.9%)	0.285
	No	73	25 (58.1%)	48 (57.1%)	
Do you enquire from your patient about whether he/she has taken a course of antibiotics in the past 1 week before prescribing antibiotics?	Yes	95	29 (67.4%)	66 (78.6%)	0.274
	No	32	14 (32.6%)	18 (21.4%)	
Do you think self-medication with antibiotics by patients to get relief from dental pain may be responsible for antibiotic resistance?	Yes	102	29 (67.4%)	73 (86.9%)	0.033*
	No	25	14 (32.6%)	11 (13.1%)	
Do you calculate the dosage of the drugs according to the age and weight of the patient?	Yes	61	21 (48.8%)	40 (47.6%)	0.94
	No	66	22 (51.2%)	44 (52.4%)	
Have you ever noticed any adverse drug reactions to antibiotics in the patients?	Yes	55	26 (60.5%)	29 (34.5%)	0.018*
	No	72	17 (39.5%)	55 (65.5%)	
Do you ask patients about any known antibiotic allergy?	Yes	110	34 (79.1%)	76 (90.5%)	0.193
	No	17	9 (20.9%)	8 (9.5%)	

The study evaluated the knowledge of house officers regarding broad and narrow-spectrum antibiotics used for treating odontogenic infections. Participants were presented with four antibiotic options for each category. For broad-spectrum antibiotics, Azithromycin and Amoxicillin with clavulanic acid were the correct choices. The results showed that while 67% of the participants correctly recognized Amoxicillin with clavulanic acid, only 18.9% recognized Azithromycin as a broad-spectrum antibiotic, meaning 81.1% were unaware of its correct classification. For narrow-spectrum antibiotics, Clindamycin and Penicillin were the correct options. An equal percentage of participants (35.4%) correctly identified both Clindamycin and Penicillin as narrow-spectrum antibiotics, leaving 64.6% who incorrectly classified them. These findings highlight significant knowledge gaps among house officers, particularly in recognizing Azithromycin as a broad-spectrum antibiotic and the correct classification of narrow-spectrum antibiotics. The detailed response distribution is summarized in (Table 3).

Table 3: Knowledge of House Officers about the Broad and Narrow-Spectrum Antibiotics

Broad Spectrum Antibiotic		
Name of Antibiotic	**Yes Frequency (%)**	**No Frequency (%)**
Azithromycin*	24 (18.90%)	103 (81.10%)
Amoxicillin with clavulanic acid*	18 (66.90%)	42 (33.10%)
Metronidazole	18 (14.20%)	109 (85.80%)
Penicillin	47 (37.00%)	80 (63.00%)
Narrow Spectrum Antibiotic		
Name of Antibiotic	**Yes Frequency (%)**	**No Frequency (%)**
Azithromycin	22 (17.30%)	105 (82.70%)
Clindamycin*	45 (35.40%)	82 (64.60%)
Moxifloxacin	38 (29.90%)	89 (70.10%)
Penicillin*	45 (35.40%)	82 (64.60%)

*Correct Answers [17]

DISCUSSION

This study aims to evaluate the knowledge of house officers regarding antibiotic prescribing practices after tooth extraction in various dental hospitals across Lahore. Antibiotics are frequently prescribed after dental procedures, including tooth extractions, to prevent or manage postoperative infections. It is still debatable

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whether to administer an antibiotic medication before or following tooth extractions to avoid issues following tooth exodontia. Regarding the efficacy and appropriateness of antibiotic prescriptions in avoiding surgical site infections, there is disagreement in the research [20]. In this cross-sectional survey, data were collected from house officers in hospitals across Lahore to assess their antibiotic prescription practices for periapical infections without systemic involvement. The results revealed that 55.1% of participants in this study prescribed antibiotics in these cases. In contrast, only 15% of participants in India prescribed antibiotics post-tooth extraction, and 47.1% of participants in Saudi Arabia did not use any antibiotics for periapical infections after drainage [18, 16]. Despite the understanding that antibiotics aren't necessary for mild to moderate pericoronitis, nearly 60% of participants prescribed antibiotics for mild cases, and 67% did so for moderate cases. However, 86.6% correctly identified the need for antibiotics in severe pericoronitis. In comparison, 78.7% of junior dentists in Sudan prescribed antibiotics for pericoronitis [2]. A study in Pakistan found 32% prescribed antibiotics, whereas a Saudi Arabian study found that 36.7% answered correctly about antibiotic use in this condition, while only 4.1% of participants in India prescribed antibiotics for pericoronitis [21, 16, 18]. Böttger S *et al.*, recommended combining surgical intervention with antibiotic treatment in cases of infection accompanied by pus discharge [22]. Additionally, it is advised that children with odontogenic cellulitis be treated with broad-spectrum antibiotics [23]. In this study, 87% of participants chose to prescribe antibiotics for cellulitis, whereas Yousufi S *et al.*, found that only 14.2% of participants in Peshawar opted for the same approach [21]. In India, 12.5% of dentists prescribed antibiotics in such cases; however, a study from Saudi Arabia reported a much higher rate of 90.8% [18, 16]. These findings highlight significant variations in antibiotic prescription practices across different studies. Many clinicians prefer to administer antibiotics and painkillers over several days to manage trismus and infection, allowing time for the symptoms of trismus to alleviate before investigating the root cause of the problem. More than 60% of participants in this study gave the right answer about the use of antibiotics in trismus, and atraumatic extraction in healthy and immunocompromised patients. Only 27.5% and 11.8% answered correctly in two other studies. [16, 24]. Al Marah ZA *et al.*, found that 51.1% of their participants prescribed antibiotics in dry Socket [24]. In this study, 25.5% of participants were prescribed antibiotics in dry sockets. 61.1% of participants in the Saudi study correctly answered that they don't prescribe antibiotics in this condition [16]. Overprescribing antibiotics can lead to various serious issues, such as bacterial resistance, gastrointestinal and blood-related complications, and disruption of bacterial flora in the body [24]. Additionally, standard infection treatments will lose their efficacy, and illnesses will continue to survive and spread more readily among people [25]. In this study, 83.7% of male and 89.3% of female participants were aware of the word drug resistance whereas 37.2% of males and 42.9% of females were aware of the latest antibiotic prescribing guideline. In a study in India, 98.5% of interns knew about drug resistance and 96.9% knew about the latest guidelines which were far better than our study's observations [19]. In Australia, dentists most frequently prescribed amoxicillin, accounting for 66.3% of all antibiotic prescriptions [26]. 66.90% and 18.9% of participants knew that amoxicillin with clavulanic (the most prescribed antibiotic in this study) and azithromycin is a broad-spectrum antibiotic. The discrepancy in antibiotic prescribing practices between the study and others, such as those conducted in India (26.6%) and Sudan (31% for dentoalveolar infections) highlights the influence of regional or institutional practices, as well as individual clinician preferences [18, 2]. Understanding these variations is crucial for identifying areas of improvement and implementing targeted interventions to promote appropriate antibiotic stewardship. The frequent prescribing of antibiotics for conditions like pericoronitis, periapical infections, cellulitis, and trismus suggests a potential for overreliance on antibiotics. This may be due to factors such as perceived patient expectations, insufficient awareness of evidence-based guidelines, or precautionary approaches to prevent complications from surgeries in oral and facial regions [25]. However, it is crucial to emphasize that antibiotics should be prescribed only when there are significant risks of complication or clear evidence of systemic involvement [26]. Studies with findings on participants' awareness and knowledge of antibiotic resistance and their adherence to prescribing guidelines reveal both strengths and areas for further improvement. The concept of antibiotic resistance is not novel anymore, but a notable number of the participants were unfamiliar with the latest prescribing guidelines and antibiotic-specific properties. This stresses the dire need for ongoing educational training programs to ensure and revise the knowledge and provide the means necessary for evidence-based decision-making. This study has, like all the other studies, had a few limitations. Since the questions were self-administered, participants might have replied with the answers they thought were correct rather than what they practice in clinics. This study focuses on one point in time, so it doesn't show how these practices have evolved or how they might be affected after educational interventions. Future studies should be longitudinal and include more intuitions across the country for a more comprehensive overview. Regular training and audits would help to ensure that guidelines are followed, and antibiotics are used responsibly in dental care.

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CONCLUSIONS

The study highlights gaps in house officers' knowledge of antibiotic prescription after tooth extractions. While most prescribed antibiotics for conditions like periapical abscess with fever and cellulitis, inconsistencies were noted. Many struggled to differentiate between broad and narrow-spectrum antibiotics. These results emphasize the need for rational antibiotic use in dental practice. Regular training and audits can help ensure adherence to guidelines and responsible antibiotic prescribing.

Authors Contribution

Conceptualization: SA, MAA
Methodology: SA, RS, IUR, AA
Formal analysis: SA, RS, IUR, AA
Writing, review and editing: MAA, TS, MAB

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Knowledge, Attitudes and Practices of Basic Life Support among University-Enrolled Undergraduate Medical Students in Karachi

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ABSTRACT

Basic Life Support (BLS) involves a core set of skills necessary to preserve life during medical emergencies. Both practical abilities and knowledge are crucial for managing life-threatening situations. **Objectives:** To assess the knowledge, attitudes and practices of BLS among undergraduate students enrolled in the medical program at a university in Karachi. **Methods:** The cross-sectional study was carried out from February 2022 to May 2022 at the Jinnah Sindh Medical University, Karachi, and included medical students of both genders from the first to the fifth year of the academic program. Data were gathered through a self-administered organized questionnaire. Data were analyzed using SPSS version 22.0. **Results:** Out of 310 medical students, 54.2% were female, and 45.8% were male. The study revealed that only 22.3% had taken the BLS course. 55.3% of medical students had adequate theoretical knowledge, while their practical skills in BLS were weak. The majority of the students, 73.4% were not confident in performing Cardiopulmonary Resuscitation (CPR), and only 8.7% had performed BLS on patients. 4% stated that they could use Automated External Defibrillators (AEDs). The attitude of medical students toward BLS was largely supportive, with 94% believing that BLS is essential for all medical students and should be integrated into the academic curriculum. **Conclusions:** It was concluded that Undergraduate medical students possess sufficient theoretical knowledge of BLS (CPR), while there is a significant gap in their practical skills. For this, continuous hands-on training in critical life-saving techniques should be included in the undergraduate program throughout their medical education.

INTRODUCTION

Worldwide, the burden of morbidity and mortality due to Cardiovascular Diseases (CVDs) is rising. The global mortality due to cardiovascular arrest rose from 12.4 million in 1990 to 19.8 million in 2022 [1]. The primary cause of death is sudden cardiac arrest. It is concerning that the survival rate is still under 10%, mainly due to sudden cardiac arrests occurring outside of hospitals [2]. Karachi's annual incidence of cardiac arrest is 166 per 100,000 people [3], with survival rates alarmingly low, 0% in traumatic cases and less than 2% in non-traumatic cases [4]. The high mortality rate can be easily reduced with some simple manoeuvres and resuscitation skills. It is important to have the knowledge and experience of cardiopulmonary resuscitation (CPR) skills to manage these emergencies effectively. Basic life support (BLS) is the fundamental set of skills required to sustain life during medical emergencies like respiratory or cardiopulmonary arrest when heartbeat or breathing has stopped. It is the most important component of the survival sequence that improves the chances of survival by CPR and increases the ratio of hospital discharges [5]. BLS includes a range of techniques to maintain vital functions such as airway patency, breathing456r, and circulation. It also involves identifying signs and symptoms of critical conditions and understanding how to apply and administer these techniques effectively [6]. Cessation of blood flow to the

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brain for just four minutes after a cardiac arrest can lead to damage, which becomes irreversible after seven minutes. BLS is a simple yet effective method that allows anyone to sustain life if administered within the first few minutes of collapse [7]. Knowledge and practice of BLS and easy CPR techniques guarantee the survival of the patient until more advanced medical intervention is available [8]. BLS requires no special resources, yet its significance is immeasurable. In the current situation, everyone should know life-saving techniques, but this knowledge and awareness are essential for healthcare professionals. Healthcare professionals are a vital part of the healthcare system. Few studies have been conducted on medical undergraduates in Pakistan, and no prior research has assessed the knowledge, attitude and practices regarding BLS among undergraduate medical students in Karachi.

This study aims to evaluate the knowledge, attitude and practices of BLS among undergraduate medical students. This study will provide baseline data and identify knowledge gaps, which will help formulate resuscitation training programs at medical institutions.

METHODS

The cross-sectional study was carried out at Jinnah Sindh Medical University (JSMU), Karachi, Pakistan, from February 2022 to May 2022, after approval of institutional review board letter no. JSMU/IRB/2021/-538. It employed a cross-sectional design, with a sample size of 310 students calculated based on 50% prevalence, 95% confidence level and 5% error margin using Open Epi software. The sample was chosen through a convenient sampling technique with inclusion criteria limited to medical students of both genders, aged 17-23 years from 1st to 5th year enrolled in the MBBS program at Jinnah Sindh Medical University. Students who refused to take part were not included. Participants were informed about the study's objectives, procedures, and their right to withdraw at any time without any negative consequences. All data collected were anonymized, and personal identifiers were removed to maintain confidentiality. Data were stored securely, with access restricted to the research team, in compliance with data protection regulations. After obtaining informed consent from the students, data were gathered using a structured questionnaire designed based on published surveys [9, 10]. A preliminary study involving 17 participants (10 medical students and seven professionals from the areas of critical care and emergency medicine) was conducted to assess the comprehensibility of the questionnaire. An anonymous questionnaire was divided into three parts. The first part, consisting of 13 questions, focused on theoretical knowledge about CPR, including, its components and the steps involved in performing it. The second part consists of 6 questions related to the training status and practices of BLS services among medical students. The third part comprises three questions related to attitudes towards the importance of BLS, opinions on including BLS as part of the curriculum and reasons for insufficient practical knowledge of BLS. The data were processed using Statistical Package for the Social Sciences (SPSS) version 22.0. Descriptive statistics was employed to summarize the study results. Frequency and proportion tables were utilized to present the categorical variables. The normality of the data distribution was assessed using the Shapiro-Wilk test. A one-sample binomial test was used to compare the observed proportions of categorical responses. A comparative analysis of BLS Knowledge Attitude and Skills (KAP) across different academic years was conducted using one-way ANOVA. Univariate and multivariate linear regression analyses were performed to identify predictors of KAP scores, with subgroups based on year of study, gender, and prior BLS experience.

RESULTS

Out of the 310 participants, 14 (45.8%) were male and 168 (54.2%) were female participants. The participant's ages varied from 17 to 23 years. Results regarding theoretical knowledge indicate that the majority of participants, 241(77.7%), identified the components of BLS, there was no statistically significant difference (p=0.249) between males and females in identifying the components of BLS, 247 (79.7%) students selected the correct location to palpate for a pulse during CPR, 283 (91.29%) students correctly identified how to recognize someone in need of CP, 249 (80.3%) students knew the first step when someone becomes unresponsive, 223 (71.9%) students identified the correct location for chest compressions in CPR. Nearly half of the students, 129 (41.6%), knew how long they should check the carotid pulse on adults, 153 (49.4%) students identified the correct steps to take when encountering a situation that requires resuscitation, 166 (53.5%) students selected the correct sequence of steps in CPR, 193 (62.3%) students knew the correct chest compression to ventilation ratio for adult CPR. However, only 60 (19.4%) students knew how frequently to check for a pulse during rescue breaths on an unconscious patient, 110 (35.5%) students identified the first response to a Choking Incident, 66 (21.3%) students selected the correct rate of chest compression in adult CPR and 108 (34.8%) students knew Automated external defibrillators (AED). A significantly higher proportion (p<0.001) of students lack knowledge about AED (Table 1).

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Table 1: Knowledge of Medical Students Regarding BLS (n=310)

Sr.no	Questions	n (%)
1.	What are the three main components of BLS?	241 (77.7%)
2.	How frequently should you check for a pulse while administering rescue breaths to an unconscious patient?	60 (19.4%)
3.	Where should you feel for a pulse on an unconscious adult while performing CPR?	247 (79.7%)
4.	How much time should you spend checking for a carotid pulse in an adult?	129 (41.6%)
5.	How will you recognize someone in need of CPR	283 (91.29%)
6.	What do you do when you encounter a situation that requires resuscitation? (Assume no scene danger)	153 (49.4%)
7.	If your friend suddenly begins showing signs of choking while eating, what would be your initial response?	110 (35.5%)
8.	Select the correct sequence of steps in CPR	166 (53.5%)
9.	If a family member suddenly complains of chest pain and becomes unresponsive at home but is still breathing, what should be your first step?	249 (80.3%)
10.	Where should chest compressions be applied during CPR?	223 (71.9%)
11.	Choose the appropriate rate for chest compressions during adult CPR.	66 (21.3%)
12.	Choose the correct chest compression to ventilation ratio for adult CPR.	193 (62.3%)
13.	Do you know about AED?	108 (34.8%)

Regarding the training status of the students, a large number of students, 241 (77.7%), did not take any training, and 235 (75.8%) students knew that their knowledge about BLS was not sufficient. Concerning the practice of BLS among medical students, 266 (85.8%) students agree that BLS should not be performed only in a healthcare facility. About half of the students, 158 (51%), have seen BLS being performed, but the majority of the students, 283 (91.3%), did not perform BLS on a patient. A significant number of students, 228 (73.5%), were not confident in performing CPR; there was no statistically significant difference in the reported confidence levels in performing CPR between participants who attended a BLS training course and those who did not (p=0.69). A significant number of students, 297 (95.8%), were not confident in using an AED (Table 2).

Table 2: Practices of BLS among Medical Students (n=310)

Sr.no	Questions	Responses	
		Yes	No
		n (%)	n (%)
1.	Have you ever participated in a BLS training course?	69 (22.3%)	241 (77.7%)
2.	Do you believe BLS should be performed only in a healthcare facility?	44 (14.2%)	266 (85.8%)
3.	Have you ever seen BLS being performed?	158 (51.0%)	152 (49.0%)
4.	Have you ever performed BLS on a patient?	27 (8.7%)	283 (91.3%)
5.	Are you confident in performing CPR?	82 (26.5%)	228 (73.54%)
6.	Can you use an AED?	13 (4.2%)	297 (95.8%)

Relating to the attitude of students towards BLS, 235 (75.8%) students responded that they do not believe their knowledge of BLS is sufficient. 292 (94.2%) students believed that all medical students need to know about BLS. A significantly higher number of students, 293 (94.5%), agreed that BLS training should be incorporated into the medical curriculum (p<0.001) (Table 3).

Table 3: Attitudes towards BLS among Medical Students (n=310)

Sr.no	Questions	Responses	
		Yes	No
		n (%)	n (%)
1.	Do you feel that your knowledge of BLS is sufficient?	75 (24.2%)	235 (75.8%)
2.	Do you believe that all medical students should be trained in BLS?	292 (94.2%)	18 (5.8%)
3.	Do you believe BLS training should be included in your medical curriculum?	293 (94.5%)	17 (5.5%)

The comparative analysis indicates a significant difference in the BLS KAP scores across different academic years (p <0.001). The mean scores progressively increase from the 1st year (12.89), 2nd year (13.58), 3rd year (13.45), 4th year (14.64), to the 5th year (16.47) (Table 4).

Table 4: Comparative Analysis of BLS Knowledge Attitudes and Skills across Different Academic Years

Sr. no	Years of Study	Frequency	Mean ± SD	p-value
1.	1st Year	19	12.89 ± 2.5	p<0.001
2.	2nd Year	38	13.58 ± 2.0	
3.	3rd Year	66	13.45 ± 2.0	
4.	4th Year	130	14.64 ± 2.0	
5.	5th Year	57	16.47 ± 1.8	
Total		310	14.49 ± 2.1	

Both BLS training and year of study significantly predict student marks, while gender has no meaningful impact. BLS training shows the strongest effect, with students who received training scoring 3.344 points higher in the univariate and 2.895 points higher in the multivariate analysis when adjusted for other variables (p<0.001). The year of study has a moderate positive effect, with marks increasing by 0.896 points per year in the univariate analysis and 0.579 points in the multivariate analysis when adjusted (p<0.001). Gender shows no significant effect in either model (p>0.05) (Table 5).

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Table 5: Univariate and Multivariate Linear Regression Analysis of Factors Influencing Knowledge, Attitudes, and Practices scores of Medical Students

Sr. no	Variables	Univariate Analysis B (95% CI)	p-value	Multivariate Analysis B (95% CI)	p-value
1.	BLS Training	3.344 (2.580-4.108)	<0.001	2.895 (2.115-3.675)	<0.001
2.	Year of Study	0.896 (0.592-1.200)	<0.001	0.579 (0.285-0.873)	<0.001
3.	Gender	-0.128 (-0.840-0.584)	0.720	-0.022 (-0.646-0.602)	0.943
Constant				11.826 (10.376, 13.276)	<0.001

DISCUSSION

Healthcare professionals must be knowledgeable about the latest protocols and guidelines based on BLS services to manage life-threatening emergencies such as sudden cardiac arrest, airway obstruction, and breathlessness. Through the BLS course, they are proficient in skills such as performing CPR, using an AED, and relieving choking. Unfortunately, the present results revealed that undergraduate medical students had adequate theoretical knowledge of BLS (55.3%), while the majority of students (73.4%) were not confident in performing CPR. This indicates a significant lack of practical training among medical students Results also highlighted that only 22.3% of medical students had taken the BLS training. CPR is the most critical step in emergencies involving sudden cardiac arrest. Insufficient training in BLS (CPR) has been identified as a key factor contributing to the limited knowledge of CPR among doctors and other healthcare professionals in Pakistan [11, 12]. The results further revealed that 51% of medical students had observed BLS being performed on patients in hospital settings, while just 8.7% had performed BLS on patients. This represents a significant gap in their practical skills, they have the theoretical knowledge but lack the hands-on experience needed to perform effectively. Medical students are the healthcare professionals of tomorrow and should be well-trained in these skills. Research shows that the majority of junior doctors are not competent in managing a resuscitation cases [13], and they are often primary doctors who attend to patients in life-threatening conditions. Medical students should undergo continuous hands-on training in life-saving skills in a simulated environment, using manikins, in skills labs or through role-playing emergency scenarios throughout their medical education. Previous study shows that the knowledge and skills of first-year medical students were improved through BLS training, supplemented by hands-on sessions [14]. If the weaknesses in the application of practical skills for life-saving emergencies are not addressed in medical students, it could result in healthcare professionals who are unable to handle life-threatening situations. Recent studies show that healthcare professional has strong BLS knowledge, but their practical application of these skills is inadequate in a tertiary care hospital [15, 16]. Pulseless ventricular tachycardia and ventricular fibrillation are leading causes of cardiac arrest, which can result in sudden death [17]. Prompt defibrillation improves the chances of survival. The results of the current study indicated that a significant number of students (65.2%) lacked knowledge about AEDs, and only 4% stated that they could use an AED, which again emphasizes the need for rehearsing BLS skills in a controlled, non-emergency environment. Implementing a BLS course along with other resuscitation courses in the medical curriculum will not only enhance student's clinical abilities but also arm medical students with life-long skills. Results indicated that 85.8% of students knew that BLS should not be performed only in healthcare settings, which shows their understanding that BLS is a critical skill that may be needed in emergencies anywhere, including public places, workplaces, or at home. The perspective of medical students in the current study toward BLS was largely supportive, with 75.8% expressing that their knowledge of BLS was insufficient. Additionally, a significant number of students (94%) believed that BLS is essential for all medical students and should be integrated into the academic curriculum. The final question of the present study explored the reasons for the insufficiency of practical knowledge of BLS, with 65.2% of students identifying the lack of professional training as the primary cause. This suggests that students have limited chances to engage in hands-on training to develop their skills. A recent study highlights the insufficient focus on BLS and/or CPR education by institutions across Pakistan, with one-third of respondents reporting that they have never attended a session on BLS and/or CPR [18]. The comparative analysis indicates a significant difference in the BLS KAP scores across different academic years. The mean scores progressively increase from the 1st year to the 5th year, suggesting that students in higher academic years tend to perform better. This finding implies that the year of study significantly influences BLS KAP scores, likely due to increased exposure, experience, or learning opportunities during clinical rotations as students' progress in their studies. Univariate and multivariate linear regression analysis of factors associated with BLS KAP scores showed that BLS training was significantly associated with the knowledge and skills of medical students. This suggests that BLS training is a strong determinant of performance, underscoring the importance of early and comprehensive BLS education in improving students' knowledge, attitudes, and practices. These findings align with prior research that emphasizes the positive impact of BLS training on students' confidence and competence in

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emergencies [19, 20]. The year of study also showed a significant positive effect on BLS KAP scores, with marks increasing as students advanced in their academic careers. This trend may reflect the cumulative nature of medical education, where students gain more exposure to clinical scenarios and practical skills during clinical rotations, which could enhance their understanding and ability to apply BLS knowledge effectively. Interestingly, gender was not found to have any significant effect on BLS KAP scores in either analysis, suggesting that both male and female students perform similarly in BLS-related assessments. Given the poor practical skills in BLS (CPR) among medical students, which can lead to incompetent doctors, it is mandatory to include training in BLS and other resuscitation courses in the medical undergraduate curriculum from the first year, with annual revisions throughout their education until students become proficient in these skills. These life-saving skills are equally important for other medical practitioners and should be included in the allied health sciences programs. When healthcare professionals gain expertise in these life-saving skills, it will result in reduced mortality and morbidity rates in emergencies, both in and outside of hospitals.

CONCLUSIONS

Based on our study, we conclude that undergraduate medical students have adequate theoretical knowledge but are deficient in practical skills regarding BLS. BLS and other life-saving techniques should be included in the undergraduate curriculum from the first year and revised annually to ensure students become competent during their studies.

Authors Contribution

Conceptualization: QI
Methodology: QI, SS, SA, BA, AI, AM
Formal analysis: QI, SS, SA, BA, AI, AM
Writing review and editing: QI, SS, SA, BA, AI, AM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Exploring Artificial Intelligence Role in Enhancing Medical Education for Future Physicians

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ABSTRACT

Artificial intelligence (AI) has the potential to completely transform medical education by improving learning outcomes through data-driven insights, simulation, and individualized instruction. **Objectives:** To determine the impact of Artificial Intelligence on Medical Education and medical students' willingness and readiness to use it. **Methods:** An analytical cross-sectional study was conducted among medical students at a private medical institute. Ethical approval and informed consent were taken. The questionnaire was distributed through social media platforms. Mann-Whitney U test was performed, mean + SD was taken and Pearson correlation was used to assess mean rank distributions, higher means among variables, and significant associations. A p-value of <0.05 was considered statistically significant. **Results:** Higher mean ranks by the Mann-Whitney U test in all perception-related questions indicated a tendency for higher values in males than females. The mean + SD of perception score was 3.63 ± 0.66 and the willingness was 3.48 + 0.69 which showed a positive perception and willingness to use AI. ANOVA was employed with the most significant association, enabling doctors to make correct decisions. Pearson correlation between readiness for AI and their perceptions, and willingness to use AI showed a strong positive correlation between them with p values significant at <0.01 level. **Conclusions:** It was concluded that AI could revolutionize medical education by enhancing learning, and clinical decision-making, and supplementing traditional teaching methods. A significant positive correlation was found between AI readiness, perceptions, and willingness to use it, recognizing its role in shaping future medical practice.

INTRODUCTION

Although AI was first introduced in 1950, early limitations in its modelling hindered its acceptance and use in medicine. Overcoming these early challenges, AI, particularly deep learning, began making significant strides in healthcare around the early 2000s [1]. Today, AI systems can analyze complex algorithms and apply self-learning techniques, opening new possibilities for clinical practice [2]. AI has gained significant adoption in recent years, with expanding applications in healthcare. On the other hand, the acceptance of AI-driven healthcare solutions is still sluggish in developing countries like Pakistan. Artificial intelligence has been broadly applied lately because its usage in the medical field has increased [3]. A multi-method approach is essential to identify the challenges that may arise with the integration of AI in healthcare. AI applications will not replace doctors but will take over many tasks currently performed by physicians and create new roles in healthcare. Medical students and physicians need to understand the fundamental principles of AI to adapt to these changes effectively [4]. In AI healthcare applications, interest is now entering a boom. In radiology, nowadays, there exist AI applications utilizing deep learning methodologies, which perform effectively [5]. With AI innovations coming into play to impact practice, increased interest in training active and future doctors in the technology is being enthused [6]. Medical students' knowledge about AI is unknown and perception is yet to be determined [7]. This study will help to answer questions regarding the perception of medical students on credibility and reliance on artificial intelligence in the medical field.

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The development of the medical AI industry will depend on the students' views on medical AI which should be understood in great depth by medical experts [8]. Although in terms of medical AI much has been advanced technically, the use of this type of study is to analyze the views of medical students on the advancement of artificial intelligence in the field of medicine. This study explores how much medical students know and perceive AI and its implications and determines the knowledge of current practices of AI. Despite the growing integration of AI in healthcare, there is limited research on medical students' perceptions regarding AI's role in clinical practice, especially in developing countries like Pakistan.

This study aims to explore these perceptions, focusing on the acceptance, credibility, and potential role of AI in shaping future medical education.

METHODS

An analytical cross-sectional study was conducted among medical students at a private medical institute. A simple random sampling technique was used to collect data from a sample size of 207 students i.e. 46-1st year, 48-2nd year, 47-3rd year, 32-4th year, 34-Final year. 1st, 2nd, 3rd, 4th, and Final year medical students are included. The study duration was 6 months i.e. from June 2024 to November 2024. Ethical approval was taken from the Aziz Fatimah Medical and Dental College, Faisalabad with reference number IEC/308-24. Informed consent was taken beforehand. A validated questionnaire was adopted from a study after obtaining the author's consent and an extensive literature review [9]. Cronbach's coefficient of at least 0.7 was used to assess the internal consistency of the questionnaire. Starting from asking questions on socio-demographics, in the next section there were questions on students' AI perceptions from strongly disagree to strongly agree. In the next two sections, there were questions regarding the impact of AI on medical Education, willingness to use it, and readiness for AI. After that, the possible effects of AI in medicine were assessed which concluded the questionnaire. Likert scale scoring was done from 1 to 5, mean + SD was taken, the Mann-Whitney U test was used, and mean ranks were calculated within the gender variable. Mann-Whitney U Test was employed instead of the t-test since the data collected was ordinal (Likert Scale) rather than interval or ratio. Also, it evaluates median ranks between 2 independent groups without positing the normality of distribution. Also, the Pearson correlation was used and a p-value of <0.05 was considered statistically significant. The data were collected through Google Forms, and the survey was distributed via social media. While cost-efficient, it might have introduced some self-selection bias. Students who were more active on social media or had a greater interest in AI-related topics may have been more inclined to respond positively. To overcome these limitations, the study worked with a random sampling of the entire student population. The Statistical Package for the Social Sciences (SPSS) Version 25.0 was considered to analyze the data.

RESULTS

By using a simple random sampling technique, the total sample size was 207. Among them, 91(44%) were male and 116(56%) were female. Most participants were day scholars, 154 (74.4%) and belonged to urban areas, 170 (82.1%). The computer literacy level of most students was literate, 113 (54.6%); while competent was 69 (33.3%) students and proficient was 25 (12.1%) students. Most of the medical students 'sometimes' 131 (63.3%) and 'always' 65 (31.4%) used computer technology for learning while 11(5.3%) never used it. Most participants 179 (86.5%) had never received any training in artificial intelligence while 28 (13.5%) had received such training. AI should be embedded into the MBBS curriculum, which should also consist of the structured introduction of courses presenting AI fundamentals and clinical AI tools. Medical colleges should partner with tech institutes to launch an AI certification program. Significant p-values show significant differences between the perception levels of male and female, while higher mean ranks in all perception questions indicated a tendency for higher values in male. The perception score and willingness to use AI had means of 3.63 ± 0.66 and 3.48 + 0.69 respectively, indicating a positive attitude towards AI among students. Associations between gender and the perception of students towards A.I. and willingness to use A.I. on a Likert scale, the Mann-Whitney U test was employed as shown in Table 1.

Table 1: Mean Rank Gender Distribution with AI Perception(n=207)

Students' Perceptions Towards AI	Gender		Mean Rank	p-value	Mean ± SD
AI will play an important role in healthcare	Male	91	119.66	<0.001**	3.63 ± 0.66
	Female	116	91.72		
Some specific specialities will be wiped out by AI in healthcare	Male	91	111.38	0.09	
	Female	116	98.21		
I understand basic AI principles and Terminologies	Male	91	112.93	0.04*	
	Female	116	96.99		
All medical students should receive AI teaching	Male	91	118.07	0.001**	
	Female	116	92.97		
At the end of my medical degree, I will be confident working with AI tools	Male	91	115.18	0.01*	
	Female	116	95.23		
Impact of AI and Willingness to Use It					
AI systems will have a positive impacton medical education	Male	91	119.66	0.01*	3.48 ± 0.69
	Female	116	91.72		
Integrating AI into medical educationwill aid the learning process	Male	91	109.32	0.19	
	Female	116	99.82		
AI will replace my future role as a physician	Male	91	108.96	0.27	
	Female	116	100.11		

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I support the use of AI in medical education	Male	91	109.47	0.21	
	Female	116	99.71		

*p-value was significant at <0.05 level. ** p-value was significant at <0.01 level.

The high perception and the preeminent willingness of male students towards AI could have been due to several factors; i.e., in certain developing countries including Pakistan, most probably male students are more exposed to technology from childhood, while females are more often restrained by traditional gender. Some specialties are more vulnerable than others from AI e.g., radiology and pathology, and their specialists ought to be trained to work with AI rather than against it. The total mean score was 3.38 + 0.64 which showed a good readiness of medical students toward AI in enhancing medical education as shown in Table 2.

Table 2: Medical Students' Readiness for AI (n=207)

Medical Students' Readiness for AI 'I Can'	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Mean ± SD	Total Mean Score
Define the basic concepts of data science	1	38	79	72	17	3.32 + 0.88	3.38 + 0.64
Explain how AI systems are taught	4	56	80	54	13	3.08 + 0.97	
Analyze AI input data in healthcare	2	42	88	59	16	3.22 + 0.89	
Articulate the significance of data collection and analysis by AI	2	33	85	74	13	3.3 + 0.84	
Use AI information with my medical knowledge.	2	23	95	69	18	3.38 + 0.83	
See AI being an excellent tool for teaching	2	12	65	119	19	3.63 + 0.77	
Explain what are the merits and demerits of these AI technologies	2	16	77	88	24	3.56 + 0.83	
Think of the opportunities and threats that AI technology can present	1	16	75	93	22	3.57 + 0.8	
Say something about the limitations of AI technology	4	20	78	82	23	3.48 + 0.88	

Medical institutions can enhance AI readiness by including computer skills & AI-related courses in the First MBBS Curriculum and through Faculty development programs that will impart AI literacy to both faculty and students. Also, the implication revealed that students positively perceive AI for decision-making (p=0.006) and for easing drug accessibility (p=0.02) while on the other hand muttering about patient confidentiality and doctor-patient relationship being threatened by AI. AI developers need to ensure that patient data is encrypted against undue access. The training needs to focus more on AI aiding doctor-patient communication instead of replacing it. Although students had moderate AI competency, practical strategies stand to better transcend the gap between theoretical AI knowledge and its practical application by including AI-assisted cases in clinical rotations and also providing internships in AI-driven healthcare startups to advance hands-on skill development. Mean + SD and associations between the computer literacy level of students i.e. literate=1 (n=113), competent=2 (n=69), proficient=3 (n=25), and possible effects of AI in medicine by using ANOVA as shown in Table 3.

Table 3: Association Between Computer Literacy and Effects of AI (n=207)

Possible Effects of AI in the Medicine	Computer literacy level	Mean ± SD	95% Confidence Interval	p-value
AI may discourage the confidentiality of the Medical Profession	1	3.5 + 0.92	3.41-3.66	0.44
	2	3.64 + 0.82		
	3	3.40 + 1.08		
AI will increase trust of people in Medicine	1	3.31 + 0.92	3.24-3.49	0.17
	2	3.35 + 0.87		
	3	3.68 + 0.8		
It may ease the patient's access to Medicine	1	3.6 + 0.82	3.51-3.74	0.02*
	2	3.52 + 0.87		
	3	4.04 + 0.79		

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AI may discourage the Doctor-Patient relationship	1	3.53 + 1.04	3.45–3.72	0.69
	2	3.65 + 0.85		
	3	3.64 + 1.03		
It may enable Doctors to make more accurate decisions	1	3.57 + 0.8	3.51–3.74	0.006*
	2	3.55 + 0.87		
	3	4.12 + 0.73		
It may increase the confidence of the Patient	1	3.42 + 0.86	3.35–3.59	0.54
	2	3.48 + 0.85		
	3	3.64 + 0.99		
Discourage the Doctor's Efforts	1	3.47 + 1.08	3.39–3.67	0.24
	2	3.7 + 0.93		
	3	3.36 + 1.11		

Pearson correlation was calculated to assess the relationship between AI readiness among medical students and their perceptions and willingness to use AI. Correlation coefficients of 0.697, and 0.642 alongside p-values of less than 0.001 (significant at <0.01 level) point toward a strong positive correlation. This means that with an increase in AI readiness on the part of the students, there tends to be an increase in positive perceptions and willingness to use AI in medical education as shown in Table 4.

Table 4: Correlation between AI Readiness with Perception and Willingness

Variables		r*	p-value
Medical Students' Readiness for AI	Perceptions Towards AI	0.697	<0.001*
	Impact of AI and Willingness	0.642	<0.001*

*p-value is significant at <0.01 level.

DISCUSSION

Positive perception and willingness among students toward AI's role in enhancing medical education were seen, with male showing more perception levels and willingness than female. Medical students' readiness towards AI was seemingly good with a higher mean found giving value to AI in education and research purposes, while also enabling doctors to make more accurate decisions. The correlation between medical students' readiness and their perceptions and willingness was found to be statistically significant. Research done by Stöhr *et al.*, showed statistically significant differences in gender perceptions of AI with male showing more optimism towards AI than female similar to the results of our study [10]. A study done by Sit et al., showed that the majority of students thought that AI teaching would benefit their careers, similar to our study results. The similarity may be due to the same study population i.e. medical students in both studies [11]. A study done by Park *et al.*, showed that similar to our study, the majority of participants agreed about the future role of AI in the medical field [12]. Research done by Yüzbaşıoğlu *et al.*, showed that students' knowledge regarding AI was less while in our study, students' knowledge was sufficient [13]. The difference may be due to dental students in other studies and also due to a very large sample size as compared to our study. A study done by Ahmed *et al.*, showed that the majority of participants thought to include AI in medical teaching, similar to the results of our study [14]. A study done by Swed *et al.*, showed that most participants do not understand AI and its significance in the medical field which is different from the results of our study, which may be due to population demographic differences and also due to a larger sample size [15]. A study done by Civaner *et al.*, showed that about half percentage of the participants thought that because of AI, there would be unemployment as it could replace many jobs, similar to our study results where although the result was not significant of this variable, many participants were having same worries [9]. A study done by AlZaabi *et al.*, showed that participants were not worried about AI taking over physicians' jobs and creating unemployment which is different from the results of our study [16]. Therefore, in most of the studies, the perception of medical students towards AI was positive. However, in a few studies, if still they were not aware or had less perception of AI, they were willing to get more knowledge and increase their perception of it. Research done by Labrague *et al.*, showed that participants had moderate readiness for AI acceptance which is less as compared to our study participants and the difference may be due to the medical vs nurses' population that only about 1/10th of participants which can have an impact on lower readiness in nurses [17]. A study done by Boilla *et al.*, showed ants had received AI training which is similar to our results, while in contrast, those participants had low AI familiarity as compared to our study [18]. Also, the study conducted by Allam *et al.*, showed that less than 10% of participants received AI training, which is almost similar to our results [19]. Research done by Wood *et al.*, showed that participants had a favorable attitude toward AI similar to our study but their AI literacy level is less as compared to our study [8]. A study done by Banerjee *et al.*, showed that participants agreed that AI would improve research and training like in our study results but different in their opinion regarding improving the diagnostics of physicians as in our study results [20].

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The most significant effect perceived by medical students in our study was to enable doctors to make more accurate decisions on an AI basis which is similar to the research done by Giordano *et al.*, which showed that AI may help overcome decision-making limitations [21]. Research done by Patil *et al.*, showed many advantages of AI and among them, one would be enhanced patient access to healthcare, similar to our study results [22]. Research done by Jackson *et al.*, showed that medical students perceive AI as an assisted healthcare technology by improving diagnosis and reducing errors, similar to our study results which may be due to a similar sample population and socio-demographics [23]. Since this is a cross-sectional study, it restricts any chances of deriving causality. Longitudinal designs would be more suitable to capture the change in students' attitudes over time. The fact that the study was limited to a single private medical college may further limit the generalizability of findings to other contexts with different curricula, resources, or levels of AI integration. In overcoming these limitations, future research could therefore include multiple universities.

CONCLUSIONS

It was concluded that AI could revolutionize medical education through enhancement of learning, clinical decision-making, and supplementing traditional teaching methods. Students exhibited a positive perception of AI, recognizing its role in shaping future medical practice and improving diagnostic accuracy and patient management. Although the study depicts the enthusiasm of students, it has also highlighted that there is no formal training on AI, with most students lacking prior structured exposure to it. Medical curricula should contain structured AI courses, AI-assisted case studies, and interdisciplinary collaborations with technology experts in the future to build the bridge between artificial intelligence knowledge to application.

Authors Contribution

Conceptualization: MA, S
Methodology: MUD, IN, AM, AR
Formal analysis: MUD, S
Writing review and editing: MUD, MA, IN, AR

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Precision in Diagnosis of Factors in Female Infertility Through Diagnostic Laparoscopy Insights from Lady Reading Hospital Peshawar

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ABSTRACT

Infertility afflicts millions worldwide and often stems from female factors. The World Health Organization reports that 60-80 million couples struggle with infertility due to blocked fallopian tubes, polycystic ovary syndrome, or endometriosis. Understanding the intricacies of infertility is paramount to addressing this prevalent issue. **Objective:** To determine factors in female infertility through diagnostic Laparoscopy. **Methods:** A cross-sectional study was conducted from Nov 2020 to April 2021 in the Gynecology Unit of Lady Reading Hospital, Peshawar. No longitudinal elements were involved; the analysis was purely observational. We included 90 infertile women aged 18-45 with normal male partner semen analysis. Exclusion criteria consisted of contraceptive use or no intercourse in a year. Participants were divided into primary (n=62) and secondary (n=28) infertility. Diagnostic laparoscopy investigated the cause. Data were analyzed by SPSS version 26.0. **Results:** Tubal blockage emerged as the leading cause at 33.3%, followed by polycystic ovaries at 21.1% and endometriosis at 13.3%. Other etiologies comprised fibroids at 6.7%, ovarian cysts at 4.4%, and pelvic inflammatory disease at 3.3%. Laparoscopy proves integral to identifying occult pathologies driving infertility. It facilitates clinical management and improves reproductive outcomes for women presenting with fertility complications. **Conclusions:** It was concluded that tubal blockage was the most common cause (33.3%). In 33.3% of cases, polycystic ovaries were found, in 13.3% endometriosis, in 6.7% fibroids, in 4.4% ovarian cysts, and in 3.3% pelvic inflammatory disease (PID).

INTRODUCTION

Infertility remains a complicated global health concern, impacting approximately 10-55% of couples worldwide. Developing nations regularly report even higher rates because of socioeconomic and healthcare barriers [1, 2]. A Pakistani study uncovered an infertility rate of 22%, with essential infertility comprising 4% of instances. The causes of infertility are multifaceted, with tubal blockages, ovulatory issues, Polycystic ovary syndrome (PCOS), and endometriosis specifically impacting female [3, 4]. Male factors for example sperm abnormalities also play a part. Laparoscopy provides an immediate view of pelvic anatomy, allowing the diagnosis of conditions for instance adhesions, endometriosis, and tubal blockages that other instruments may miss [5, 6]. Infertility involves deep psychosocial implications, specifically in cultures with powerful expectations of fertility [7]. Pakistani women confronting infertility frequently experience melancholy, anxiety, and emotions of inadequacy. Societal pressures surrounding motherhood can amplify distress, potentially leading to stigmatization, marital strain, and isolation. A multifaceted, integrated response that we already use for medical and psychological issues is the answer. Experiences are also shaped by socioeconomic status and education through access to and choices made within the healthcare system [8]. Research also shows the psychological impact of infertility spreads beyond women,

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with relationships often strained and family dynamics altered. Support, emotional and social, thus become important for those undergoing fertility remedies [9]. Support systems help alleviate the psychological burden and emphasize the importance of integrated care where therapy and counselling coexist. This is especially important in areas like Pakistan, where fertility is tied to social expectations [10, 11].

This study aims to investigate the causes of primary and secondary infertility in female of the Peshawar region with the help of diagnostic laparoscopy.

METHODS

A cross-sectional study was conducted from Nov 2020 to April 2021 in the Gynaecology Unit of Lady Reading Hospital, Peshawar. Ethical permission was taken from the ethical review committee of Lady Reading Hospital and was granted ethical permission Ref no: 604 ILRH/ MTI. In consideration of infertility frequency, an adequate sample size was figured out to guarantee a reliable investigation with 95% confidence adjacent to a 5% margin of error. This formula helped with estimating the test probably going to differentiate the estimated infertility prevalence, with worldwide between 20-40%. Screening estimated unlike Follicle-Stimulating Hormone (FSH), luteinizing hormone (LH), and progesterone levels, essential pointers singular of ovarian records rises and falls, ovulation circumstances, luteal stage capacities' rises and falls. These tests offered significant knowledge of regenerative richness and propelled demonstrative and remedial translations. Ultrasound was linked to the identification of anatomical anomalies such as cysts, polycystic ovaries, and fibroids, which can impact fertility. It also measured the thicknesses of the endometrial lining, which is important for embryo implantation. High ethical principles were strictly adhered to, ensuring patient privacy, informed consent, and anonymous data, preserving trust and transparency during the investigation. Data were isolated depending on infertility type (essential or auxiliary), socioeconomic status, family arranging learning, and mental factors. This isolation permitted an intensive comprehension of how these viewpoints impact fertility and treatment viability. The connection between Socioeconomic status (SES) and infertility results was inspected, acknowledging that admittance to human services, instructive assets, and natural introductions differ by socioeconomic position. The investigation investigated the job of family arranging information and past contraceptive utilization in infertility. Ladies with more prominent information and earlier intercessions may have had a superior possibility of analyzing and treating infertility sooner. FSH levels were measured using chemiluminescent immunoassay (CLIA), LH via radioimmunoassay (RIA), and progesterone using enzyme-linked immunosorbent assay (ELISA). For diagnostic methods, ultrasonography (both transabdominal and transvaginal) was employed to detect anatomical abnormalities and measure endometrial thickness. Laparoscopy was used to identify causes of infertility, such as tubal obstruction, endometriosis, and polycystic ovaries, aiding in the development of targeted treatments. Laparoscopy uncovered different infertility variables, including tubal hindrance (33.3%), polycystic ovaries (21.1%), endometriosis (13.3%), and fibroids (6.7%). These discoveries helped decide the fundamental drivers of infertility, zeroing in on tending to tubal hindrance through medical or helped regenerative strategies. Pelvic inflammatory disease (PID) was analyzed in over 3% of members and was generally connected to tubal factor infertility that can diminish fertility potential. Mindful conclusion through laparoscopy was critical for recommending focused remedies to conceivably improve the chances of the idea. This sorted out and diligent strategy guaranteed the legitimacy of the investigation, considering an assortment of infertility drivers and giving a comprehensive way to approach regenerative well-being investigation. Initial factual examinations of the investigation incorporated different tests to ensure strong outcomes and important ends. Descriptive measurements were initially connected to summarize the information, like focal patterns (normal, middle) and dissemination (standard deviation). Data were analyzed by SPSS version 26.0. The chi-squared test was utilized to survey the relationship between class factors, for example, infertility type and socioeconomic status, while t-tests and ANOVA were connected to look at means between different gatherings for case those with essential versus auxiliary infertility. To inspect the connections between constant factors, connection coefficients were estimated, and different relapse investigations were utilized to perceive indicators of infertility results. The typicality of the information was tried utilizing the Shapiro-Wilk test, and the noteworthy level was set at 0.05 for all tests, affirming the factual intensity and legitimacy of the discoveries.

RESULTS

The data reveals the following descriptive statistics for the given variables: The average age of the participants was 29.39 ± 4.83, indicating a relatively narrow age range. The mean weight was 76.27 ± 5.34, suggesting a moderate variation in weight. The mean average height was 1.64 ± 0.07, indicating little variation in height. The mean BMI was 28.54 ± 3.64, implying that most participants fall within a similar range of BMI but there was some variation. The average duration of infertility was 3.98 ± 2.11, suggesting a wide range of infertility durations. Lastly, the average hormonal profile (FSH IU/L) was 12.26 ± 4.56, indicating a

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moderate variation in FSH levels among the participants (Table 1).

Table 1: Analysis of Female Infertility Descriptive Statistics and Stratified Laparoscopic Findings at Lady Reading Hospital Peshawar 2022

Subcategory	Mean ± SD
Age (Years)	29.39 4.83
Weight (kg)	76.27 ± 5.34
Height (Meters)	1.64 ± 0.07
BMI (kg/mÂ²)	28.54 ± 3.64
Duration of Infertility	3.98 ± 2.11
Hormonal Profile (FSH IU/L)	12.26 ± 4.56

The distribution of participants across different age groups was as follows: 48.9% of the participants fall in the 18 to 28 age group, making it the largest group. The 29 to 35 age group comprises 37.8% of the participants, while the 36 to 45 age group includes 13.3% of the participants. This indicates that most participants are younger, with a significant portion in the middle age range and a smaller proportion in the older category (Table 2).

Table 2: Age Distribution Breakdown: Insights into the Demographic Landscape

Age Group	Frequency (%)
18 to 28	44 (48.9%)
29 to 35	34 (37.8%)
36 to 45	12 (13.3%)

The distribution of education levels among participants shows that 68.9% have completed their education at the primary level, while 31.1% have completed secondary education. This suggests that most participants have a primary education, with a smaller proportion pursuing education at the secondary level (Table 3).

Table 3: Education Level Distribution at Primary vs. Secondary

Subcategory	Frequency (%)
Primary	62 (68.9%)
Secondary	28 (31.1%)

The analysis of laparoscopy findings related to reproductive health conditions reveals the following distribution: 33.3% of participants were diagnosed with tubal blockage, making it the most common condition. Polycystic ovaries were observed in 21.1% of participants, while 17.8% had normal findings. Endometriosis was found in 13.3% of the participants, and pelvic inflammatory disease was present in 3.3%. Fibroids were identified in 6.7% of cases, and ovarian cysts were found in 4.4%. This shows that tubal blockage and polycystic ovaries are the most prevalent conditions, with other conditions occurring less frequently (Table 4).

Table 4: Key Laparoscopy Findings Analysis of Reproductive Health Conditions

Laparoscopy Findings	Frequency (%)
Normal	16 (17.8%)
Tubal Blockage	30 (33.3%)
Polycystic Ovaries	19 (21.1%)
Endometriosis	12 (13.3%)
Pelvic Inflammatory Disease	3 (3.3%)
Fibroid	6 (6.7%)
Ovarian Cyst	4 (4.4%)

The data exploring the relationship between health conditions and social class shows the following distribution: 32.2% of participants reported a history of depression, while 67.8% did not. Regarding hypothyroidism, 46.7% of participants have a history of it, and 53.3% do not. In terms of social class, 48.9% of participants belong to the high social class, 35.6% belong to the middle class, and 15.6% are in the low social class. The stratification of depression and hypothyroidism by social class and history follows the same distribution, with 48.9% of participants in the high class, 35.6% in the middle class, and 15.6% in the low class for both conditions. This indicates a relatively even distribution of depression and hypothyroidism across social classes, though most participants belong to the higher social class (Table 5).

Table 5: Exploring Health and Social Stratification of Depression, Hypothyroidism, and Social Class

Category	Subcategory	Frequency (%)
History of Depression	Yes	29 (32.2%)
	No	61 (67.8%)
History of Hypothyroidism	Yes	42 (46.7%)
	No	48 (53.3%)
Social Class	High	44 (48.9%)
	Middle	32 (35.6%)
	Low	14 (15.6%)
Stratification with Social Class	High	44 (48.9%)
	Middle	32 (35.6%)
	Low	14 (15.6%)
Stratification with History of Depression	Yes	29 (32.2%)
	No	61 (67.8%)
Stratification with History of Hypothyroidism	Yes	42 (46.7%)
	No	48 (53.2%)

The analysis of family planning knowledge, experiences, and BMI stratification reveals the following: 40% of participants have high family planning knowledge, while 60% have low family planning knowledge. In terms of family planning experience, 42.2% of participants have used family planning methods, while 57.8% have never used them. When stratified by family planning knowledge, 40% of participants fall under the high knowledge category and 60% under the low knowledge category. Regarding family planning experience, 42.2% have used family planning

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methods, while 57.8% have not. For BMI stratification, 71.1% of participants have a BMI of less than 30, while 28.9% have a BMI greater than 30, indicating a significant proportion of participants fall within the normal weight range. The analysis suggests that family planning knowledge and usage are evenly distributed across categories, while a larger proportion of participants have a BMI under 30 (Table 6).

Table 6: Analyzing Family Planning Knowledge and Experiences Knowledge, Usage, and BMI Stratification

Category	Subcategory	(%)
Family Planning Knowledge	High	40%
Family Planning Knowledge	Low	60%
Family Planning Experience	Ever Used	42.2%
Family Planning Experience	Never Used	57.8%
Stratification with Family Planning Knowledge	High	40%
Stratification with Family Planning Knowledge	Low	60%
Stratification with Family Planning Experience	Ever Used	42.2%
Stratification with Family Planning Experience	Never Used	57.8%
Stratification with BMI	<30	71.1%
Stratification with BMI	>30	28.9%

DISCUSSION

Infertility is a meaningful issue afflicting public health, especially in developing nations where female factors substantially contribute. The World Health Organization estimates globally around 60–80 million couples do battle with infertility, with 8-12% confronting fertility problems. This analysis aimed to identify primary infertility causes in a sample of 90 women in Peshawar by using diagnostic laparoscopy, widely seen as a gold standard for diagnosing female factor infertility. The results of the present study found that Tubal blockage was the most common cause (33.3%). The results of the present study are not those of Zeb and Malik, where blocked tubes were present in 23 (14.43%) [12]. The present study had endometriosis at 13.3% the results are also consistent with a study conducted by Rizvi SM *et al.*, where endometriosis was found in 8 (13.3%) of the total cases of infertility [13]. The present study used Laparoscopy for diagnosis the results are n consistent with a study carried out Garg *et al.*, Laparoscopy is the gold standard for the diagnosis of these disorders and has the advantage of performing corrective surgery in the same sitting [14]. While socioeconomic factors did not directly influence decisions regarding laparoscopy procedures in the study cohort, it remains true that greater access to healthcare and education often correlate with superior healthcare choices overall. This relationship could easily affect the timing of seeking infertility treatments, as diagnostic costs pose challenges in many developing nations that may unfortunately delay necessary diagnosis and care. Our findings identified polycystic ovarian syndrome as the most prevalent endocrine disorder in those struggling with infertility, impacting 21.1% of participants. Previous investigations similarly show polycystic ovarian syndrome impacts 16-33% of women experiencing infertility issues. Given its pervasive nature and sizable effects on ovulation, careful monitoring and treatment of polycystic ovarian syndrome constitutes a key aspect of infertility management and therapy. Endometriosis occurred in 13.3% of our patients, which was consistent with the study by Mahmood, who reported a 13.6% portion in infertile women [15]. This destruction results in changes in normal ovarian, fallopian, and pelvic anatomy, which can then compromise fertility; endometriosis can "indirectly" compromise fertility. It is often difficult to diagnose because of symptomless initial stages, making laparoscopy an important tool for recognition and treatment during this critical moment. And while it remains the subject of considerable debate as a leading cause of fertility issues, there is no doubt that endometriosis greatly complicates the fertility journey. An additional common infertility consideration, fibroids, affected 6.7% of cases, in line with Khaula's Lahore-based investigation results. Although fibroids frequently are asymptomatic, they can block fallopian tube pathways or alter the shape of the uterine cavity, which can interfere with fertility. The prevalence of fibroids in this category highlights the importance of diagnostic laparoscopy for identifying uterine anomalies that adversely affect fertility. The most striking result we found in our study is that tubal blockages appear to be widespread, occurring in 33.3% of the individuals we studied [16]. Tubal blockage is an important cause of impaired fertility, often due to pelvic inflammatory disease (PID). Impact of Tubal Damage: Tubal damage is responsible for 15-20% of cases of primary infertility and up to 40% of secondary infertility [4]. PID was found in 3.3% of our cohort, suggesting that infection-related tubal injury is a relevant factor for this population, not by a study carried out by Mascagni where Pelvic inflammatory disease (PID) was found in 1 (3.1%) [17]. The tubal factor was the most common etiology in our study carried out by Kumar *et al.*, the Tubal factor is the most common cause of infertility followed by endometriosis and ovarian factor [18]. Laparoscopy was used for the evolution of the results by Shanmugham *et al.*, who confirmed that Laparoscopy is an effective diagnostic tool in the evaluation of infertility [19]. A retrospective study on 151 patients by Chanu *et al.*, shows that the most common abnormalities found during laparoscopy in both the primary and secondary infertility group were features of PID (adnexal adhesion and hydrosalpinx) The results are not by our study where PID was found by 3.3% [20].

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CONCLUSIONS

It was concluded that tubal blockage was the most common cause (33.3%). In 33.3% of cases, polycystic ovaries were found, in 13.3% endometriosis, in 6.7% fibroids, in 4.4% ovarian cysts, and in 3.3% PID.

Authors Contribution

Conceptualization: IU
Methodology: HNM, NH, FJ
Formal analysis: NA
Writing review and editing: PN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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Assessing the Correlation between Hearing Loss and Diabetic Retinopathy Severity in Patients at A Tertiary Care Hospital in Pakistan

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ABSTRACT

Diabetes frequently results in sensorineural hearing loss (SNHL), although little is known about its root causes and risk factors. **Objectives:** To evaluate the association between the severity of diabetic retinopathy and sensorineural hearing loss in patients with type 2 diabetes mellitus. **Methods:** Data were collected from 150 patients with type 2 diabetes between June and August 2024. Participants were recruited via consecutive sampling. Audiological assessments were conducted using pure-tone audiometry, and the severity of diabetic retinopathy was graded by the Early Treatment Diabetic Retinopathy Study scale. Statistical analysis was performed using the Kruskal-Wallis test to assess the association between diabetic retinopathy severity and sensorineural hearing loss. **Results:** 33.3% of participants had normal hearing, while 37.3% had mild sensorineural hearing loss, 20% had moderate sensorineural hearing loss, and 9.3% had severe sensorineural hearing loss. Hypertension prevalence increased with DR severity ($p=0.002$), and a longer duration of diabetes was associated with more severe retinopathy ($p<0.001$). Significant differences were found in albumin, creatinine, and HbA1C levels ($p<0.05$), indicating worsening metabolic control with disease progression. sensorineural hearing loss severity showed a significant correlation with retinopathy stages ($\chi^2=25.47$, $p<0.001$), with the highest prevalence of severe sensorineural hearing loss in proliferative diabetic retinopathy. **Conclusions:** It was concluded that this study demonstrates a significant association between diabetic retinopathy severity and sensorineural hearing loss, with increased sensorineural hearing loss severity in more advanced stages of diabetic retinopathy.

INTRODUCTION

One of the main causes of blindness and disability among diabetics is diabetic retinopathy. Despite advances in diabetes management, diabetic retinopathy (DR) remains a significant public health concern, particularly in low- and middle-income countries like Pakistan. According to estimates, approximately 5% of people with diabetes have a severe form of the condition, while 25% of those with diabetes mellitus have diabetic retinopathy [1, 2]. According to a recent meta-analysis, among Iranian patients with type 2 diabetes mellitus (T2DM), the prevalence rate of retinopathy was 37.8% (95% CI: 32.8%, 43.0%) [3]. Diabetic retinopathy (DR) is divided into two types: proliferative diabetic retinopathy (PDR), which develops with additional retinal ischemia and is characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous, and non-proliferative diabetic retinopathy (NPDR), which is characterized by micro-aneurysms, retinal hemorrhages,

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cotton-wool spots, or venous beading. While DR primarily affects vision, growing evidence suggests that similar microvascular and neuropathic mechanisms may also contribute to hearing loss in diabetic patients [4]. Hearing loss is a prevalent condition that can affect people of all ages and has a significant negative impact on their quality of life. Over 1.5 billion people, or 20% of the world's population, are currently thought to be affected by hearing loss. Of these, over 430 million have moderate or greater hearing loss in their better hearing ear. By 2050, that number is predicted to increase to over 700 million [5]. There are three types of hearing loss: mixed, sensorineural, and conductive. Chronic exposure to loud noises is one of the main causes of sensorineural hearing loss (SNHL). Nevertheless, genetic predisposition, specific drugs, and illnesses including diabetes mellitus (DM) and hypertension (HTN) are other contributing variables [6]. High blood sugar levels are a typical sign of diabetes mellitus, resulting in complications including diabetic retinopathy (DR) and neuropathy. Damage to the blood vessels of the retina leads to DR, which directly or indirectly impairs vision. On the other hand, neuropathy is damage to the nerves that can result in impairments in motor and sensory abilities. According to earlier studies, diabetic patients with retinopathy had a higher chance of acquiring SNHL [7]. Another prevalent medical condition that can raise the risk of SNHL is hypertension which directly affects the blood vessels and nerve fibers in the inner ear [8, 9]. Despite existing literature on diabetes-related complications, the relationship between the severity of diabetic retinopathy and the degree of hearing loss remains inadequately explored, particularly in the Pakistani population. In Pakistan, both diabetic retinopathy and hearing loss are common conditions that significantly impact independence, function, and quality of life. However, the extent to which the severity of DR correlates with hearing impairment remains unclear.

This study aims to assess the degree of hearing loss at different stages of diabetic retinopathy.

METHODS

This hospital-based cross-sectional study analysed data from patients with diabetes mellitus (DM) at Jinnah International Hospital, Abbottabad, Pakistan. Data collection was carried out over three months (June 2024 to August 2024). Ethical approval was taken from the Institutional Review Board (IRB), IRB number JIHA-EYE-01-2024. The sample size was calculated using a significance level of 0.05, power of 80%, and an anticipated SNHL prevalence rate of 70.4% using Open Epi software [10]. 150 patients were recruited via random sampling methods from ophthalmology clinics and referrals by primary care physicians and internists within the medical centre. Written informed consent was obtained from each patient before participation. The study followed the principles outlined in the Declaration of Helsinki. Patients aged ≥18 years, with a confirmation of DM according to the criteria set by the American Diabetes Association and any grade diabetic retinopathy (DR) following the criteria set by the Early Treatment Diabetic Retinopathy Study (ETDRS) scale, were included [5,6]. Exclusion criteria encompassed patients with a history of ear surgery, use of hearing aids, known non-DM-related causes of hearing loss, or retinal vein or artery occlusions. The demographic and medical history included age, gender, DM duration, hypertension (HTN) status, and severity of retinopathy (no DR, mild non-proliferative DR, moderate non-proliferative DR (NPDR), severe NPDR, proliferative DR) according to ETDRS scale, were included [5, 6]. Audio-logical assessments were performed in a soundproof closed area using a standardised audiometer by a qualified audiologist. Pure-tone audiology was conducted at different frequencies from 0.5 to 8 kHz, and the mean hearing threshold for each ear was measured by adding all the values of the threshold at 500, 1000, 2000, 4000, and 8000 Hz and dividing by five. Sensorineural hearing loss (SNHL) was grouped as normal, mild, moderate, or severe according to the criteria set by the World Health Organization. Only cases with SNHL were considered, and patients with mixed or conductive hearing loss were excluded. The worst ear of each patient was evaluated, and SNHL was correlated with the eye with the most severe retinopathy. Data were analysed using SPSS version 24.0, version 28.0 (IBM Corp., Armonk, NY). Descriptive statistics summarised the clinical and demographic characteristics of the study population. The association between retinopathy severity and SNHL was assessed using the Kruskal-Wallis non-parametric test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

This study included 150 participants with type 2 diabetes, with a male-to-female ratio of 56% to 44%. Regarding diabetic retinopathy (DR), 26.7% of the participants had no DR, 16% had mild non-proliferative DR (NPDR), 17.3% had moderate NPDR, 9.3% had severe NPDR, and 30.7% had proliferative DR. Among the participants, 33.3% had normal hearing, 37.3% had mild sensorineural hearing loss (SNHL), 20% had moderate SNHL, and 9.3% had severe SNHL (Table 1).

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Table 1: Distribution of Diabetic Retinopathy Severity and Sensorineural Hearing Loss (SNHL) by Gender

Category	Severity	Male n (%)	Female n (%)	Total n (%)
Diabetic Retinopathy	No DR	22 (14.7%)	18 (12.0%)	40 (26.7%)
	Mild NPDR	10 (6.7%)	14 (9.3%)	24 (16.0%)
	Moderate NPDR	14 (9.3%)	12 (8.0%)	26 (17.3%)
	Severe NPDR	8 (5.3%)	6 (4.0%)	14 (9.3%)
	Proliferative DR	30 (20.0%)	16 (10.7%)	46 (30.7%)
	Total	84 (56.0%)	66 (44.0%)	150 (100%)
Sensorineural Hearing Loss	Normal Hearing	28 (18.7%)	22 (14.7%)	50 (33.3%)
	Mild SNHL	30 (20%)	26 (17.3%)	56 (37.3%)
	Moderate SNHL	18 (12%)	12 (8%)	30 (20%)
	Severe SNHL	8 (5.3%)	6 (4%)	14 (9.3%)
	Total	84 (56.0%)	66 (44.0%)	150 (100%)

Among participants with no diabetic retinopathy (DR), 10.7% had normal hearing, while 8%, 3.3%, and 1.3% had mild, moderate, and severe sensorineural hearing loss (SNHL), respectively. For mild non-proliferative DR (NPDR), 5.3% showed normal sense of hearing, 6.7% showed slight SNHL, 3.3% showed modest SNHL, and 1.3% showed severe SNHL. In moderate NPDR, 4.0% had normal hearing, 8% had mild SNHL, 4% showed moderate SNHL, and 1.3% had severe SNHL. Among severe NPDR cases, normal hearing was observed in 1.3%, while 2.7%, 1.3%, and 0.7% had mild, moderate, and severe SNHL, respectively. Proliferative DR showed the highest proportions of SNHL, with 8% having normal hearing, 13.3% mild SNHL, 8% moderate SNHL, and 7.3% severe SNHL (Table 2).

Table 2: Distribution of SNHL Assessment with Diabetic Retinopathy Severity

Retinopathy Severity	Normal Hearing n (%)	Mild SNHL n (%)	Moderate SNHL n (%)	Severe SNHL n (%)	Total n (%)
No DR	16 (10.7%)	12 (8%)	5 (3.3%)	2 (1.3%)	35 (23.3%)
Mild NPDR	8 (5.3%)	10 (6.7%)	5 (3.3%)	2 (1.3%)	25 (16.7%)
Moderate NPDR	6 (4%)	12 (8.0%)	6 (4.0%)	2 (1.3%)	26 (17.3%)
Severe NPDR	2 (1.3%)	4 (2.7%)	2 (1.3%)	1 (0.7%)	9 (6.0%)
Proliferative DR	12 (8%)	20 (13.3%)	12 (8%)	11 (7.3%)	55 (36.7%)
Total	44 (29.3%)	58 (38.7%)	30 (20%)	18 (12%)	150 (100%)

The prevalence of hypertension significantly increased with retinopathy severity (p=0.002), with 88.2% of patients in the Severe NPDR/PDR group having hypertension. The duration of diabetes was significantly longer in patients with more severe retinopathy (p<0.001), with the Severe NPDR/PDR group having an average of 18.4 years of diabetes. The analysis revealed significant differences in albumin (p=0.04), creatinine (p=0.01), and HbA1C (p<0.001) levels across retinopathy stages, indicating worsening metabolic control with disease progression. Hearing loss severity showed a significant correlation with retinopathy stages ($\chi 2=25.47$, p<0.001). Patients with Severe NPDR/PDR had the highest prevalence of moderate (29.4%) and severe (35.3%) hearing loss, while those with No DR predominantly had no hearing loss (61.7%) (Table 3).

Table 3: Demographic, Clinical Characteristics, and Hearing Loss Severity Across Retinopathy Stages

Variables	No DR (n=81)	Mild NPDR (n=52)	Moderate NPDR (n=25)	Severe NPDR/PDR (n=17)	Median (IQR)	χ^2	p-Value
Age (Years)	59.6 ± 8.0	61.5 ± 6.9	62.4 ± 10.4	58.8 ± 8.4	60 (55–65)	3.42	0.33
Albumin (g/dL)	4.2 ± 0.8	4.2 ± 0.5	4.3 ± 0.7	3.7 ± 0.9	4.2 (3.9–4.4)	8.13	0.04*
Creatinine (mg/L)	7.3 ± 34.3	1.0 ± 0.2	11.2 ± 40.3	1.2 ± 0.4	1.0 (0.9–1.2)	10.72	0.01**
HbA1C (%)	7.2 ± 1.6	8.1 ± 1.7	8.0 ± 2.0	8.9 ± 1.8	8.0 (7.1–9.0)	18.65	<0.001**
Hypertension n (%)	25 (30.9%)	34 (65.4%)	18 (72.0%)	15 (88.2%)	60 (50–70)	14.39	0.002**
Duration of Diabetes (Years)	12.5 ± 6.4	14.2 ± 6.1	16.3 ± 7.2	18.4 ± 8.1	13 (10–15)	22.61	<0.001**
No Hearing Loss n (%)	50 (61.7%)	15 (28.8%)	5 (20.0%)	2 (11.8%)	0.0 (0.0–1.0)	–	–
Mild Hearing Loss n (%)	20 (24.7%)	20 (38.5%)	7 (28.0%)	4 (23.5%)	1.0 (1.0–2.0)	25.47	<0.001**
Moderate Hearing Loss n (%)	8 (9.9%)	12 (23.1%)	8 (32.0%)	5 (29.4%)	2.0 (1.0–3.0)	–	–
Severe Hearing Loss n (%)	3 (3.7%)	5 (9.6%)	5 (20.0%)	6 (35.3%)	3.0 (2.0–3.0)	–	–

Data are presented as mean ± standard deviation, n (%), or median (interquartile range). Statistical analysis was performed using the Kruskal-Wallis test, with χ^2 and p-values reported. Significant differences are indicated by *(p<0.05) and **(p<0.01).

DISCUSSION

In 1990, an estimated 158.8 million people worldwide had diabetes, a number that surged to 459.9 million (6.18% of the global population) by 2019 [11]. It is a metabolic disease that has a major impact on health because it doubles or triples the risk of heart attacks and strokes [12], is one of the main reasons for renal failure [13], and results in DR, which is a major reason of blindness due to the growth of retinal vessels [14]. Diabetes may also be associated with other morbidities, such as sensorineural hearing loss. SNHL was more common in diabetics than in non-diabetics of the same age and sex, according to several studies [15]. Uncertainty surrounds the precise mechanism by which hyperglycemia may cause SNHL. SNHL linked to diabetes mellitus is thought to be caused by the microvascular alterations and inflammation linked to this metabolic disorder, which may also impact the auditory system and cause cochlear microangiopathy, articular vascular degeneration, and loss of cochlear outer hair cells [16].

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Since microvascular alterations are the cause of both diabetic retinopathy and sensorineural hearing loss, the current study aims to investigate the association between the degree of DR and the occurrence of sensorineural hearing loss and its severity. Our findings showed a strong correlation of the severity of DR with the evaluation of sensorineural hearing loss. Specifically, it was discovered that those with comparatively more severe DR were more prone to have worse hearing test scores. Patients who had more severe DR or moderate non-proliferative diabetic retinopathy were more likely to have moderate SNHL or worse, which was clear from the data. Similarly, Alizadeh *et al.*, AM *et al.*, and Carlson *et al.*, observed a direct relationship between the progression of DR and hearing impairment, further supporting our findings [1, 17, 18]. A significant relationship was also found between age and hearing loss level. This result is consistent with earlier studies that indicated a high correlation between hearing loss and age. According to Lin *et al.*, systematic review and meta-analysis, the prevalence of hearing loss rises with each decade of life [19]. In a similar vein, a different study conducted by Wasano *et al.*, discovered that the prevalence of hearing loss rose dramatically with age, peaking in people over 80 [20]. To avoid or lessen the effects of age-related hearing loss, these findings emphasize the significance of routine hearing tests and hearing protection measures for older people. A notable finding in our study was the strong correlation between hypertension (HTN) and SNHL severity. This suggests that HTN may be an independent risk factor for hearing loss, consistent with Abraham *et al.*, who highlighted the vascular contributions of hypertension to cochlear dysfunction. Furthermore, SNHL severity tended to increase with the duration of HTN, reinforcing the hypothesis that chronic vascular stress exacerbates auditory impairment [21]. The number of years the patient had diabetes may have been underestimated because the duration of diabetes was determined from the year of diagnosis. However, this computed DM length and DR severity showed a strong correlation in the multinomial cumulative logit model. A review of the literature revealed conflicting and inconsistent findings; whereas some studies found no significant link [22], others identified a favourable correlation between DM duration and SNHL severity [23, 24]. To confirm these findings and understand the reasons behind the connection, longer-term studies are needed. Despite the limitations, current research provides a useful understanding of the link between diabetic retinopathy and hearing loss and more research is required to explore this further and find ways to prevent or reduce hearing loss in people with diabetic retinopathy.

CONCLUSIONS

It was concluded that this study underscores a significant association between DR severity and SNHL, with proliferative DR (PDR) emerging as a strong predictor of hearing impairment. Male gender, advancing age, longer diabetes duration, and hypertension were also identified as independent risk factors for worsening SNHL. Notably, for every additional year of age, the likelihood of severe SNHL increased by 9.2%.

Authors Contribution

Conceptualization: MAK
Methodology: MAK, ZF, WA
Formal analysis: AQ, KF
Writing review and editing: MF

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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Dental Caries Prevalence among Undergraduate Students Attending Medical and Dental College

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ABSTRACT

Dental caries is a chronic and widespread infectious disease that affects billions of people worldwide. The most prevalent chronic illness is one that, if left untreated, becomes worse over time. **Objective:** To determine the prevalence of the dental caries in the undergraduate student in medical and dental college of Jamshoro. **Methods:** With permission from Liaquat University of Medical and Health Science's Ethical Committee vide number ERC-19/2024/11, this observational cross-sectional study was carried out between April 2024, and November 2024. All students of Medical and Dentistry who were willing to participate in the study were included with 17-25 age range. Epi Info Software was used to calculate the sample size. 500 of the students were included as per the sample size calculation. **Results:** 300 (60%) of the participants were day scholars. The first, second, third, and fourth/final years were represented by students 105 (21%), 90 (18%), 175 (35%) and 130 (26%) respectively. 97 students (19.4%) had no DMFT score, whereas 403 students (80.6%) had dental caries with a DMFT score (>1). The test-takers' DMFT scores were as follows: 97 (19.4%) for a score of 0 and 139 for a score of 1 (27.8%). The DMFT scores were 102 (20.4%) for a score of 2, 136 (27.2%) for a score of 3, and 26 (5.2%) for a score of 4. **Conclusion:** This study demonstrated that the population's prevalence of dental caries was relatively low.

INTRODUCTION

Dental caries is a microbiological and infectious disease [1]. It is the result of tooth demineralization, which can lead to cavitation and pulp injury if treatment is not received. The combination of several problems, such as tooth demineralization, dental plaque bacteria, processed carbohydrates, and weak teeth from external sources [2]. Dental caries is a chronic and widespread infectious disease that affects billions of people worldwide. The most prevalent chronic illness is one that, if left untreated, becomes worse over time [3]. Because they make it difficult to eat, chew, smile, and communicate, teeth that are broken, decayed, or missing have a major impact on day-to-day living. Dental caries is the third most prevalent oral health issue that affects people of all races, according to the World Health Organization (WHO). Dental caries affects around 100% of adults in most nations worldwide, particularly in developed nations [4]. In Pakistan, dental caries is seven times more common than hay fever and five times more common than asthma, which has concerning consequences for oral health in the nation. It is presently a

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significant problem for community health in developing countries because of inadequate oral hygiene practices, excessive sugar consumption, and ignorance regarding fluoride additions [5, 6]. Thus, it is not unexpected that the WHO is urging pledges for ongoing oral and dental health improvement. The Decayed, Missing, Filled (DMF) index has been used for about 80 years and is well recognized as a significant indication of caries experience in dental epidemiology [7]. The DMFT index is used for teeth, and each person's score can be anywhere from 0 to 28 or 32. The DMFT results will be interpreted using the DMF scoring system. The traits that make women more susceptible to dental caries are a matter of debate, and some of these traits may differ among communities [8]. A study of medical and dentistry students in Taxila revealed a mean DMFT score of 1.64 ± 1.66 among participants. This shows generally decent oral health, but it also emphasizes unmet treatment requirements for untreated cavities. The study highlighted the importance of education and preventative practices in treating dental caries [9]. Yadav K *et al.*, conducted another research in Nepal to analyze medical students' knowledge, attitudes, and practices about dental caries at Janaki Medical College Teaching Hospital.It stated that while these students have enough understanding of oral hygiene principles, greater attention should be made on practical applications [10]. Despite substantial studies [5, 9] on dental caries prevalence, there are still numerous gaps in the literature. Firstly, gender disparities in dental caries have been frequently reported, the underlying biological, behavioral, and environmental variables that contribute to this disparity in Pakistani medical student populations have received little attention. Furthermore, stress levels, academic burden, and psychological aspects influencing medical and dental students' dental hygiene practices have not been well investigated.The objective of the current study was to determine the prevalence of the dental caries in the undergraduate student in medical and dental college of Jamshoro.

METHODS

With permission from Liaqat University of Medical and Health Science's Ethical Committee vide number ERC-19/2024/11, this observational cross-sectional study was carried out at Liaqat University of Medical and Health Sciences Jamshoro between April 2024, and November 2024. All students of who were willing to participate in the study were included with 17-25 age range. While students who had history of orthodontic treatment or ongoing orthodontic treatment were excluded. To validate external generalizability, a Kolmogorov-Smirnov test was conducted, confirming that the age distribution of the sample did not significantly differ from the general student population ($p = 0.076$). Epi Info Software was used to calculate the sample size. Population size was taken as 957 with an expected frequency of 50% and CI 95%. 500 of the students were included as per the sample size calculation. The students were selected randomly. The participant signed a written consent form. The students were told there were no risks or disadvantages. To record the oral health status for dental caries, three examiners from dental college filled out the DMFT performa and demographic data, making sure to check for any inaccuracies by looking at dental carries. (D) indicates decaying teeth, (M) indicates caries-related tooth loss, (F) indicates carious tooth filling, and (T) indicates teeth. The WHO-recommended procedure was followed i.e. (Examiners were trained and calibrated to minimize inter-examiner and intra-examiner variability. WHO-recommended tools, such as mouth mirrors, explorers, and periodontal probes (e.g., WHO probe), were used. Proper lighting (natural) was used. Infection control measures, including the use of Personal Protective Equipment (PPE) like gloves, masks, and eyewear, were followed, with instruments sterilized or disposable ones utilized. Patients were seated comfortably in a well-lit area, ensuring their head remains stable throughout the examination). Students who met the requirements for inclusion were evaluated in the classroom near the window under natural light. The SPSS version 26.0 was used to enter and analyze the date. The relationship between gender and dental caries prevalence was evaluated using the chi-square test. An independent t-test and chi square test were used to analyze the differences in average DMFT, dental caries or decaying, missing, and fillings among many groups. Both the 95% confidence level and the P-Value 0.05 criterion were used.

RESULTS

Among the 500 subjects, 255 (51%) were males and 245 (49%) were females. Maximum of the students belong to the age group 22-23 years 167 (53.4%) followed by 24-25 years 103 (46.6%) (Table 1).

Table 1: Characteristics of the Subjects Involved in the Study

Age	Male Frequency (%)	Female Frequency (%)	Total Frequency (%)
<18	51 (49.5%)	52 (50.5%)	103 (20.6%)
19-21	40 (37.4%)	67 (60.6%)	107 (21.4%)
22-23	84 (50.3%)	83 (49.7%)	167 (33.4%)
24-25	80 (65%)	43 (35%)	123 (24.6%)
Total	255 (51%)	245 (49%)	500 (100%)

Three hundred (60%) of the participants were day scholars. The first, second, third, and fourth/final years were represented by students 105 (21%), 90 (18%), 175 (35%) and 130 (26%) respectively. 97 students (19.4%) had no DMF score, whereas 403 students (80.6%) had dental caries with a DMFT score (>1). The test-takers' DMFT scores were as follows: 97 (19.4%) for a score of 0 and 139 for a score of 1

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(27.8%). The DMFT scores were 102 (20.4%) for a score of 2, 136 (27.2%) for a score of 3, and 26 (5.2%) for a score of 4. The differences between genders were statistically significant (p=0.003). Logistic regression analysis revealed age and gender as significant predictors of caries presence (p<0.05)(Table 2).

Table 2: Characteristics of the Participants Involved in the Study

Variables	Category	Frequency (%)	p-value
Gender	Male	245 (49%)	0.003*
	Female	255 (51%)	
Class	1st Year	105 (21%)	0.045*
	2nd Year	90 (18%)	
	3rd Year	175 (35%)	
	4th/Final Year	130 (26%)	
Residence	Hostilities	200 (40.0%)	
	Day Scholars	300 (60.0%)	
DMFT Categories	Low (0-1)	236 (47.2%)	<0.001*
	Moderate (2-3)	238 (47.6%)	
	High (4+)	26 (5.2%)	
Caries Presence	DMFT = 0	97 (19.4%)	<0.001*
	DMFT > 0	403 (80.6%)	

*Statistically Significant

The correlation between the DMFT index score and gender over time is presented. This connection with the average number of students having decayed teeth among male and female students are statistically significant, with a p-value of 0.003. Furthermore, across students in different graduation years, the average number of missing teeth was 0.000.00 for male students and 0.0360.29 for female students. Female students exhibited slightly higher DMFT scores, and difference was statistically significant, with a p value of 0.003 (Table 3).

Table 3: Gender associated with the DMFT Index Score

Gender	Class (Year)	Mean of Decayed Teeth	Mean of Missed Teeth	Mean of Filled Teeth	DMFT Score
Male	1st	1.40 ± 0.05	-	0.64 ± 0.63	2.04 ± 0.68
	2nd	0.27 ± 1.01	-	1.59 ± 0.19	1.86 ± 1.20
	3rd	0.13 ± 1.06	-	0.41 ± 0.13	0.54 ± 1.19
	4th/Final	1.30 ± 1.06	-	0.01 ± 0.29	1.31 ± 1.35
Female	1st	1.51 ± 0.59	0.03 ± 0.01	0.51 ± 0.43	2.05 ± 1.03
	2nd	0.19 ± 1.16	-	0.21 ± 0.81	0.40 ± 1.97
	3rd	1.01 ± 0.01	-	0.94 ± 0.71	1.95 ± 0.72
	4th/Final	0.03 ± 0.19	0.01 ± 0.18	1.46 ± 0.35	1.50 ± 0.72
p-Value	-	0.003*	-	-	0.27

*Statistically Significant

Effect size measures were calculated to clarify the clinical significance of group differences. The effect size for gender differences in DMFT scores was Cohen's (d = 0.42), indicating a moderate effect size. Additionally, Cramér's V for the chi-square test between gender and caries presence was 0.28, suggesting a moderate association. The odds ratio (OR) for females having a DMFT > 0 compared to males was 1.34 (95% CI: 1.12 – 1.57, p = 0.002), indicating that female students were 34% more likely to have dental caries than males (Table 4).

Table 4: Statistical Tests and Effect Sizes Evaluating the Clinical Significance of Group Differences

Variable Comparison	Test Used	Effect Size	p-value	Interpretation
Gender vs DMFT score	Independent t-test	Cohens d=0.42	0.003*	Moderate Effect
Gender vs Caries	Chi-square test	Cramér's V=0.28	<0.001*	Moderate Association
Female vs Male	Logistic Regression	OR= 1.34 (95% CI: 1.12 – 1.57)	0.002*	Female more likely to have caries by 34%

*Statistically Significant

DISCUSSION

The research involved 500 students aged 17 to 25 from medical & dental college, revealing that approximately 80.6% of participants exhibited dental caries, as indicated by a DMFT score. Interestingly, while female students showed a higher prevalence 255(51%) of caries compared to males 245 (49%). Given that the mean DMFT of 0.27, it was determined that the amount of caries suffered was extremely minimal. Since many parts of Sindh are classified as being in the fluorotic belt, using ground water for drinking, which may be higher in fluoride, might be one of the causes of the low DMFT. Regarding age and gender, the results of this survey were in line with those of another study conducted on Peshawar undergraduate dental students [11]. Female students 255 (51%) had a higher prevalence of caries than male students, according to other studies that used the same study design. The average total DMFT score for boys and girls did not differ statistically significantly, according to this study. With a p-value of 0.003, the quantity of dental caries, which affects the DMFT average, was statistically significant. According to the present study's findings, dental caries is prevalent in both men and women. Several studies conducted in Saudi Arabia, the United Kingdom, India, Pakistan and Saudi Arabia produced similar results [5, 6, 12-17]. Based on these findings, caries was found to be lower. Among the included

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studies, there were differences in the reported dental caries rates [18]. This supported the findings of Tsuchida S *et al.*, who discovered that the prevalence of dental caries varies greatly between studies because of things like (a) the age, socioeconomic status, and availability of examination of the subjects; (b) racial and cultural factors; and (c) diagnostic criteria [19]. It is hard to extrapolate findings from one ethnic group inside another due to the significant regional variations in dental caries prevalence. Current research findings in some ways support the World Health Organization's 2022 World Oral Health Report, which indicates that emerging nations have low Mean DMFTs (1.7) [20]. This analysis found that the frequency of dental cavities was trending increasing in developing nations and lower in industrialized ones. This is mostly since industrialized nations have better self-care habits, fluoride exposures, and preventative care programs, whereas underdeveloped nations lack those [21]. Qureshi A *et al.*, conducted another survey in underprivileged regions of Karachi, revealing variances in the mean DMFT, which is around 4 among rural populations [22]. The socioeconomic status of two distinct areas is the cause once more. Since Karachi is Pakistan's largest metropolis, there are more economic prospects there than in Jamshoro. Once more, the results showed that there were relatively few teeth filled because of caries.Reliability of the DMFT performa was enhanced through examiner calibration and adherence to standardized procedures.The natural light conditions and sterile instruments minimized variability in caries detection.

CONCLUSIONS

This study demonstrated that the population's prevalence of dental caries was relatively low. It demonstrated how oral hygiene education aided medical and dentistry students in maintaining and practicing good oral hygiene. Larger- longitudinal scale studies should be conducted, to explore caries determinants in diverse populations and evaluate the long-term effectiveness of preventive strategies

Authors Contribution

Conceptualization: AQM
Methodology: AQM, MFC
Formal analysis: SWB, YH, MZ
Writing, review and editing: AS, SWB, SAAZ, YH, MFC

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

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Exploring the Relationship between Achievement Emotions and Academic Performance in Dental College

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ABSTRACT

Achievement emotions, such as anxiety, enjoyment, and confidence, significantly influence students' academic performance. Understanding these emotions can enhance educational strategies and student outcomes, especially in high-stress environments like dental colleges. **Objective:** To investigate the achievements and emotions effects on academic performance in Pakistani dental colleges. **Methods:** A cross-sectional study was conducted at Islamic International Dental College, using convenient sampling across all professional years. Students scoring 50% or higher were classified as "pass," while those below 50% were labeled as "fail." Achievement emotions were measured using the Achievement Emotions Questionnaire, and logistic regression was used to analyze their impact on performance. Data were processed using Jaffery Amazing Statistical Package (JASP). **Results:** The study included 212 students (average age 21.25 years, 73.6% female). Females had higher average scores (375.64 vs. 342.79) and pass rates (75.6% vs. 67.9%) compared to males. Day scholars outperformed hostilities (377.70 vs. 358.41). Anxiety was common, with 60.9% of students experiencing moderate to high levels. While 35.8% disliked exams, 34.4% felt moderate pressure, and 54.2% were moderately confident. Concerns about grades were prevalent, with 36.3% worrying about poor grades and 47.2% caring about good grades. Negative emotions significantly reduced the likelihood of passing ($p = 0.040$), whereas positive emotions did not have a significant effect ($p = 0.367$). **Conclusion:** Negative emotions significantly decreased the likelihood of passing exams, while positive emotions did not have a significant impact.

INTRODUCTION

The relationship between achievement emotions and academic performance has garnered increasing attention in educational research, particularly in the demanding fields of medical and dental education. Achievement emotions, which encompass students' emotional responses to success or failure in academic tasks, play a crucial role in shaping their motivation, learning strategies, and overall academic success. Emerging evidence indicates that Emotional Intelligence (EI) is linked to improved academic outcomes across various professions [1]. Individuals with higher levels of EI are better equipped to maintain stability and navigate social challenges effectively. EI is described as "the capacity to recognize, understand, and manage one's own emotions, as well as those of others, and to use this emotional awareness to guide thought and behavior [2]." A strong correlation has been identified between Emotional Intelligence (EI) and academic success among medical students [3]. Academic performance is closely tied to a range of achievement emotions, which are feelings linked to success or failure in academic contexts. Among dental students, these emotions often carry an added weight due to the rigorous

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nature of their studies and the high standards expected in their field. Achievement emotions feelings directly linked to success or failure in academic settings play a significant role in dental students' educational experiences. Positive emotions such as enjoyment and pride can enhance motivation and learning, while negative emotions like anxiety and shame may impede academic performance [4]. Positive emotions like pride and hope can drive motivation and enhance learning, while negative emotions such as anxiety, shame, and frustration may hinder academic performance and overall well-being [5, 6]. The demanding curriculum, competitive environment, and clinical responsibilities unique to dental education amplify these emotions, making it essential to address their impact on students' academic and personal lives. Learning medicine is a complex process that involves acquiring medical knowledge, developing clinical skills, and cultivating professional attitudes. Research has shown that emotions play a leading role in this process [7]. Specific emotions in educational settings influence academic performance, assessments, feedback reception, exam results, and overall satisfaction with the learning experience [8]. Medical students, in particular, face a range of emotions due to challenging circumstances such as heavy academic workloads, high competitiveness, memorizing large volumes of information, managing busy schedules, taking difficult exams, and fearing failure [9]. During clinical years, anxiety may arise when dealing with suffering, sick, or dying patients, and collaborating with other healthcare professionals.

This study aimed to explore the intricate connections between different achievement emotions such as anxiety, pride, and hopelessness and their impact on academic outcomes among medical and dental students. By analyzing these relationships, we seek to provide valuable insights into emotional regulation and its potential to enhance student performance, well-being, and educational success in health-related disciplines.

METHODS

This cross-sectional study was conducted among students of International Islamic Dental College Rawalpindi over six months (June to December 2023) using a convenient sampling technique. The study included participants from all professional years who provided informed consent and completed the study questionnaire. The sample size was calculated using OpenEpi (Version 3) for a finite population of 470, with a hypothesized frequency of 50%, a margin of error of ± 5%, and a 95% confidence level, resulting in a required sample size of 212. Achievement Emotions Questionnaire (AEQ): The AEQ comprised 24 items, assessing students' emotional responses during exams. Total scoring ranged from 24 to 120, with higher scores indicating greater emotional intensity. The AEQ is validated with a Cronbach's alpha of 0.89, demonstrating high reliability. The study included students enrolled in all professional years at the college who provided informed consent and completed the AEQ. Exclusion criteria comprised students who did not provide consent, had incomplete questionnaires, or were on leave or not actively attending classes during the study period. Academic performance data were available for all included participants. Ethical approval was obtained from the Ethical Review Committee (ERC) at Islamic International Medical and Dental College (Ref: Riphah/IIMC/IRC/23/3025, dated 30th January 2023). Informed verbal consent was obtained from all participants in accordance with the Helsinki Declaration. Academic performance was categorized as "pass" for scores of at least 50% and "fail" for scores below 50%. Descriptive statistics (mean, standard deviation) were used for continuous variables such as age and obtained marks, while frequency distributions were employed for categorical variables like AEQ scores, gender, results, residence, and professional year. For inferential analysis, logistic regression was used to assess the effects of positive and negative emotions on academic performance, with results presented as odds ratios with 95% confidence intervals and a 5% significance level. Data were analyzed using JASP (Jeffrey's Amazing Statistical Package).

RESULTS

The study's findings offer a detailed analysis of the demographic and academic performance of medical students, alongside their emotional responses to exams and the impact on academic outcomes. Table 1 summarizes the demographic characteristics and academic performance of the participants. The sample comprised predominantly female students, who displayed slightly higher average marks and pass rates compared to males. Performance varied based on professional year and residence type, with day scholars outperforming hostelites on average.

Table 1: Demographic and Academic Performance Analysis of Dental Students

Variables	Frequency (%)	Mean ± SD	Range
Age			
Age	212 (100%)	21.25 ± 1.707	17-25
Gender-Wise Distribution of Age			
Female	156 (73.585%)	21.929 ± 1.745	17-25
Male	56 (26.415%)	21.536 ± 1.572	18-25
Total	212 (100%)	-	-
Gender-Wise Distribution of Age Examination Results Outcome (Pass)			
Female	118 (75.641%)	-	-
Male	38 (67.857%)	-	-
Total pass	156	-	-

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Gender-wise distribution of Age Examination Results Outcome (Fail)			
Female	38 (67.86%)	-	-
Male	18 (32.14%)	-	-
Total fail	56 (100%)	-	-
Grand total	212 (100%)	-	-
Gender-Wise Distribution of Obtain Marks			
Female	156 (73.585%)	375.641 ± 91.026	128-544
Male	56 (26.415%)	342.786 ± 104.254	88-520
Total	212 (100%)	366.962 ± 95.554	88-544
Professional			
1st Year BDS	51 (24.057%)	339.902 ± 104.689	80-620
2nd Year BDS	51 (24.057%)	396.745 ± 96.933	162-520
3rd Year BDS	55 (25.943%)	364.509 ± 67.423	176-488
4th Year BDS	55 (25.943%)	386.891 ± 103.672	128-544
Total	212 (100%)	-	-
Obtain Marks Residence Wise			
Day Scholar	94 (44.340%)	377.702 ± 91.060	88-544
Hostelite	118 (55.660%)	358.407 ± 98.534	88-520
Total	212 (100%)	-	-

Table 2 presents the distribution of students' perceptions regarding various aspects of exams based on a Likert scale. A significant proportion reported moderate to high anxiety levels during exams, with 32.1% feeling moderately anxious and 28.8% feeling very anxious. The majority did not enjoy taking exams, as 35.8% reported not enjoying them at all. Pressure during exams was prevalent, with 34.4% feeling moderate pressure and 33.5% feeling very pressured.

Table 2: Distribution of Students' Perceptions of Exam-Related Factors using Achievement Emotion Questionnaire (AEQ) (n=212)

Variables	Frequency (%)				
Likert Scale	**Not at all**	**Slightly**	**Moderately**	**Very Much**	**Extremely**
How anxious do you feel when you are taking an exam?	17 (8.019%)	37 (17.453%)	68 (32.075%)	61 (28.774%)	29 (13.679%)
How much do you enjoy taking exams?	76 (35.849%)	52 (24.528%)	58 (27.358%)	22 (10.377%)	4 (1.887%)
How much pressure do you feel when you are taking an exam?	12 (5.660%)	29 (13.679%)	73 (34.434%)	71 (33.491%)	27 (12.736%)
How confident do you feel about your ability to perform well in exam?	18 (8.491%)	26 (12.264%)	115 (54.245%)	45 (21.226%)	8 (3.774%)
How much do you worry about getting a bad grade in exam?	13 (6.132%)	34 (16.038%)	51 (24.057%)	77 (36.321%)	37 (17.453%)
How much do you care about getting a good grade in exam?	8 (3.774%)	14 (6.604%)	47 (22.170%)	100 (47.170%)	43 (20.283%)
How much do you feel that the exam accurately reflects your knowledge and skills?	23 (10.849%)	35 (16.509%)	98 (46.226%)	45 (21.226%)	11 (5.189%)
How much do you feel that the exam is fair?	20 (9.434%)	40 (18.868%)	94 (44.340%)	47 (22.170%)	11 (5.189%)
How much do you feel that the exam is important?	13 (6.132%)	32 (15.094%)	56 (26.415%)	89 (41.981%)	22 (10.377%)
How much do you feel that the exam is challenging?	1 (0.472%)	21 (9.906%)	73 (34.434%)	94 (44.340%)	23 (10.849%)
How much do you feel that the exam is interesting?	41 (19.340%)	68 (32.075%)	76 (35.849%)	25 (11.792%)	2 (0.943%)
How useful do you feel that the exam is?	18 (8.491%)	30 (14.151%)	75 (35.377%)	76 (35.849%)	13 (6.132%)
How much do you feel that the exam is a waste of time?	82 (38.679%)	51 (24.057%)	46 (21.698%)	24 (11.321%)	9 (4.245%)
How much do you feel that the exam is too difficult?	10 (4.717%)	39 (18.396%)	94 (44.340%)	50 (23.585%)	19 (8.962%)
How much do you feel that you are prepared for the exam?	13 (6.132%)	42 (19.811%)	112 (52.830%)	43 (20.283%)	2 (0.943%)
How much do you feel that the exam is a good measure of your understanding of the subject?	18 (8.491%)	46 (21.698%)	83 (39.151%)	58 (27.358%)	7 (3.302%)
How much do you feel that the exam is an effective way to evaluate your progress in the subject?	15 (7.075%)	47 (22.170%)	70 (33.019%)	67 (31.604%)	13 (6.132%)

Table 3 presents the logistic regression analysis examining the impact of negative emotions on passing outcomes. Negative emotions significantly reduced the likelihood of passing (β = -0.467, p = 0.040), though the overall effect size was modest (Nagelkerke $R^2 = 0.030$).

Table 3: Logistic Regression Analysis for Negative Emotion Impact

Variables	Estimate	Standard Error	Z	Wald Statistic	df	p-Value
(Intercept)	2.482	0.739	3.356	11.264	1	< 0.001
Negative Emotions	-0.467	0.228	-2.051	4.207	1	0.040

Table 4 summarizes the logistic regression analysis for positive emotions. Positive emotions did not significantly impact the likelihood of passing (β = 0.218, p = 0.367), indicating a minimal role in predicting academic outcomes.

Table 4: Logistic Regression Analysis for Positive Emotion Impact

Variables	Estimate	Standard Error	Z	Wald Statistic	df	p-Value
(Intercept)	0.390	0.710	0.540	0.290	1	0.580
Negative Emotions	0.210	0.240	0.900	0.810	1	0.360

DISCUSSION

The current study provides a detailed overview of medical students' demographics, academic performance, and emotional responses to exams. The Achievement Emotion Questionnaire revealed that many students experienced moderate anxiety and pressure during exams, with mixed

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perceptions about fairness and usefulness. Studies further showed that negative emotions significantly reduced the likelihood of passing, while positive emotions had no significant effect on pass/fail outcomes. Addressing negative emotions is crucial for enhancing academic success among medical students. The findings from this study provide valuable insights into the relationship between emotional factors and academic outcomes among medical students. The demographic analysis indicates that female students represent the majority of the sample, and they demonstrate slightly higher academic performance in terms of average marks and pass rates compared to their male counterparts. Some studies reported that males had higher Emotional Intelligence (EI) scores, while others indicated that females achieved higher EI scores [10-12]. However, many studies did not find a statistically significant gender difference in EI. Results on gender and EI also varied by region. Notably, males scored better in self-awareness, social awareness, and social skills, suggesting they may possess slightly higher EI capacities in these areas [13-15]. Additionally, day scholars appear to slightly outperform hostilities, although performance differences between residence types are minimal. Emotional responses to exams, as captured by the Achievement Emotion Questionnaire (AEQ), revealed significant levels of anxiety, pressure, and concern regarding grades among students. A substantial portion of students reported moderate to high levels of anxiety and pressure during exams, with a strong emphasis on achieving good grades. These findings underscore the importance of emotional factors in the academic experience of medical students, with many feelings anxious and worried about their performance. The scientific literature showed that anxiety and depression can have both negative and positive effects on the academic performance of medical students. Severe anxiety often hinders performance by impairing memory, concentration, and cognitive function. Most studies link anxiety and depression with lower academic outcomes, such as lower GPAs and more failed courses [16, 17]. However, some studies suggest that moderate levels of anxiety may boost motivation and academic performance, as students tend to study harder and aim for higher scores when feeling manageable anxiety [15, 18]. The results were similar to these findings. Negative emotions, significantly reduced the likelihood of passing. This suggests that students who experience higher levels of negative emotions, such as anxiety and stress, are at a greater risk of academic underperformance. The model fit improved significantly with the inclusion of negative emotions as a predictor, indicating that these emotions have a meaningful and detrimental effect on passing rates. Most studies indicated similar results to the study by showing a negative correlation between test anxiety and academic performance, with higher test anxiety linked to lower exam scores and overall academic achievement [19, 20]. According to the control-value theory, test anxiety arises from a student's negative appraisal of exam difficulty and outcome expectations. A meta-analysis by Von der EMBSE revealed moderate negative correlations between test anxiety, test performance, and GPA [21]. Cultural differences also play a significant role, influencing how students experience and express test anxiety. Studies showed variations between countries in physiological and cognitive responses to anxiety, emphasizing the need for culturally validated tools and further research to explore these complexities in diverse settings [22]. Positive emotions did not show a significant influence on pass/fail outcomes. While positive emotions were associated with a small increase in the likelihood of passing, this effect was not statistically significant. The findings suggest that while negative emotions have a clear and direct impact on academic performance, positive emotions alone may not be enough to significantly improve outcomes. The minimal influence of positive emotions could indicate that they do not substantially buffer against the detrimental effects of negative emotions in high-pressure exam situations. Previously published studies explored the link between emotions and medical students' academic performance. Behrens *et al.*, in 2019 found that students felt more positive and motivated in challenging, manageable clinical cases, with mild anxiety being beneficial [21]. However, frustration reduced interest, decision-making, and self-esteem, showing weak correlations between emotions and performance. Overall, positive emotions correlated with academic success, while negative emotions led to poor outcomes, aligning with control–value theory. The limited sample size and single setting place was the major limitation of this study.

CONCLUSIONS

In conclusion, this study emphasizes the importance of addressing negative emotions to improve academic performance among medical students. While positive emotions do not appear to significantly enhance the likelihood of passing, mitigating the impact of negative emotions may be key to fostering better academic outcomes. Interventions aimed at reducing stress, anxiety, and other negative emotions could play a critical role in enhancing both the emotional well-being and academic success of students in rigorous medical programs.

Authors Contribution

Conceptualization: MOS
Methodology: ES, FA
Formal analysis: ES
Writing, review and editing: SA, MA, WS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Comparison of "Mucopexy with Haemorrhoidal Artery Ligation with Open Hemorrhoidectomy in Terms of Effectiveness and Outcome

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ABSTRACT

Traditional haemorrhoidectomy techniques are effective in the treatment of haemorrhoids but are associated with an increased risk of postoperative bleeding, pain, and longer recovery time. Our study on Mucopexy with haemorrhoidal artery ligation compares the outcomes in both procedures. **Objective:** To compare operating time, postoperative pain and bleeding, and postoperative urinary retention with both methods. **Methods:** This randomized control trial was conducted at the Department of General Surgery at the Pakistan Railway Hospital from January 2023 to December 2023. **Results:** In the hemorrhoidectomy group, the median age was 44.6 ± 14.54 years and the mean age of 50.91 ± 17.23 years for the other group. The mean operating time for the Hemorrhoidectomy group was 56.04 ± 7.52 minutes, while for the Mucopexy group, it was 40.36 ± 6.85 minutes. The difference was significant (p=0.0000000000000000078). On the 1st day, the mean pain score (numerical rating scale for pain) for the Hemorrhoidectomy group was 7.00 ± 1.17, whereas for the Mucopexy group, it was 3.59 ± 1.15 with a significant difference (p=0.000000000000000578). On the 7th postoperative day, the mean score on the numerical rating scale for pain for the Hemorrhoidectomy group was 2.37 ± 1.10, as compared to the mucopexy group, which was 1.07 ± 0.25, (p=0.0000000000258). No statistically significant difference was found for Postoperative bleeding and urinary retention between the two groups. **Conclusions:** It was concluded that HAL with Mucopexy has shown significant improvement in postoperative pain and operating time as compared to the open haemorrhoidectomy.

INTRODUCTION

Conventional hemorrhoidectomy has been the standard option for the management of haemorrhoidal disease and it is effective against 3rd-degree hemorrhoids. However significant postoperative pain, prolonged recovery periods, and other complications like postoperative bleeding can result in notable morbidity [1, 2]. Reported literature has shown that newer dearterialization procedures are the least painful as compared to the traditional open haemorrhoidectomy [3, 4], but the research is still ongoing and more data is required to formulate guidelines with consensus, especially in our procedure where we are doing haemorrhoidal artery ligation (HAL) without the use of Doppler ultrasound. Similarly, post post-operative bleeding has been a major concern after haemorrhoidectomy especially delayed bleeding after discharge, highlighting the need for safer alternatives. New minimally invasive procedures, such as stapled haemorrhoidopexy, laser therapy, and hemorrhoidal artery ligation [5]. offer promising alternatives that minimize these risks while effectively addressing the condition. These more recent procedures aim at dearterialization of hemorrhoids rather than extensive dissection [6]. Keeping in mind the limited resources of under-developed countries it is essential to

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focus on newer and minimally invasive methods that are least dependent on technology and can be implemented with existing equipment, while at the same time, these methods are equally or more effective in the treatment of 3rd-degree hemorrhoids with improves rates of post-operative complications like pain and bleeding. Hemorrhoid artery ligation with Mucopexy has emerged as a promising technique, offering effective relief with reduced recovery times and minimal discomfort [5, 7]. However, this method requires specifically designed ultrasound equipment to accurately locate the hemorrhoidal artery for ligation, which may be replaced with the surgeon's ability to locate the position using the palpatory method and surface anatomy. Our study questions the necessity of using specifically designed equipment for the localization of the haemorrhoidal artery. We aim to establish the fact that our technique could potentially be more effective than open haemorrhoidectomy and it can also demonstrate better results in terms of outcomes and post-operative complications. Furthermore, this method could reduce costs significantly, allowing more patients to benefit from effective treatment while minimizing the reliance on expensive technology.

This study aims to assess whether we can offer our technique as a viable option for patients seeking effective relief with an improved rate of complications like pain, postoperative bleeding, and urinary retention.

METHODS

The randomized controlled trial (RCT) was started at the Pakistan Railway Hospital Rawalpindi, from January 2023 to December 2023 after approval of the hospital's ethical committee (reference no: Riphah/IIMC/IRC/22/2086). Informed consent was obtained from all participants. The trial was registered with the Iranian Registry for Clinical Trials (IRCT) ID: IRCT20241220064108N. G*Power software version 3.1.9.7 was used to detect significant differences in postoperative pain, operating time, and length of hospital stay between the two groups, with an alpha error of 0.05, a power of 0.8, and assuming a medium effect size (Cohen's d=0.5); for sample size calculation.. The formula used was $n=2.(Za/2+Z\beta)2.\sigma2/\Delta2$, where Za/2 corresponds to the alpha level (0.05), Zβ corresponds to the power (0.8), σ represents the standard deviation, and Δ represents the minimum detectable difference, resulting in a required total of 90 participants (45 in each group). A total of 90 patients diagnosed with 3rd-degree hemorrhoids were enrolled. Patients were divided between the two groups randomly: The Mucopexy group and the conventional hemorrhoidectomy group. Patients who were unfit for surgery, those with previous anorectal surgeries, those with 1st or 2nd-degree hemorrhoids, and those below 16 years and above 65 years of age were excluded from the study. Randomization was conducted using a computer-generated sequence. Concealment was ensured using sealed envelopes. Assessors were blinded to the treatment allocation. An objective assessment of outcomes was done throughout the study to ensure blinding. Both groups underwent spinal anesthesia. Both groups received preoperative antibiotic prophylaxis with IV ceftriaxone Ig and IV metronidazole 500mg. All patients were in the lithotomy position. The diagnosis was confirmed and other pathologies were ruled out on initial examination and proctoscopy. The haemorrhoidal artery was ligated with figure-of-8 vicryl 1 suture was performed after finger-guided palpation of the artery without Doppler. After Figure eight suture ligation of the artery, a continuous suture is placed up to and just superior to the dentate line for mucopexy. The consultant surgeons performed all cases. Patients were kept in the hospital for one day and were discharged on 1st postoperative day. All patients were given routine analgesia with IV Panadol and non-steroidal anti-inflammatory drugs (NSAIDs) during their hospital stay. No postoperative antibiotics were prescribed. The conventional hemorrhoidectomy group underwent traditional open hemorrhoidectomy, involving clamping of hemorrhoidal tissue at the base. An inverted V-shaped incision is made and haemorrhoidal tissue is dissected from surrounding tissue and sphincter using scissors or electrocautery. Ligating the vascular pedicle and excision of hemorrhoids. Hemostasis was secured using cautery. Data were collected using pre-designed proformas, recording patient demographics, clinical presentation, and outcome variables, including operating time, length of hospital stay, and postoperative pain on days 1 and 7 measured using the Numerical rating scale, which is a rating scale for pain from 0 to 10, while 0 is no pain and 10 is worse pain. Statistical analysis was performed using SPSS version 26.0, with descriptive statistics calculated for all variables. Mean ± standard deviation (SD) was calculated for continuous variables and analyzed using the independent t-test. In contrast, frequencies and percentages were calculated for categorical variables. The chi-square test or Fisher's exact test was used to analyze categorical variables. With a confidence interval of 95%, a p-value of less than 0.05 was taken as significant.

RESULTS

Data of patients who underwent either Hemorrhoidectomy or Mucopexy was analyzed. The primary variables considered were age, gender, operating, length of hospital stay, postoperative pain on days 1 and 7, postoperative bleeding, and postoperative urinary retention. The data were segregated into two groups based on the type of procedure performed. In the Haemorrhoidectomy Group,

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45 patients were included, with a mean age of 48.4 ±13.9 years for female patients and 43.8 ± 14.7 for male patients as shown in Table 1.

Table 1: Age and Gender Distribution Hemorrhoidectomy Group

Gender	Mean ± SD
Female	48.4 ± 13.9
Male	43.8 ± 14.7

45 patients were included in the mucopexy group with a mean age of 47.8 ± 16.1 years for female patients and 51.8 ± 17.7 years for male patients. This group also had a higher number of male, with 35 male and 10 female, as shown in Table 2.

Table 2: Age and Gender Distribution Mucopexy Group

Gender	Mean ± SD
Female	47.8 ± 16.1
Male	51.8 ± 17.7

These results have shown that the average age of patients undergoing Mucopexy was higher as compared to those undergoing Hemorrhoidectomy. Both groups have a higher proportion of male patients. The mean operating time for the Hemorrhoidectomy group was (56.04 ± 7.52) minutes, while for the Mucopexy group, it was (40.36 ± 6.85) minutes. It was statistically significant (p=0.00000000000000078). The mean length of stay for the Hemorrhoidectomy group was (1.11 ± 0.31) days, compared to (1.02 ± 0.15) days for the Mucopexy group. This difference was not statistically significant (p=0.104). On the first postoperative day, the mean pain score for the Hemorrhoidectomy group was (7.00 ± 1.17), whereas for the Mucopexy group, it was (3.59 ± 1.15). This difference was statistically significant (p=0.000000000000000578). On the 7th postoperative day, the mean pain score for the Hemorrhoidectomy group was (2.37 ± 1.10), compared to (1.07 ± 0.25) for the Mucopexy group. This difference was also statistically significant p=0.0000000000258, as shown in Table 3.

Table 3: Summary of Continuous Variables in Both Groups

Variables	Hemorrhoidectomy (Mean ± SD)	Mucopexy (Mean ± SD)	p-value
Operating Time (min)	56.04 ± 7.52	40.36 ± 6.85	0.000000000000000078
Length of Stay (Days)	1.11 ± 0.31	1.02 ± 0.15	0.104
Postoperative Pain Day 1	7.00 ± 1.17	3.59 ± 1.15	0.000000000000000578
Postoperative Pain Day 7	2.37 ± 1.10	1.07 ± 0.25	0.0000000000258

Hemorrhoidectomy group, post-operative bleeding was observed in 6.6% of cases and 0.0% of patients in the Mucopexy group. It was not statistically significant with a p-value of less than 0.05 (p=0.256). 15.2% of patients in the Hemorrhoidectomy group had urinary retention after surgery and 2.2% of patients in the Mucopexy group. It was not statistically significant p=0.074, as shown in Table 4.

Table 4: Summary Categorical Variables Both Groups

Variable	Hemorrhoidectomy	Mucopexy	p-value
Postoperative Bleeding	3/45 (6.5%)	0/45 (0.00%)	0.256
Postoperative Urinary Retention	7/45 (15.2%)	1/45 (2.22%)	0.074

DISCUSSION

This study provides a comparative analysis of hemorrhoidectomy and Mucopexy with hemorrhoidal artery ligation (HAL) in terms of perioperative and postoperative outcomes. The findings highlight significant differences between the two procedures, with Mucopexy with HAL demonstrating advantages in key clinical parameters, particularly in reducing postoperative pain and operating time. The literature on minimally invasive treatment of haemorrhoidal diseases is growing and these results will add further to it [8, 9]. In our study, both groups consisted of 45 patients each. The mean age in the Hemorrhoidectomy group was 48.4 ± 13.9 years for female and 43.8 ± 14.7 years for male. The mean age was 47.8 ± 16.1 years for female and 51.8 ± 17.7 years for male, with a higher proportion of male (35 male, 10 female) in mucopexy with the HAL group. Alemrajabi *et al.*, reported a mean patient age of 40.9 ± 8.3 years, nearly similar to our study and almost equal male-to-female ratio [10]. Median age for HAL-RAR in another study was 47 years, while 52 years for the Milligan-Morgan hemorrhoidectomy group [11]. The demographic trends in our study align with previous studies, showing a slightly higher representation of male patients in surgical hemorrhoidal treatments [12]. Current study showed a significantly lower mean operating time for the Mucopexy with HAL group (40.36 ± 6.85 minutes) compared to the Hemorrhoidectomy group (56.04 ± 7.52 minutes) (p<0.000000000000000078). This was consistent with Sobrado *et al.*, who reported a mean operating time of 22 minutes for mucopexy procedures [12]. The faster surgical time associated with mucopexy and HAL may contribute to reduced perioperative morbidity and faster recovery. Patients in the Mucopexy with HAL group experienced significantly lower postoperative pain. The mean pain score was 7.00 ± 1.17 in the Hemorrhoidectomy group and 3.59 ± 1.15 in the Mucopexy group (p<0.000000000000000578) on the first postoperative day. By the 7th postoperative day, the pain scores had decreased to 2.37 ± 1.10 and 1.07 ± 0.25, respectively (p=0.0000000000258). These findings align

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with previous studies reporting reduced pain with Mucopexy and artery ligation techniques, likely due to the minimally invasive nature of the procedure, which involves less tissue dissection and trauma [13-15]. Alemrajabi *et al.*, reported an initial postoperative pain score of 7.06 ± 1.58 at 48 hours, consistent with our findings for the Hemorrhoidectomy group [10]. Symeonidis *et al.*, observed adequate pain control with oral analgesics but reported two cases requiring readmission for severe pain in each group [11]. Chivate *et al.*, noted that most patients undergoing mucopexy had minimal pain (VAS 1-2) [16]. Significantly lower pain scores in our study highlight the advantage of Mucopexy with HAL in reducing postoperative discomfort. Current study showed the mean length of stay for the Hemorrhoidectomy group as 1.11 ± 0.31 days, compared to 1.02 ± 0.15 days for the Mucopexy group. This difference was not statistically significant (p=0.104). Chivate *et al.*, and some other literature reported that patients undergoing transanal suture mucopexy could return to normal activities within 48-72 hours [16], whereas Milligan-Morgan hemorrhoidectomy patients required 1-6 weeks [17]. Similar trends were observed in Hemorrhoidal artery ligation has shown a lower postoperative complication rate and faster recovery than conventional hemorrhoidectomy in previously reported literature [18]. The postoperative urinary retention rate of 15.2% and 2.2% was reported in the Haemorrhoidectomy group and mucopexy group respectively with a non-significant p-value of 0.074. Reported literature has also shown non-significant results [19]. Postoperative bleeding was observed in 6.6% of cases in the Hemorrhoidectomy group, while no cases were reported in the Mucopexy group (p=0.256). Symeonidis *et al.*, recorded 2 cases of significant postoperative bleeding in the mucopexy group and 5 cases in the other group, with one case needing surgical intervention [11]. Alemrajabi *et al.*, found a bleeding incidence of 22.2% at one month in patients undergoing HAL with mucopexy, though no cases were reported at three months [10]. Chivate *et al.*, reported no recurrent bleeding with transanal suture mucopexy [16]. Overall, our findings, in conjunction with existing literature, suggest that Mucopexy with HAL offers several advantages over conventional hemorrhoidectomy, particularly in terms of reduced postoperative pain and shorter operative duration [20].

CONCLUSIONS

It was concluded that Mucopexy with HAL WAS associated with significantly reduced operating time, lower postoperative pain scores, and faster recovery compared to conventional hemorrhoidectomy. Although the difference in postoperative complications such as urinary retention and bleeding was not statistically significant, the overall trend suggests a favorable outcome with HAL-Mucopexy. These findings align with previous studies, reinforcing the benefits of less invasive surgical techniques in the management of hemorrhoidal disease. Further studies with larger sample sizes and longer follow-up periods may provide additional insights into the long-term efficacy and recurrence rates of these procedures.

Authors Contribution

Conceptualization: MA
Methodology: KR, MIS, BA, AH, SR
Formal analysis: KR, MI, BA, AH, SR
Writing review and editing: MA, KR, MIS, MI

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Immunohistochemical Demonstration of COX2 in Various Lesions of Oral Cavity

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ABSTRACT

Cyclooxygenase enzyme facilitates the conversion of arachidonic acid into pro-inflammatory compounds, resulting in formation of prostaglandins, which contributes substantially to the carcinogenic process. **Objective:** To analyze the immunohistochemical COX2 enzyme expression in various lesion of oral cavity. **Methods:** A total of 60 formalin fixed, paraffinized blocks (including 10 healthy oral mucosa cases, 10 cases of leukoplakia. 10 cases of oral sub mucosal fibrosis, 10 cases of dysplasia, 10 cases of well differentiated carcinoma, 10 cases of highly aggressive invasive squamous carcinoma) were randomly selected during the period of Jan, 2022 till Dec, 2023. Immunohistochemistry was done on each case for analyzing COX2 expression. Data was statistically analyzed by using chi square test. P value < 0.05 was taken as substantial. **Result:** It was found that the expression level was high in invasive carcinoma as compared with other oral lesion. **Conclusion:** Present study strongly supported the involvement of COX2 in the advancement of precancerous lesions of oral cavity to malignant one.

INTRODUCTION

Benign and malignant lesion of oral cavity are major health issue in developed and undeveloped countries. Because they are linked to a higher risk of oral cancer, especially Oral Squamous Cell Carcinoma (OSCC), Oral Potentially Malignant Disorders (OPMDs) pose a serious threat to global health. Globally, OPMD prevalence varies, with South Asian nations reporting greater rates. Given that OSCC's five-year survival rate is still less than 50%, early detection and intervention are essential [1]. In 2020, there were about 0.37 million new instances of oral cancer worldwide, with Asia accounting for a large portion of these cases [2]. High-risk lesions with a higher chance of malignant development, such as erythroplakia and non-homogeneous leukoplakia, are included in the classification of OPMDs [3].According to national cancer registry, Pakistan data Oral Cavity (OC) cancer is the leading No. 1 cancer in males of Pakistan and number three in females [4]. It has been observed that the percentage of progression from premalignant lesion of oral cavity to malignant is increasing despites marvelous advancement in diagnostic and surgical fields. Therefore, it is a dire need to search new molecular targets to prevent the progression of oral lesion toward malignancy [5]. In South East Asia especially in Pakistan the leading cause of oral lesions are mainly smoking, alcohol, betel nuts chewing and gutka eating. All these risk factors are somehow involved in

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causing chronic inflammation in buccal mucosa. In 1863, Virchow first hypothesized the connection between inflammatory process and carcinogenesis. An environment rich in inflammatory cells along with certain growth factors, enhance the potential for malignant transformation in proliferating cells [5].Although inflammation has been regarded as a protective mechanism of body to various types of injurious stimuli, there has been growing evidence of its strong role in initiation or progression of various diseases especially cancer. It has been observed that inflammation accompanies many premalignant and malignant lesion of oral cavity. This results in elevation of COX 2 enzyme in local tissue, which converts into Prostaglandins (PGs) especially PGE2 (prostaglandin E2). It amplifies several key processes in tumor formation, such as angiogenesis, invasive capabilities, and cell proliferation [6]. COX2 mRNA has been found many folds high in oral cancer tissues compared with non-cancerous tissues. Likewise, buccal tissues of tobacco or gutka eaters expresses significant upregulation of COX2 mRNA levels than non-users. These patients exhibit increased COX-2 expression which has been linked to increased incidence of tumor progression from premalignant to malignant one resulting in lower 5-year survival rate [7].

This study aimed to evaluate the expression levels of COX2 in premalignant and malignant oral lesions.

METHODS

This was a retrospective observational study with immunohistochemical analysis, conducted at the Life Care Molecular and Polymerase Chain Reaction (PCR) Lab Services, Karachi, from January 2022 to December 2023, in collaboration with Fazaia Ruth Pfau Medical College, Karachi. Ethical approval was obtained from the Institutional Review Board (IRB) of Fazaia Ruth Pfau Medical College with reference number FRPMC/002/IRB/21. Permission for data collection was granted as per institutional guidelines. Since this was a retrospective study, informed consent was waived in compliance with institutional policies, ensuring strict confidentiality and anonymity of patient data. For sampling, a total of 60 Formalin-Fixed Paraffin-Embedded (FFPE) tissue blocks were retrieved from the Histopathology Department, Life Care Molecular Lab, covering the period from January 1, 2020, to December 31, 2023. These blocks contained tissues diagnosed as leukoplakia, oral submucosal fibrosis, dysplasia, carcinoma in situ, and invasive cancer, as well as ten blocks of large intestinal mucosa used as a control group. Since oral lesion biopsies are typically small and received for diagnostic purposes, normal mucosa from unaffected areas of the oral lesion could not be reliably used as a control. Instead, normal colonic mucosa was selected as a control group due to its larger tissue size and established expression of COX2, ensuring robust comparison of COX2 staining between normal and pathological samples. The colonic mucosa was obtained from biopsies submitted for unrelated diagnostic purposes, with care taken to sample areas confirmed as histologically normal. Tissue blocks from patients diagnosed with oral lesions, including leukoplakia, oral submucosal fibrosis, dysplasia, carcinoma in situ, and invasive cancer, large intestinal mucosa samples with histologically normal findings from diagnostic biopsies and cases with well-preserved histopathological features and complete clinical records were included for the study. Incomplete or degraded tissue samples and cases lacking essential clinical data or diagnostic confirmation were excluded. Furthermore, patients with a history of prior chemoradiotherapy or immunosuppressive therapy for oral lesions were also excluded. The sample size was calculated using data from a comparable study evaluating immunohistochemical expression of COX2 in similar oral lesions. The equation for sample size was derived using a single proportion formula: Using a single proportion formula:

$$n = \frac{Z^2 \times P \times (1-P)}{d^2}$$

Where:

n= required sample size

Z = 1.96 (standard normal value corresponding to a 95% confidence level)

P=(Prevalence of Oral submucous fibrosis) 4.9% or 0.049 .

d=5% (margin of error)

Substituting the values into the formula

n=(1.96)2 x0.049x(1-0.049)(0.05)2

n=71.84

Since this could not get enough tissue samples and 60 samples for this study instead of the calculated 72. Although the ideal number is determined to be 72 by statistical power for necessary optimality, practical sample availability constraint forced us to use 60 as the sample size. In the same time, even when the sample size is 60, this number gives a quite meaningful insight and robust outcomes. Histopathological analysis was performed using fresh five-micron histopathological slides prepared from the retrieved tissue blocks, stained with hematoxylin and eosin (HandE), and examined independently by two consultant pathologists. HandE staining was performed as per the method described by Bancroft and Gamble (Theory and Practice of Histological Techniques, 8th edition) [9]. Large intestinal tissue from the colonic mucosa was used as a positive control for COX2 immunohistochemical staining. This tissue was chosen due to its reliable and established expression of COX2 in normal glandular epithelium and inflammatory contexts [10]. Sampling was

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limited to histologically confirm normal areas. Immunohistochemistry was performed from four-micron thick sections obtained from all tissue blocks. Sections were mounted on positively charged slides and underwent routine deparaffinization and antigen retrieval using an automated water bath (CytoTest, China). The primary antibody used was anti-COX2 monoclonal antibody (Clone CX-294, Dako, Denmark) at a dilution of 1:100. A secondary antibody conjugated with Horseradish Peroxidase (HRP) was used for signal amplification. A substrate (H_2O_2) and chromogen (3, 3'-diaminobenzidine; DAB) were added to form a brightly colored, insoluble product localized to antigenic areas. Positive expression was indicated by brown staining in tumor cells, visualized and photographed using a Leica 2500 optical microscope (Leica Microsystems, Germany). From each paraffin-embedded block, 3–5 slides were prepared to ensure adequate representation of tissue. For each slide, four fields were captured for analysis at a magnification of 40×. Images included a scale bar of 50 µm for reference. To ensure background or nonspecific staining did not interfere with results, negative controls were used, and antigen retrieval, antibody dilutions, and blocking steps were optimized. Endogenous enzyme activity was inhibited, and high-specificity antibodies were applied. Normal large intestinal tissue served as a control, and two pathologists independently reviewed the slides for consistency. Representative images were captured from three different paraffin-embedded tissue blocks, showcasing COX2 staining patterns in dysplasia, carcinoma in situ, and invasive cancer. Each image highlights the intensity and localization of staining at a magnification of 40× with a 50 µm scale bar. Immunohistochemical staining for COX2 expression was graded on a scale of 1–3 as 1+: Weak staining, 2+: Moderate staining, and 3+: Strong staining. The statistical analysis was conducted to evaluate the relationship between COX2 expression and the morphological grades of oral lesions. Descriptive Statistics was used to summarize COX2 expression across different lesions, calculating frequencies and proportions of staining intensities (+1, +2, +3, +4). Chi-Square Test was used to assess the association between lesion grade and COX2 expression intensity. A threshold of $p < 0.05$ was considered statistically significant, indicating the presence of a meaningful correlation.

RESULTS

The immunohistochemical analysis of COX2 expression in various oral lesions revealed significant variations across different morphological types. A higher intensity of COX2 expression was observed in more advanced lesions such as poorly differentiated Oral Squamous Cell Carcinoma (OSCC), as compared to less aggressive lesions like leukoplakia and normal buccal mucosa. In normal buccal mucosa, 90% of cases exhibited weak (+1) COX2 expression, with only 10% showing moderate (+2) expression. Leukoplakia showed a notable increase in COX2 expression, with 60% of cases displaying moderate (+2) staining. Oral submucosal fibrosis showed a mix of moderate (+2) and strong (+3) expressions in 50% of cases. Dysplastic lesions had a balanced distribution across mild, moderate, and strong expressions (+1 to +3). Well-differentiated OSCC and poorly differentiated OSCC demonstrated the highest levels of COX2 expression, with the majority of cases showing strong (+3) and very strong (+4) staining (Figure 1). Table 1 presents the distribution of COX2 cytoplasmic expression in different oral lesions, categorized by proportional value. A significant increase in COX2 expression is observed from normal mucosa to invasive carcinoma.

Table 1: COX-2 Cytoplasmic Expression in Different Oral Lesions

Morphological Type of Specimen	Total Cases Analyzed	Proportional Value				Probability Value
		+1	+2	+3	+4	
Normal Mucosa	10	09	01	-	-	0.001
Leukoplakia	10	04	06	-	-	
Oral Submucosal Fibrosis	10	02	03	05	-	
Dysplasia	10	01	02	02	05	
Well Differentiated OSCC	10	-	01	03	06	
Poorly Differentiated OSCC	10	-	-	03	07	

Proportional value was designated as +1: 5-10% of cells positive, +2: 11-40% of cells positive, +3: 41-70% of cells positive, and +4: 71-100% of cells positive.

Table 2 categorized COX2 expression by morphological grade. A statistically significant correlation was found between the grade of the oral lesions and the intensity of COX-2 expression ($p < 0.05$). Higher grades of lesions showed an increase in the intensity of COX2 staining.

Table 2: Graded Analysis of COX-2 Cytoplasmic Expression in Oral Lesion

Morphological Type of Specimen	Total Cases Analyzed	Proportional Value				Probability Value
		0	+1	+2	+3	
Normal Mucosa	10	10	-	-	-	0.001
Leukoplakia	10	00	10	-	-	
Oral Submucosal Fibrosis	10	00	04	06	-	
Dysplasia	10	00	02	03	05	
Well Differentiated OSCC	10	00	00	04	06	
Poorly Differentiated OSCC	10	00	00	02	08	

Grading was designated a proportional values as Grade 0: Negative COX-2 expression, Grade +1: Mild COX-2 expression, Grade +2: Moderate COX-2 expression, and Grade +3: Strong COX-2 expression. A and B represented negative COX-2 staining in normal mucosa of grade 0 indicating no significant expression in normal Mucosa. C and D represent mild positive COX-2 immunostaining expression in an oral fibrotic lesion (oral submucosal

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fibrosis) showing mild oral fibrosis of grade 1. E and F represent moderate immunostaining in a dysplastic lesion, showing an increased number of positive cells of grade 2. G and H represent strong expression in a well-differentiated OSCC,severe positive immunostaining in poorly differentiated OSCC of grade 3 with significant tumor cell show intense staining.

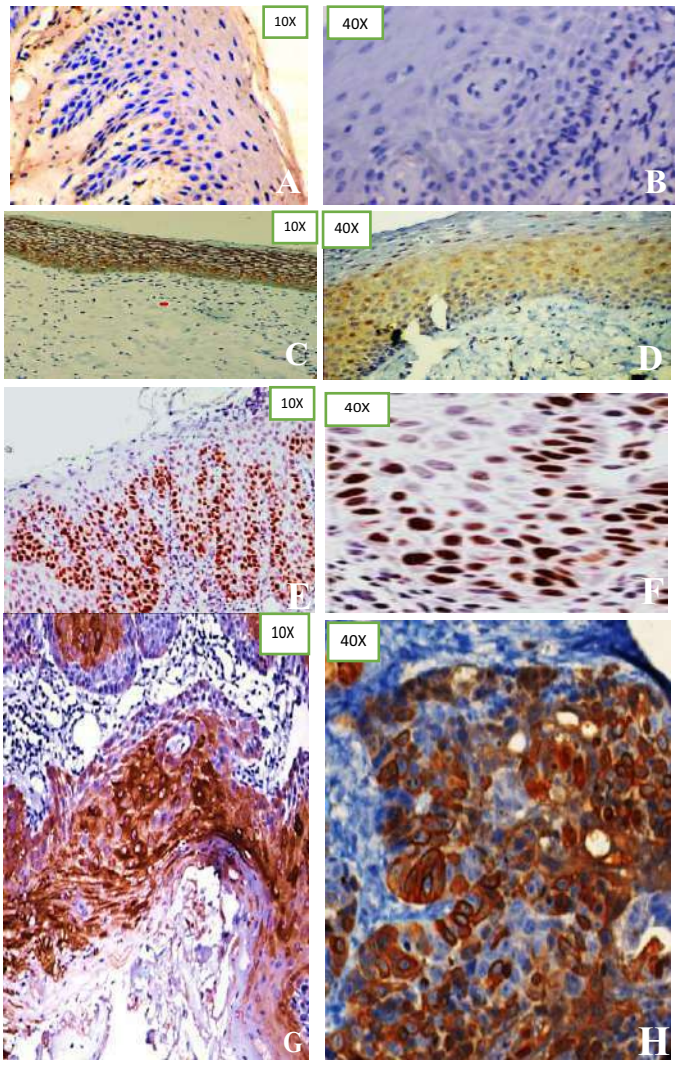

Figure 1: Immunohistochemistry of COX-2 Expression in Oral Lesions

DISCUSSION

The current study's findings revealed a progressive upregulation of COX2 expression in oral cavity lesions, transitioning from premalignant to malignant stages, as well as in normal buccal mucosa, thereby substantiating the involvement of COX2 in the carcinogenic process (Figure 1). Cyclooxygenase (COX) is a member of myeloperoxidase family which is involve in the synthesis of prostaglandins from arachidonic acid [11]. The Cyclooxygenase (COX) enzyme exists in three isoforms, namely COX1, COX2, and COX3, each with distinct properties and functions. COX 1 and COX3 are encoded by the same gene. Difference in both COX enzyme is that COX3 is a posttranscriptional modification of COX1. The expression of COX1 is predominantly localized to the Central Nervous System(CNS)and the aortic wall. While the full significance of COX3 remains to be fully understood, it is known to possess important pathophysiological properties that contribute to various biological processes [12]. COX1 is responsible for the maintenance of normal bodily homeostasis. Somehow, it is also being found involved in the pathogenesis of atheromatous plaques and inflammatory foci in rheumatoid arthritis [13]. In humans, COX 2 is present in very low concentration and is rarely detected in healthy individuals. Nevertheless, it is involved in various physiological functions in GIT, renal, CVS, CNS, Eye and the reproductive system. Upregulation of COX-2 has been implicated in the development and progression of various cancers, including esophageal cancer, urinary bladder cancer, and notably, head & neck cancers, as well as oral cancers [14]. Over expression of COX2 genetically and phenotypically change premalignant cells to a malignant one. It also disturbs cell growth cycle, apoptosis and the immune response enabling cancer cells to proliferate, survive, enhancing neovascularization, and promotes cancer cell invasion [15]. This study revealed the presence of COX2 expression in normal buccal mucosa as well as various benign and malignant lesions of oral cavity. Or results showed negative expression in healthy oral mucosa while COX 2 expression was found to be raised as disease progress from benign to malignant conditions. Table 1 and 2 results are in accordance with the study of which stated that simultaneous upregulation of COX2 expression was detected as the disease progress from dysplasia to invasive oral squamous cell cancer. This suggests a crucial role for this enzyme in the progression of premalignant lesions to malignancy [16]. Similar results were also stated by their research also revealed that COX-2 expression is significantly higher in oral OSCC (Oral Squamous Cell Carcinoma) compared to premalignant lesions [17]. These results are in accordance with the study of which also showed COX2 expression is significantly higher in dysplasia and oral squamous cell carcinoma as compared to normal mucosa [18]. Same results have been reported by for head and neck SCC and by and about OSCC [19]. These results are in accordance with the study of that a significant variation in COX2 expression was also noted among OSCC (Oral Squamous Cell Carcinoma), oral leukoplakia, and oral fibrous lesions. Higher expression was found in oral squamous carcinoma than leukoplakia and fibrosis[20].

CONCLUSIONS

This study investigates the expression of COX2 in various oral lesions, including normal oral mucosa, to provide a comprehensive understanding of its role in oral pathology. The results obtained clearly demonstrate the increasing

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level of expression of COX2 among benign to cancerous oral cavity lesions. This clearly point toward the positive role of COX2 in progression of premalignant to malignant oral cavity lesions. Since COX 2 enzyme has a rate limiting function in inflammation, anti COX2 medicines could be used to prevent the transformation of pre malignant lesions to malignant one. Additionally, these drugs may potentiate the effects of chemotherapy, allowing for reduced treatment durations and minimizing the risks associated with prolonged exposure to chemotherapeutic agents.

Authors Contribution

Conceptualization: SZ
Methodology: NQ, HK, MS, SS, FM
Formal analysis: NQ, HK, MS, SS, FM
Writing, review and editing: NQ, HK, MS, SS, FM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Diagnostic Accuracy of Chest Ultrasonography in Diagnosing Pneumothorax Taking CT Chest as A Gold Standard

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ABSTRACT

Ultrasound of the lung is an emerging diagnostic technique for diagnosing pneumothorax in patients with traumatic injury which is faster, safer, or more accessible than a conventional computed tomography scan. **Objectives:** To assess the diagnostic accuracy of chest ultrasonography in diagnosing pneumothorax using computed tomography chest as a gold standard. **Methods:** A cross-sectional validation study was conducted at the Radiology Department of Holy Family Hospital, from Nov 2022 to May 2023. Adult patients of either gender, with clinical suspicion of pneumothorax either traumatic or spontaneous, were included. Patients undergone chest ultrasound and pneumothorax were confirmed by the presence of sonographic features. Plain computed tomography chest imaging was done to confirm the diagnosis and compare it with ultrasound results. **Results:** There were ninety patients included. The ultrasound technique was found to have 92.8% sensitivity and 91.7% specificity to correctly diagnose pneumothorax as compared to chest computed tomography. The positive and negative predictive values were found to be 94.5% and 88.5% respectively, and overall diagnostic power was 92.2%. **Conclusions:** It was concluded that the diagnostic accuracy of chest ultrasonography in detecting pneumothorax is comparable to computed tomography Chest gold standard and this technique can be utilized in emergency care settings.

INTRODUCTION

Pneumothorax is a medical term used to describe a serious condition where there is air trapped inside the pleural cavity [1]. The most common reason resulting in pneumothorax is trauma which can occur due to any external factor or accident with a direct forceful hit to the chest, followed by other iatrogenic causes. As a result of injury, the parietal or visceral pleura ruptures allowing air entry into the pleural space [2, 3]. Other than post-traumatic pneumothorax, pneumothorax can occur in intensive care unit patients, post-intervention pneumothorax, pneumothorax due to lung disease, residual pneumothorax associated with intercostal chest tube drainage, and spontaneous pneumothorax in adults and paediatric population [4, 5]. Due to entrapment of air in the pleural cavity, there is a drop in negative pressure which is necessary to keep the lung inflated and assist in proper breathing. A drop in negative pressure leads to improper breathing, severe pain and even collapsing of the lung can occur in severe situations [6]. An early diagnosis can play an important role in the timely management of pneumothorax which can be life-saving. Clinically pneumothorax is presented with severe dyspnoea, extreme air hunger, and chest pain. All trauma patients are recommended to be examined for pneumothorax during initial clinical examination [7]. In routine, patients who are clinically suspicious of pneumothorax undergo chest X-rays for evidence of trapped air and/or collapsed lungs. For critically ill patients who cannot stand, undergo a supine

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chest x-ray which can cause pneumothorax, or sometimes undergo a chest Computed Tomography (CT) [8, 9]. It is reported in the literature that at times supine chest X-ray might not be enough to diagnose pneumothorax which can pose the patients at risk of developing complications; whereas, chest CT is an established gold standard test for diagnosing pneumothorax [10]. CT scan is an expensive and time-consuming procedure, which exposes the patients to high doses of ionizing radiation and sometimes is not feasible for unstable patients. In addition to that CT scans might not be available at every accident and trauma center in resource-constrained developing countries like Pakistan. Ultrasound of the lung is an emerging diagnostic technique for diagnosing pneumothorax in patients with traumatic injury or other causes with fairly decent sensitivity and specificity. Literature showed that it has the advantage of being simple, is portable, can provide real-time imaging, and is more easily accepted by patients [11]. A systematic review reported 91% specificity and 99% sensitivity of chest ultrasound to diagnose pneumothorax [12]. Some major advantages of chest ultrasound over chest CT scan include; less time-consuming, less expensive, no exposure to harmful radiations, handy, portable, available at most healthcare facilities, and suitable for repeated examinations [13]. Despite of literature supporting the efficiency of chest ultrasound in establishing the diagnosis of pneumothorax, very few studies are reported from Pakistan in this context. In a developing country like Pakistan with constrained resources, chest ultrasound can prove to be cost-effective in the diagnosis of pneumothorax.

This study aims to assess the performance of chest ultrasonography in diagnosing patients with pneumothorax against the CT Chest images as the reference standard.

METHODS

A cross-sectional diagnostic validation study was conducted in the Department of Radiology of Holy Family Hospital, Rawalpindi, for a period of six months from Dec 2022 to May 2023. Before executing the research, ethical approval was taken from the College of Physicians and Surgeons Pakistan (Ref no. CPSP/REU/RAD-2021-126-3489). A sample of 90 patients was calculated by the WHO sample size calculator considering 89.6% sensitivity [14]. 95.6% specificity [14]. 40.6% prevalence of pneumothorax in accident and trauma patients 95% confidence, 80% power and 6% precision. Patients presenting to the emergency department with traumatic chest injury and complaining of sudden shortness of breath were considered for enrolment using a consecutive sampling method. Those fulfilling the inclusion criteria of any age group, either gender, clinical suspicion of pneumothorax, whether traumatic or spontaneous, willing to participate in the study were included. Patients who were critically ill, required urgent surgery, had tension pneumothorax, experienced hemodynamic instability, or were pregnant were excluded. Before data collection the study objectives and procedures were explained to the participants and consent for participation was taken. Socio-demographic and clinical data were recorded for each patient. All included patients were undergone chest ultrasound using Honda HS-2600 ultrasound machine having 5-10 MHz frequency. A single operator performed all the ultrasound tests. The patients were scanned in a supine position by an ultrasound machine with a high-frequency linear probe (5-10 MHZ) placed perpendicular to two rib spaces in the anterior chest region in the midclavicular line in the second and third intercostal spaces. The ribs were characterized as hyperechoic and their acoustic shadows visible as hypoechoic rays were considered stationary structures. This was defined as interspace which is the location of the pleural line that appears as an echogenic line obtained at the inferior border of the space between two ribs. Pneumothorax was diagnosed from the sonographic signs, such as the lack of a seashore sign, absent lung sliding sign, lung point sign, and presence of a barcode sign at that particular site. The presence or absence of A-lines was also noted. All of the included patients were then followed up with plain CT chest imaging modality to confirm the diagnosis. The results were reported by a radiologist who was unaware of the ultrasound findings. Data were extracted from a data collection tool, and data management software IBM SPSS version 23.0 was used for data analysis. The ultrasound findings of pneumothorax were reported as present or absent in percentage and confirmed with gold standard chest CT scan findings. Diagnostic accuracy was measured. A p-value of ≤0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 33.37 ± 14.90 years. The majority of the patients, accounting for 59 individuals (65.56%), were above 40 years of age. Among the 90 patients that were included in the study, the total male patients were 52 (57.78%), while the total female patients were 38 (42.22%), resulting in a male-to-female ratio of 1.4:1. Demographic characteristics are shown in Table 1.

Table 1: Socio-Demographics of Study Participants (n=90)

Characteristics	Frequency (%)
Age	33.37 ± 14.90
Age Categories	
≤40 Years	59 (65.6%)
>40 Years	31 (34.4%)

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Sex Distribution	
Female	38 (42.2%)
Male	52 (57.8%)

All patients underwent chest ultrasonography followed by computed tomography (CT) for confirmation of the diagnosis. The frequency and percentage of ultrasound signs observed among study participants are given in table 2.

Table 2: Distribution of Ultrasound Signs (n=90)

Pneumothorax Positive (n=55)	n (%)
Absent Lung Sliding Sign	53 (96.0%)
Lung Point Sign	11 (29.1%)
Barcode Sign (M-Mode)	52 (94.5%)
A-Lines	23 (44.0%)
Pneumothorax Absent (n=35)	
Present Lung Sliding Sign	33 (94.2%)
Seashore Sign (M-Mode)	32 (91.0%)
A-Lines	26 (74.2%)

Present lung sliding and seashore sign (M-mode), Pneumothorax absent. The specific ultrasound signs are shown in figure 1.

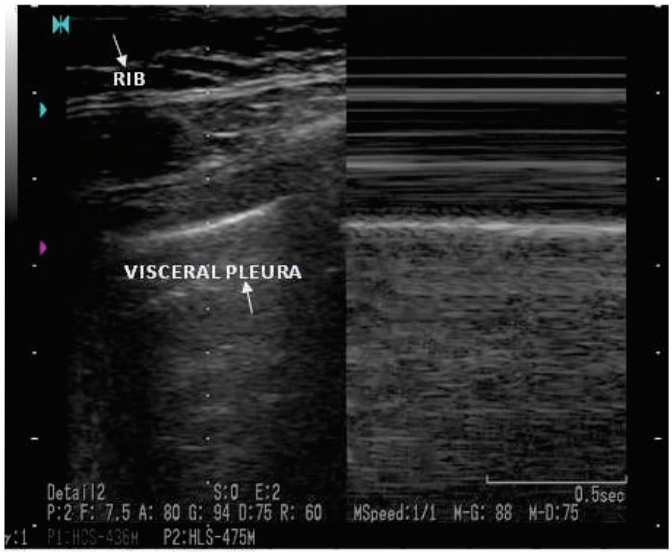

Figure 1: Present Lung Sliding and Seashore Sign (M-Mode), Pneumothorax Absent

Absent lung sliding sign and barcode sign (M-Mode), Pneumothorax present are shown in figure 2.

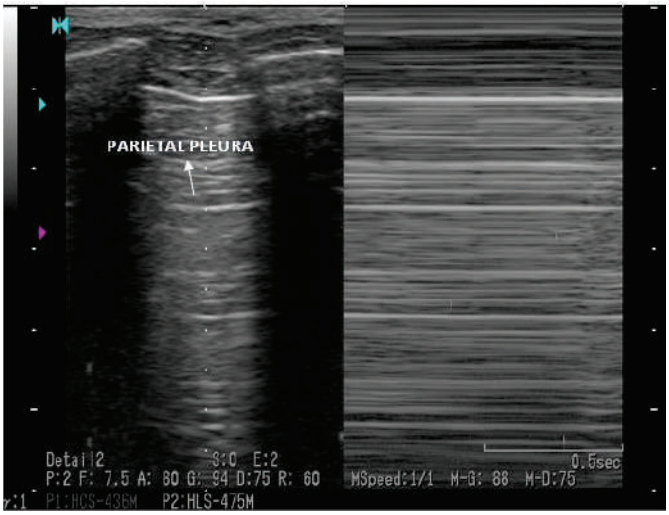

Figure 2: Absent Lung Sliding Sign and Barcode Sign (M-Mode), Pneumothorax Present

Results show lung point sign (right image, arrow) and absent point sign (left image, star) in figure 3.

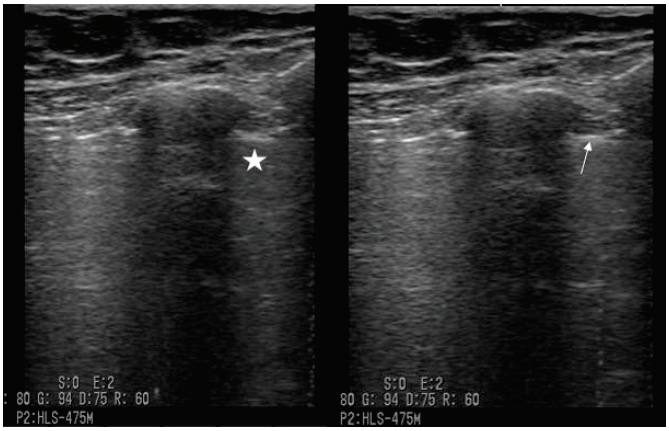

Figure 3: Showing Lung Point Sign (Right Image, Arrow) and Absent Point Sign (Left Image, Star)

A line, Pneumothorax absent is shown in figure 4.

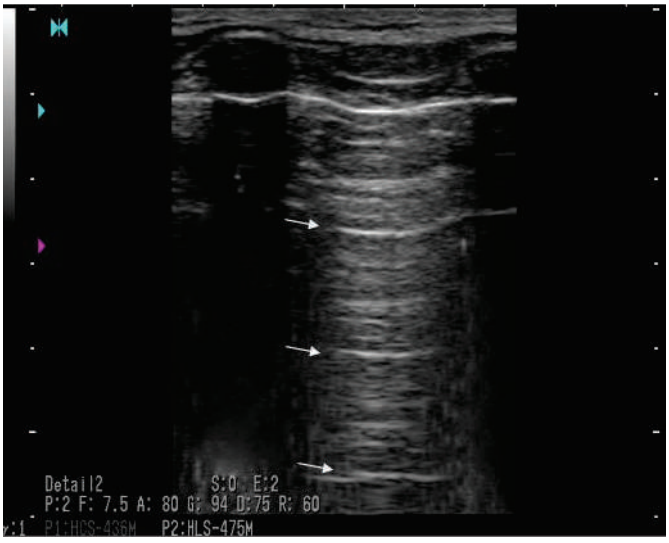

Figure 4: A-Line, Pneumothorax Absent

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CT left-sided pneumothorax is shown in figure 5.

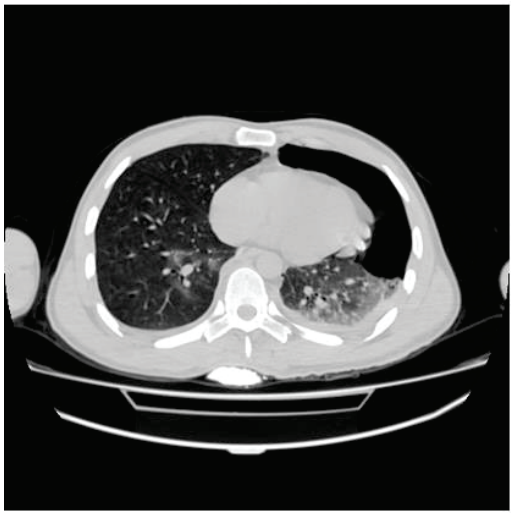

Figure 5: CT, Left-Sided Pneumothorax

Among the cases that tested positive via ultrasonography, 52 were confirmed as true positives, while 3 were identified as false positives. In the ultrasonography-negative group, 31 were confirmed as true negatives, and 4 were classified as false negatives as shown in Table 3.

Table 3: Distribution of Patients as Per Test and Confirmed Diagnosis

Variables	Pneumothorax Present On CT	Pneumothorax Absent On CT	p-value
Pneumothorax Present On USG Scan	52 (TP)*	03 (FP)***	0.0001
Pneumothorax Absent On USG Scan	04 (FN)**	31 (TN)****	

*-TP=True Positive, **-FP=False Positive, ***-FN=False Negative, ****-TN=True Negative

The diagnostic performance of chest ultrasonography in detecting pneumothorax, using CT chest imaging as the gold standard, revealed a sensitivity of 92.85%, specificity of 91.17%, positive predictive value of 94.54%, negative predictive value of 88.57%, and an overall diagnostic accuracy of 92.22% as given in Table 4.

Table 4: Diagnostic Parameters for Ultrasound Technique to Diagnose Pneumothorax

Parameters	Value
Sensitivity	92.8%
Specificity	91.7%
Positive Predictive Value	94.5%
Negative Predictive Value	88.5%
Diagnostic Accuracy	92.2%

DISCUSSION

Ultrasound of the lung is an emerging diagnostic technique for diagnosing pneumothorax in patients with traumatic injury or other causes with fairly decent sensitivity and specificity. It has many advantages over chest radiography and CT scanning it does not use ionizing radiations, is movable, is capable of real-time imaging, and is ideal for repeated tests. Also, it is easily accessible, and the cost is relatively low.Despite of literature supporting the efficiency of chest ultrasound in establishing the diagnosis of pneumothorax, very few studies are reported from Pakistan in this context. The goal of this research work is to establish the diagnostic efficacy of chest ultrasonography in diagnosing pneumothorax using a CT chest as the reference. Ninety patients were included in this study and the ultrasound technique was found to have 92.8% sensitivity and 91.7% specificity to diagnose pneumothorax as compared to chest CT correctly. The positive and negative predictive values were found to be 94.5% and 88.5% respectively, and overall diagnostic power was 92.2%.Several studies done in different countries have demonstrated that the ultrasound method has comparatively high sensitivity and specificity in diagnosing pneumothorax in trauma patients [14]. Similar results were demonstrated in the current study where we reported fairly high sensitivity and specificity of the same method compared with CT as the gold standard. According to Bhoil et al., the sensitivity of the ultrasound method was 89.6% as compared to gold standard chest CT, with higher reported predictive values as well [14]. The results of the current study match with those reported by Staub *et al.*, in a systematic review, identified the role of the ultrasound method in chest trauma including both haemothorax and pneumothorax [15].The author reported sensitivity and specificity of 81% and 98% respectively and overall accuracy of 97.9%.The results reported were slightly different than the current study, a slightly lower value of sensitivity was reported by the authors and the reason can be that they included patients with both pneumothorax and haemothorax in their study whereas we included patients with pneumothorax only.Another systematic review by Netherton et al., reported the pooled estimate specificity and sensitivity of ultrasound to be 69% and 99% respectively for pneumothorax [16]. The sensitivity found in the current study is comparatively higher may be due to the characteristics of the study population and sample size. The study by Abdalla *et al.*, in Egypt, revealed that ultrasound was also found to be more sensitive as compared to chest X-ray with a sensitivity of 86.1% and sensitivity of 52.7% respectively [17]. These results align with the findings and results of our current study. It was concluded by Undziakiewicz *et al.*, that there is a high utility potential of chest ultrasound to diagnose pneumothorax among trauma patients presenting in emergency settings, and the author reported a specificity of 91% and sensitivity of 99% [18]. The results are very similar to what was reported in the current study. A local study conducted in Lahore by Naseem *et al.*, reported that ultrasound can be used to diagnose pneumothorax with specificity of 97.9% and sensitivity of 83.6% as compared to a chest CT scan [19]. These local results are somewhat similar to what we reported because the population dynamics are almost the same within the country. Another local study reported by Imran *et al.*, included 275 cases of tension pneumothorax presenting to the emergency department before cardiac

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arrest. The authors explored the utility of the ultrasound technique to diagnose tension pneumothorax in such patients and reported a sensitivity of 78.2% and specificity of 96.8% [20]. The results might vary from the current study because the authors considered specific cases retrospectively who later on developed cardiac arrest. The current study highlighted the importance of using ultrasound techniques in diagnosing pneumothorax in comparison with a CT scan. Being a non-invasive and cost-effective imaging modality, ultrasonography eliminates the need for ionizing radiation exposure, making it a safer alternative to traditional methods like chest radiography and computed tomography. Similarly, given its wide availability, affordability, and capacity for bedside application, chest ultrasonography proves to be of high importance in emergency settings and in areas with limited access to advanced imaging techniques.This can contribute toward enabling clinicians to make timely and accurate diagnoses and thus improve patient outcomes.

CONCLUSIONS

It was concluded that the diagnostic accuracy of ultrasonography is comparable with the CT scan gold standard. Therefore, it can be utilized to detect pneumothorax in trauma patients presenting in emergency care settings, or in other resource-constraint settings where the availability of CT scans is limited.

Authors Contribution

Conceptualization: NK
Methodology: MHN, NK
Formal analysis: AZ
Writing review and editing: MHN, SBK, RR, BN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Gender Predilection in Post-Graduation among Dental House Officers in a Public Tertiary Care Hospital

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ABSTRACT

Pakistan is characterized as a developing nation with 25000 registered dentists. Confronting issues as the demand and dental needs are rising, so grasping the knowledge for career choices is vital. **Objectives:** To determine the Post-graduate career choices and factors involved in career selection by gender among dental house officers in a public tertiary care hospital. **Methods:** This cross-sectional study was conducted at the Dow University of Health Sciences, Karachi, for six months using a convenient sampling technique by Self-administered questionnaire after consenting from the administration and house officers while maintaining privacy and approval from the Ethical Review Board. A sample size of n=82 was calculated at 50% proportion keeping the confidence limit at 10 using Open Epi Software Version 3.01. House Officers were inducted except those who had a gap of more than one year after graduation. Using SPSS version 28.0, the mean and standard deviation for numerical data were calculated for categorical data. **Results:** There were 11 (13.1%) male and 73 (86.9%) female. Male 10 (90.9%) and female 64 (87.7%) opted for post-graduation. Both genders opted for Oral Surgery and Restorative dentistry. In male, 11 (100%) wanted clinical dentistry while 52 (71.3%) female wanted it, 9 (12.3%) health management, 3 (4.1%) academics, 2(2.7%) business rest were undecided. **Conclusions:** Clinical dentistry and FCPS exams were chosen irrespective of gender and marital status. Among female Oral Surgery and Restorative Dentistry while in males Oral Surgery, Restorative Dentistry and Orthodontics departments were favoured.

INTRODUCTION

Over time dental students' career choices are sprouting. Studies have demonstrated and recommended earlier that factors for career selection among dentists modify by time and among nations, and understanding the current aspirations and perceptions of students is vital for the healthcare system leading to health policies for education and post-graduation [1]. In Karachi, 810 students pass out amongst 13 colleges. Information on dental graduate's inclination towards specialization is still scanty [2]. In many developed countries in the past quarter of the century female gender has considerably increased in the field, especially in Germany, Finland and Turkey where more than half were female [3]. Research in Saudi Arabia that more than half of both genders wanted to continue postgraduate studies [4]. However large dental cohort alone is not an assurance towards high quality dental care system until proficiencies and expertise are attained [5]. Studies in Australia and New Zealand reinforce previous research with this concept that practice and experience an essential step for graduating dental students [6]. In Turkey

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equilibrium is maintained when it comes to specialization among dentists as female opt equally for it [7]. In China, no difference was seen by gender to specialization [8]. Another study in Karachi in private and public institutes showed that intentions to specialize after graduation and choice of specialization are diverse. Cultural factors in the locality affect these choices among graduates [9]. A study in Saudia displayed that in male Endodontics, Prosthodontics and Orthodontics have favoured choices while in female's Restorative Dentistry, Prosthodontics, Orthodontics and Surgery were popular [1]. Persuasion by close family members and less rigid working hours, lower on-call requirements and maintaining work-life balance were some of the major factors considered by female to continue into dentistry [10]. A study in Turkey showed gender differences where 33% of male but 67% of female wanted to continue humanitarian service [7]. Due to the massive number of females in the field who were prospectively viewing their careers based on family life hence adjustable work timings for specialization was another dominant factor quoted by a study in South Africa [11]. It is of supreme significance to recognize what motivates dental students while accelerating their career pathways, which specializations they prefer to choose and their satisfaction with this field [12]. Researching these house officers their assessment, and gender differences professionally is essential for academic palaces and those in policy-making to attenuate the hurdles faced by dentists. This will safeguard the dental cohort and keep them enthused, prepared and stimulated for their career-related endeavors [13]. Less studies have been conducted locally and internationally on future career choices and their determinants [1]. It is superlative to conceive the attitude by gender to propel institutes and policy settings for attenuating barriers among dentists. This will assure a future professional cohort that is equipped to handle health system dynamics [13].

This study aims to assess gender wise career preferences among dental house officers along with their marital status and reasons.

METHODS

A cross-sectional study was conducted for six months from 31 Oct 2023 to 31 Mar 2024. among dental house officers working at Dow University of Health Sciences, Karachi. Approval was taken from the Ethical Review Board with reference no: DME/2023/DCE/G-09761. Prior informed consent was taken from all participants. The principal researcher visited the respective hospital departments after consenting from the administration and arranging time with the participants. Data were collected by utilizing a convenient sampling technique however individuals who were absent and completing house jobs after a gap of more than one year of graduation were excluded along with undergraduates. Both male and female house officers who were graduates only from the respective Public Medical colleges were included in the study. Basic objectives were detailed to the participants and they were assured that privacy will be maintained and how the research will be used. Sample size was calculated at 50% proportion keeping the confidence limit at 10 using Open Epi Software Version 3.01. After taking a 20% dropout rate our total sample size was 82 house officers. The relevant researches were downloaded, consulted and in the light of accepted scientific literature questionnaire was formed. Students rated the factors on a three-point Likert scale; Agree, neutral or disagree. The responses from the participants were entered into a Microsoft Excel worksheet and then coded, cleaned, double-checked and analyzed using SPSS (Statistical Package for Social Sciences) Version 28.0. The normality of the distribution of continuous variables was tested by the Shapiro-Wilk test. Univariate analysis was carried out to present an overview of the findings from the study. Frequency and percentages were used for categorical data. For association chi square was used. p-value less than 0.05 was taken as significant.

RESULTS

Out of the total 84 participants, 11 (13.1%) were male house officers and 73 (86.9%) were female house officers. When seen by marital status 8 (9.5%) were married and 69 (82.2%) were unmarried and 7 (8.3%) were engaged. Among male, 11 (100%) had started searching for programs while among female, 59 (80.8%) had begun while 14 (19.2%) had not. p-value=0.012 Among the married, 4 (50%) had begun searching while the remaining had not, in unmarried 60 (87%) had started it while 9 (13%) had not, in engaged 6 (85.7%) had begun while 1 (14.3%) had not. p-value=0.124. Specialization preference by gender is displayed in Table 1.

Table 1: Postgraduate Specialty Preference by Gender

Variables	Male	Female	p-value
	n (%)		
Special Care Dentistry	1 (9.1%)	4 (5.5%)	0.001
Oral Surgery	6 (54.5%)	37 (50.7%)	0.811
Orthodontics	6 (54.5%)	10 (13.7%)	0.001
Pediatric Dentistry	2 (18.2%)	9 (12.3%)	0.592
Endodontics	5 (45.5%)	19 (26%)	0.184
Periodontics	2 (13.3%)	13 (17.8%)	0.976
Prosthodontics	3 (27.3%)	11 (15.1%)	0.311
Restorative Dentistry	6 (54.5%)	28 (38.4%)	0.308
Dental Public Health	3 (27.3%)	10 (13.7%)	0.246
Oral Medicine	4 (36.4%)	9 (12.3%)	0.040
Oral and Maxillofacial Pathology	3 (27.3%)	12 (16.4%)	0.642
Dental and Maxillofacial Radiology	2 (18.2%)	4 (5.5%)	0.295

When seen by gender with regards to future career side it was seen that among male, 11 (100%) wanted to move to

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Clinical dentistry while none of them chose for Academic side, Health Management, Business or undecided option. Among female, 52 (71.3%) went for clinical dentistry, 9 (12.3%) health management, 2 (2.7%) business, 3 (4.1%) academics and the rest were undecided. p-value=0.481. Among married, 5 (62.5%) wanted Fairfax County Public Schools (FCPS) remainder were taking foreign exams. Among unmarried, 39(56.5%)voted for FCPS, 7(10.1%)were undecided, and 23(33.4%)were attempting foreign exams. In female, 41(56.2%)were willing for hospital jobs, 13(17.8%) in private practice, 10 (13.7%) in government jobs, 8 (11%) NGO and 1 (1.4%) in basic sciences. Reasons for Post-Graduate Specialization by gender have been displayed in Table 2.

Table 2: Reasons for Postgraduate Specialization

Reasons	Male			Female			p-value
	Agree	Neutral	Disagree	Agree	Neutral	Disagree	
	n(%)			n(%)			
Financial	5(45.4%)	3(27.3%)	3(27.3%)	29(39.7%)	25(34.3%)	19(26%)	0.235
Clear in Career	5(45.4%)	3(27.3%)	3(27.3%)	37(50.7%)	28(38.4%)	8(10.9%)	0.363
Advised by Family	4(36.4)	4(36.4%)	3(27.%3)	30(41.1%)	17(23.3%)	26(35.6%)	0.838
Family and Friends Expectations	6(54.5%)	5(45.5%)	0(0%)	32(44%)	23(31.4%)	18(24.6%)	0.064
Work Independence	7(63.6%)	3(27.3%)	1(9.1%)	43(59%)	24(32.8%)	6(8.2%)	0.966
Personal Interest	5(45.5%)	4(36.4%)	2(18.1%)	57(78.1%)	9(12.3%)	7(9.6%)	0.04
For Community	7(63.6%)	4(36.4%)	0(0%)	44(60.2%)	18(24.7%)	11(15.1%)	0.357
Talent in the Field	5(45.5%)	2(18.1%)	4(36.4%)	38(52.1%)	27(37%)	8(10.9%)	0.013
Social Status	6(54.5%)	3(27.3%)	2(18.2%)	34(46.6%)	29(39.7%)	10(13.7%)	0.942
Rewards	6(54.5%)	2(18.2%)	3(27.3%)	34(46.6%)	22(30.1%)	17(23.3%)	0.497
Low Stress	2(18.2%)	2(18.2%)	7(63.6%)	21(28.8%)	22(30.1%)	30(41.1%)	0.202
Flexible work schedule	6(54.6%)	2(18.2%)	3(27.2%)	33(45.2%)	23(31.5%)	17(23.3%)	0.851
Early Settlement	5(45.5%)	3(27.3%)	3(27.3%)	29(39.7%)	28(38.4%)	16(21.9%)	0.207
Job Availability	4(36.4%)	2(18.2%)	5(45.5%)	32(43.8%)	23(31.5%)	18(24.7%)	0.01
Good Opportunities	4(36.4%)	4(36.4%)	3(27.2%)	34(46.6%)	28(38.4%)	11(15%)	0.615

Findings depict the future career preference among married, unmarried and engaged participants. When seen by Marital status in future career preference, results are shown in Figure 1.

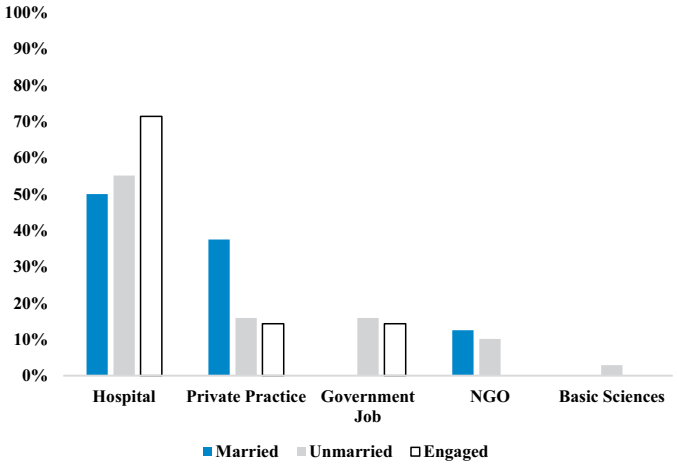

Figure 1: Future Career Preference by Marital Status(%)

When inquired if the rising number of medical colleges is a threat, 11 (100%) male agreed while in female, 50 (68.5%) agreed. The remaining 23 (31.5%) disagreed. p-value=0.05. When investigated regarding continuation immediately post house job, 11(100%) male was affirmative whereas, in female, 67 (91.8%) agreed while 6 (8.2%) negated. p-value=0.324. Regarding the need for career counselling among male, 9 (81.8%) agreed while 2 (18.2%) disagreed. While female, 62 (84.9%) accepted it and 11 (15.1%) did not feel the need for it. p-value=0.790. When assessed if sufficient postgraduate perspectives were present among male, 4 (36.4%) agreed while 7 (63.6%) denied it. In female 22 (30.1%) perceived it while 51 (69.9%) denied it. p-value=0.677. When asked about field saturation, 9 (81.8%) males stated it while 2 (18.2%) gave contrary answers. When seen by marital status among unmarried, merely 2 (2.8%) stated parents will not approve Post-graduation while 67 (97.2%) did not have this issue. Among married, 8 (100%) and engaged 7 (100%) denied any such issue. (p-value=0.979) When inquired if disapproval for post-graduation would come from in-laws, 8 (100%) married and 7 (100%) engaged denied any such issue. (p-value=0.896). The same results among married and engaged were received when husband disapproval was inquired. (p-value=0.954).

DISCUSSION

If the dental workforce is to be managed it needs a thorough understanding of graduating student's perceptions and presumptions about post-graduation, specialization and career as recommended by previous studies [1]. The choice of career in the long term affects the behaviour, outlook, earnings and societal interactions [14]. Specialization selection is significant for the maintenance of dental pools [15]. In our study most participants were female. A study on dental students in Germany, Finland and

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Turkey demonstrated that 55.2% in Germany, 61.5% in Finland, and 69.2% in Turkey were female students [3]. A recent study in Saudia showed that 62% of the participants were female, which demonstrates that female were more likely to opt for this field [16]. The study in Rawalpindi also reflected the same with three-quarters of female participants [17]. However, a study in Trinidad found no connection of gender with post-graduate career selection [11]. This was similar to our research where no statistically significant association was found. Both genders agreed that Post-graduation is a necessity similar findings were seen by marital status. Likewise, most participants irrespective of gender and marital status planned for post-graduation. A study in Turkey stated resembling results with 69% stating post-graduation a necessity [7]. Another research showed a similar ratio of male and female intended to go into a speciality [8]. In our study, both genders mostly preferred Clinical Dentistry. Female, showed a predilection for Health Management and Academics side as well. In both genders, Hospital jobs were most preferred followed by private practice and government jobs. In China study revealed career selection varies among genders [8]. Research in Pakistan demonstrated that in the Public sector, university jobs and research females were more inclined than male in Private practice, defence and Healthcare Management [13]. A study in Turkey showed that 64.1% of male and 69.4% of female intended to work in some institute or hospital or someone else work workplace, whereas 22.9% male and 12.7% female planned to start their clinical practice [7]. In our study male's Oral Surgery, Orthodontics and Restorative surgery while female's Oral surgery, Restorative surgery and endodontics were favoured choices. Simulating findings came from a study in China where among males 63.6% wanted to go for Prosthodontics, 52.3% for Maxillofacial and Oral surgery and 43.2% for Orthodontics. In female 58.6% chose Orthodontics, 56.6% planned for Prosthodontics and 40.7% Periodontics [8]. Another research in Saudia segregated by gender choices that among female 17.8% chose Restorative dentistry, 13.8% chose Orthodontics, Prosthodontics and surgery. Lowest on the list were Oral biology and Radiology. In male, endodontics was favored by 19%, 18.1% Stated Prosthodontics and 14.6% Orthodontics. Oral Biology, public health and Pathology were the lowest on the list [1]. Among male work independence, serving the community and social status were the most quoted reasons for continuation while in female's interest, serving the community and work independence were the most dominant reasons. This was similar to a study where females narrated altruistic reasons more compared to male as the basis for continuation [7]. Further study elicited that a prominent reason for continuation was minimum on-call duty [10]. and family-related obligations [18]. Job security was another factor affecting career choice [11]. In another study in Saudia, patient affiliation was observed in both genders equally, one-third were convinced by close ones and time duration of training, and community benefit were other prominent reasons stated by both genders. Males mentioned more job benefits, salary, adjustable timings and personal skills as compared to female [1]. The majority of female in our study agreed to the influence of a mentor. A recent study in Turkey also found the same that personal liking was the main reason, however, influence by mentors, parents, senior professionals and supervisors was also noted [7]. Another study added an interesting angle where most female 68% wanted to do their work on the same gender whereas 97.7% of male did not show any gender predilection for performing dental procedures [16]. Research at Cornell University pointed that male overrated their working capabilities and female undervalued their performance at work [19]. This is further evidenced when a study displayed that male even with less than standards or requisite criteria went for jobs or promotions and female only did it if they fulfilled all criteria [20]. Our study had an imbalance of gender although the entire batch was inducted. However, this has been an issue in recent studies [18]. Single public tertiary care hospital was included which limits generalizability along with the cross-sectional nature of the survey. To our knowledge, very few studies have been conducted based on gender and marital status when viewing career selection. Data was personally collected by the primary investigator. Perceptions and determinants for future post-graduation will provide information to academicians and policy setters about educational framework, students satisfaction, their plans and requirements [21]. Once factors affecting career decisions are known policy policymakers can fix, carve and develop the essentials for curriculum and training. This will form a conduit among the house officers and the professional arcade [8]. Upgradation of the health system cannot be achieved unless equivalent steps are taken for research, curriculum and education irrespective of gender. Further studies and research need to be done to cover gender prejudices, financial gains, job promotions, specializations, job needs and mentorship available in the market [16]. Studies have suggested that new graduates in dentistry should be observed for a long time as it gives an idea of the working personnel and for future planning [16].

CONCLUSIONS

It was concluded that by gender and marital status most opted for FCPS exam and hospital-based jobs, clinical dentistry while in female health management was also of interest, Oral Surgery and restorative dentistry were opted for by both while Orthodontics by male.

Authors Contribution

Conceptualization: AS, SHD
Methodology: AS, SHD, AKH
Formal analysis: AKH
Writing review and editing: AS, SHD, NF, FP, AM

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Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Outcome of Open Versus Closed Reduction of Unilateral Mandibular Sub-Condylar Fracture

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ABSTRACT

Condylar fractures are among the most common types in the maxillofacial area, yet their optimal treatment approach remains debated. **Objectives:** To compare occlusion and mouth opening between open and closed reduction for unilateral mandibular sub-condylar fractures in adults. **Methods:** This quasi-experimental study was conducted on 68 patients in Jamshoro using a non-probability sampling technique. Patients aged 18–50 years with unilateral non-comminuted sub-condylar fractures within 48 hours and sufficient dentition for fixation were included, while those with bilateral fractures, undisplaced condyles, or other exclusion criteria were excluded. Participants were divided into two groups: Group A underwent closed reduction with maxillomandibular fixation, and Group B underwent open reduction with internal fixation using titanium mini-plates under general anesthesia. Occlusion, range of motion, and mouth opening were evaluated at 3-month follow-ups. **Results:** Pre-operative assessments showed limited mouth opening (15–20 mm) in 97.1% and 100%, poor occlusion in 100%, and poor range of motion in 100% of patients in both groups. Post-operatively, mouth opening improved to 20–30 mm in 8.8% vs. 67.6% and 30–45 mm in 73.5% vs. 85.3%. Good occlusion improved to 58.8%, 88.2%, and 97.1% in Group A vs. 82.4%, 94.1%, and 100% in Group B over 1, 2, and 3 months, respectively. Range of motion also improved, reaching 94.1% vs. 100% by the 3rd month. **Conclusions:** It was concluded that open reduction with internal fixation was a superior therapeutic option compared to closed reduction for unilateral mandibular sub-condylar fractures.

INTRODUCTION

Approximately 35% of mandibular fractures occur worldwide among facial injuries treated by oral and maxillofacial departments [1]. The condyle is the most frequently involved site, followed by fractures of the angle, symphysis, and para-symphysis [2]. Mandibular condyle fractures may present as unilateral or bilateral injuries [3], with common etiological factors including road accidents, falls, firearm injuries, assaults, sports incidents, and industrial mishaps [4]. The distal portion of the condylar process, anatomically referred to as the subcondylar region, is defined superiorly by a line crossing the sigmoid notch and anteriorly by a line obliquely joining the masseter tuberosity to the sigmoid notch. Given its proximity to critical structures such as the temporomandibular joint and facial nerve, fractures in this region have significant clinical implications. Both the fracture itself and the surgical intervention pose risks of functional impairment. If left untreated, subcondylar fractures may lead to serious functional deficits, including limited mouth opening, malocclusion, impaired lateral excursion of the condyle,

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and deviation upon mouth opening [5]. Management of unilateral sub-condylar fractures includes conservative treatment through observation, closed reduction with maxillomandibular fixation, or open reduction and internal fixation [6]. According to a clinical observation, the patient may exhibit minor to severe symptoms, all of which are based on how much the broken pieces have moved. Condylar fractures are uncommon to occur alone and are often linked to fractures in other facial bone locations [7, 8]. A unilateral condylar fracture is characterized by limited mobility, ear haemorrhage, Battle's sign, otorrhea, haematoma around the broken condyle, displacement of the jaw towards the side of the fracture, and edema above the temporomandibular joint [9]. Patients with bilateral condylar fractures may also have limited mobility, occlusion abnormalities, and related symphysis or para-symphysis fractures; as a result, a thorough examination is required (Contre-coupe fracture) [10-12].

This study aims to determine the outcomes of two different techniques, open reduction internal fixation with closed reduction maxillomandibular fixation in unilateral mandibular sub-condylar fracture in terms of occlusion and mouth opening in adult patient.

METHODS

This quasi-experimental study was conducted on 68 subjects at the Oral and Maxillofacial Surgery Department, Institute of Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro from 1-05-2022 to 30-04-2023. Informed written consent was obtained from all patients. The minimum sample size was calculated using the OpenEpi calculator, based on the mean difference in mouth opening after closed reduction maxillomandibular fixation (28.73 ± 2.8 mm) [13] versus open reduction internal fixation (33 ± 2.61 mm) [13] in mandibular sub-condylar fractures. With a 95% confidence interval and 95% power, the total sample size was determined to be 22 (11 in each group). However, to satisfy the assumption of normality, a sample size of 68 (34 per group) was used. Patients from the age group 18-50 years with either gender having unilateral non-comminuted sub-condylar fracture in the last 48 hours and with ample bilateral dentition to permit Maxillomandibular Fixation are included in this study whereas patients with bilateral sub-condylar fracture, undisplaced condyle with normal occlusion, multiple facial injuries, medically incapable or not willing take part in the research in this study were excluded. Ethical approval for this study was granted by the Research Ethics Committee of Liaquat University of Medical and Health Sciences, Jamshoro (LUMHS/REC/-70). All patients were assessed clinically and radiographically using orthopantomography (OPG) and posteroanterior (PA) views. The participants were divided into two groups: Group A, treated with closed reduction and maxillomandibular fixation, and Group B, treated with open reduction and internal fixation. Patients who received treatment were kept nothing per oral six hours before and after surgery. To gain access to the fracture area, sterile surgical blade no. 15 carbon steel was used for a preauricular, submandibular, and retromolar incision. All surgical procedures were performed under general anesthesia with nasopharyngeal route intubation. Local anaesthesia was administered using Xylocaine with 2% adrenaline 1:100,000. Mini-plates (5 holes' titanium mini-plates with 4 screws of the size of 6 mm) were used to repair the fractured bone after the fracture had been reduced for preventing post-pain and reducing the risk of bleeding. The incision was then stitched in two layers using sterile surgical sutures (Vicryl 3-0) and (Prolene 4-0). The wound was then cleaned out with regular saline. The sufferer received a five-day prescription for antibiotics, an analgesic, and mouthwash; after two days, the patient was released. following up to evaluate the functional impacts, such as range of motion and occlusion. In closed reduction with maxillomandibular fixation 1.8 ml cartridges of local anaesthetic, Xylocaine with adrenaline 1:100000 were administered to the fracture site. First, the length of the mandibular and maxillary arches' arch bars was measured using a hook. The arch length in each jaw should ideally start with the first molars. Stainless steel wires (24 or 26 gauge) were used to fasten the arch bar to the mandibular and maxillary facial/buccal cervical levels of the teeth. Crossed intermaxillary wires were employed to provide pre-injury occlusion and fixation when the arch bar was attached. For four to six weeks, the patient's mouth was closed completely. For five days, standard antibiotics with analgesic syrup were provided, and a soft diet was suggested. During maxillomandibular fixation, patients followed a liquid or pureed diet, consuming food through a straw or syringe. For oral hygiene, they used a small, soft-bristled toothbrush and antiseptic mouth rinses to maintain cleanliness. On follow-up for assessment of functional effects and after five weeks of follow-up, the maxillomandibular fixation was removed. Occlusion was recorded as good if there was maximum intercuspation and poor in cases of deviation or open bite. Range of motion was recorded as good if there was a 10 mm protrusion of the mandible and poor in cases of less than 8mm. Mouth opening was measured in millimetres using a ruler, from the upper incisal edges to the lower incisal edges at maximum opening. SPSS-21 was used for data analysis. Frequency and percentage were calculated for qualitative outcomes such as gender, age groups, mouth opening, occlusion, and range of motion at the 1st, 2nd, and 3rd months. A comparison between the two groups (closed reduction and open reduction) was conducted using the

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Chi-square/Fisher's exact test. p≤0.05 was a significant threshold.

RESULTS

The gender and age distribution of participants in the two intervention groups showed no significant differences. Among those undergoing closed reduction, 26 (76.5%) were male, compared to 31 (91.2%) in the open reduction group (p=0.1). Female comprised 8 (23.5%) of the closed reduction group and 3 (8.8%) of the open reduction group. In terms of age, 24 (70.6%) in the closed reduction group and 22 (64.7%) in the open reduction group were aged 18–30 years. Participants aged 31–40 years accounted for 9 (26.5%) in the closed reduction group and 6 (17.6%) in the open reduction group, while those aged 41–50 years were 1 (2.9%) and 6 (17.6%), respectively (p=0.119) (Table 1).

Table 1: Distribution of Demographics in Both Interventions (n=68)

Variables	Characteristics	Closed Reduction	Open Reduction	p-value*
Gender	Male	26 (76.5%)	31 (91.2%)	0.1
	Female	8 (23.5%)	3 (8.8%)	
Age Categories in Years	18 to 30	24 (70.6%)	22 (64.7%)	0.119
	31 to 40	9 (26.5%)	6 (17.6%)	
	41 to 50	1 (2.9%)	6 (17.6%)	

*Chi-square test

Mouth opening between the two interventions at various time points was compared. Pre-operatively, both groups had similar mouth openings, with most participants in both groups (97.1% in closed reduction, 100% in open reduction) having 15–20mm (p=0.31). At 1-month post-surgery, a significant difference was observed (p<0.001), with 91.2% of the closed reduction group at 15–20mm, compared to 67.6% of the open reduction group at 20–30mm. By the 2nd month, both groups showed similar improvement (p=0.31). At 3 months, both groups showed further progress, with no significant difference (p=0.23), as 73.5% of the closed reduction group and 85.3% of the open reduction group had mouth openings of 30–45mm (Table 2).

Table 2: Comparison of Mouth Opening Between Two Interventions at Various Time Points

Time Point	Intervention	Mouth Opening			p-value*
		15–20mm	20–30mm	30–45mm	
Pre-Operative	Closed Reduction	33 (97.1%)	1 (2.9%)	0 (0%)	0.31
	Open Reduction	34 (100%)	0 (0.0%)	0 (0%)	
Post-Operative 1st Month Follow-Up	Closed Reduction	31 (91.2%)	3 (8.8%)	0 (0%)	<0.001
	Open Reduction	11 (32.4%)	23 (67.6%)	0 (0%)	
Post-Operative 2nd Month Follow-Up	Closed Reduction	0 (0%)	34 (100.0%)	0 (0.0%)	0.31
	Open Reduction	0 (0%)	33 (97.1%)	1 (2.9%)	
Post-Operative 3rd Month Follow-Up	Closed Reduction	0 (0%)	9 (26.5%)	25 (73.5%)	0.23
	Open Reduction	0 (0%)	5 (14.7%)	29 (85.3%)	

*Fisher exact test

Occlusion between the two interventions at various time points was compared. Pre-operatively, both groups had poor occlusion (100%). At the 1st-month follow-up, a significant difference was observed (p=0.033), with more patients in the open reduction group showing good occlusion. By the 2nd month, no significant difference was found (p=0.393), with both groups showing similar improvements. In the 3rd month, both groups showed further improvement, with no significant difference (p=0.314) (Table 3).

Table 3: Comparison of Occlusion Between Two Interventions at Various Time Points

Time Point	Intervention	Occlusion		p-value*
		Good	Poor	
Pre-Operative	Closed Reduction	0 (0.0%)	34 (100%)	–
	Open Reduction	0 (0.0%)	34 (100%)	
Post-Operative 1st Month Follow-Up	Closed Reduction	20 (58.8%)	14 (41.2%)	0.033
	Open Reduction	28 (82.4%)	6 (17.6%)	
Post-Operative 2nd Month Follow-Up	Closed Reduction	30 (88.2%)	4 (11.8%)	0.393
	Open Reduction	32 (94.1%)	2 (5.9%)	
Post-Operative 3rd Month Follow-Up	Closed Reduction	33 (97.1%)	1 (2.9%)	0.314
	Open Reduction	34 (100%)	0 (0.0%)	

*Fisher exact test

The range of motion between the two interventions at various time points was compared. Pre-operatively, both groups had poor range of motion (100%). At the 1st-month follow-up, a significant difference was observed (p=0.05), with 73.5% of the open reduction group showing a good range of motion compared to 50% in the closed reduction group. By the 2nd month, no significant difference was found (p=0.07), with both groups showing improvement. At the 3rd-month follow-up, 100% of the open reduction group and 94.1% of the closed reduction group had a good range of motion, with no significant difference (p=0.15) (Table 4).

Table 4: Comparison of Range of Motion Between Two Interventions at Various Time Points

Time Point	Intervention	Range of Motion		p-value
		Good	Poor	
Pre-Operative	Closed Reduction	0 (0.0%)	34 (100%)	–
	Open Reduction	0 (0.0%)	34 (100%)	
Post-Operative 1st Month Follow-Up	Closed Reduction	17 (50.0%)	17 (50.0%)	0.05
	Open Reduction	25 (73.5%)	9 (26.5%)	
Post-Operative 2nd Month Follow-Up	Closed Reduction	24 (70.6%)	10 (29.4%)	0.07
	Open Reduction	30 (88.2%)	4 (11.8%)	
Post-Operative 3rd Month Follow-Up	Closed Reduction	32 (94.1%)	2 (5.9%)	0.15
	Open Reduction	34 (100%)	0 (0.0%)	

*Chi-square/Fisher exact test

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DISCUSSION

Mandibular fractures comprise 57% of all craniofacial fractures, with the condylar region being the most common site, accounting for approximately 18–57% of cases [14, 15]. In this research, male subjects were more in number as compared to female. Likewise, similar studies have also reported higher male patients such as Hassan *et al.*, [17] report 75.0% male and 25.0% female patients, Hakim *et al.*, [18] report 66.67% male and 33.33% female patients and Balouch *et al.*, report 80.0% male and 20.0% female patients [19]. It has been proved through reporting that male patients are mostly affected with unilateral mandibular sub-condylar fracture as compared to female patients. In this study, pre-operative assessment showed similar results in both groups: mouth opening of 15-20 mm in 97.1% of Group A and 100% of Group B, with poor occlusion and range of motion in 100% of patients in both groups. All similar studies report the deviation from standards in pre-operative assessment after unilateral mandibular sub-condylar fracture [16, 17]. Patel *et al.*, reported similar issues, with a mean mouth opening of 26.6 mm (range: 24–30 mm) in their closed treatment group and 22.66 mm (range: 21–25 mm) in the open reduction group [20]. Hassan *et al.*, also found occlusal disturbances and restricted mandibular movement in condylar fractures [16]. In this study, postoperative assessment shows notable variation between both groups at first-month follow-up, whereas no notable variation between both groups at second and third-month follow-up. Open reduction shows better outcomes at first-month follow-up in terms of mouth opening, occlusion and range of motion as compared to closed reduction. Hakim *et al.*, reported a significant difference between maximal mouth opening, lower extremity functional scale, lateral excursion on the non-fractured side, pain and anatomical reduction in both groups [18]. Patel *et al.*, reported a better but non-significant difference between interincisal opening, mouth opening, occlusion, facial nerve function, and ramus height among both groups [20]. Balouch *et al.*, reported a significant difference between the adequacy of mouth opening at the third and sixth months of follow-up in Group A and Group B [19].

CONCLUSIONS

It was concluded that open reduction with internal fixation is a superior therapeutic option for managing unilateral mandibular sub-condylar fractures compared to closed reduction with maxillomandibular fixation. Patients in the open reduction group demonstrated better outcomes in terms of occlusion, range of motion, and mouth opening at 3-month follow-ups.

Authors Contribution

Conceptualization: SK
Methodology: SK
Formal analysis: MS, MAC
Writing review and editing: AH, AS, AA, MAC

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Association Between Hypertensive Disorder in Pregnancy and Postpartum Depression

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ABSTRACT

Gestational hypertension, preeclampsia, and eclampsia are suspected of spontaneously developing and being particularly critical for maternal and infant health. New research indicates that these disorders may also elevate the probability of developing Postpartum Depression (PPD), which remains one of the serious mental health challenges in new mothers. **Objective:** To evaluate the prevalence of PPD in women with hypertensive disorders during pregnancy and to examine further the association of PPD with hypertensive disorders of pregnancy. **Methods:** This comparative cross-sectional study was conducted at the Obstetrics and Gynaecology Department, LMH, Kohat. A total of 155 postnatal women between the ages of 15 and 40 between 2-6 weeks postpartum were included. PPD was evaluated using the Urdu translation of Edinburgh Postnatal Depression Scale (EPDS), with depression indicated by scores >10. SPSS version 25 for statistical analysis, Chi-square tests ($p < 0.05$) were performed. **Results:** Women suffering from hypertensive disorders showed significantly higher EPDS scores (mean value of 11.85 ± 3.00) in comparison to those of normotensive women (mean value of 8.71 ± 2.03, $p = 0.001$). Emotional neglect ($p = 0.001$) and previous depression ($p = 0.001$) as risk factors were significantly related to PPD. Hypertensive pregnancies were also linked to adverse neonatal outcomes, including lower birth weights ($p = 0.001$) and increased neonatal admissions ($p = 0.001$). **Conclusions:** Hypertensive disorders in pregnancy significantly increase the risk of PPD. Integrating mental health support into prenatal and postnatal care for hypertensive women may improve maternal psychological well-being and neonatal health outcomes.

INTRODUCTION

Pregnancy induces significant physiological and psychological changes. Many complications can result in hypertensive disorders which are dangerous to the health of both the mother and the fetus. Among the many challenges in maternal care that exist throughout the world, hypertensive disorders during pregnancy, including gestational hypertension, preeclampsia and eclampsia remain most often linked with negative outcomes for the mother and the fetus [1]. However, little attention has been paid to the mental health effects of these hypertensive disorders in the postpartum period, especially those related to PPD [2, 3]. PPD is one of the most widespread mental health conditions that affects women within twelve months after delivery [4]. Together, these factors impede a mother's ability to care for herself and her infant, as she may experience prolonged feelings of sadness, anxiousness, and fatigue. Studies indicated that 15% of women are possibly affected, indicating that PPD is considered comparatively common in certain populations [5, 6]. A combination of hormonal changes, family history, psychological stressors, and sociocultural factors can contribute to PPD. Complications of pregnancy, including hypertensive disorders, are linked to higher risks of Postpartum Depression (PPD) [7]. Such emotional disorders are often associated with other psychosomatic disorders like placental abruption and fetal growth restriction, along with more severe ones like preterm birth. Collectively, these pose a greater physical, emotional and psychological burden on women suffering from these disorders [8]. There is a notable increase in the risk of

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developing PPD after childbirth in women suffering from hypertension and pregnancy complications. These forms of hypertension have been linked to several complications including placental abruption, fetal growth restriction and preterm birth which adds severe emotional and psychological stress to the burdened women. In PPD, stress and anxiety management during pregnancy is shown in research to contribute to the development of hypertension causing depression after childbirth [9]. Pregnancy related hypertension and systemic inflammation as well as oxidative stress accompanying it could establish a link between PPD and hypertension. The link between hypertensive disorders and PPD is still unclear, especially with some research indicating that the management of stress and anxiety during pregnancy can lead to hypertension, which then aids in the manifestation of depressive tendencies postpartum. In addition, It has been suggested that systemic inflammation and oxidative stress that often accompany pregnancy hypertension may contribute to linking hypertension with PPD. Despite growing evidence, the association between various hypertensive disorders and PPD risk remain unclear. This research examines the prevalence of PPD in pregnant women with hypertensive disorders and compares these findings with normotensive pregnant women to fill the existing knowledge gap. The primary objective of this study is to evaluate the prevalence and correlation of hypertensive disorders during pregnancy with the onset of PPD. This research investigates how psychological and social stressors combined with a lack of emotional support and a history of mental health problems raise the PPD risk for women who have hypertension.

The research evaluated how hypertensive disorders affect neonatal outcomes such as birth weight and neonatal hospital admissions while examining their influence on maternal mental health.

METHODS

The comparative cross-sectional study was conducted at the LMH Kohat obstetrics and gynaecology department over a period of three months. The aim of the study was to determine the incidence of PPD in women suffering from hypertensive disorders in pregnancy and its relationship with the neonatal outcomes. Employing the WHO software, the sample size has been estimated with 95% confidence level, and expecting proportion of PPD among women with hypertensive disorders to be 27%, and absolute precision set at 7%, resulting in a total sample size of 155 participants [10]. The recruitment of participants was achieved using a non-probability sampling and consecutive sampling strategy. This strategy is suited to a clinical context and permits comprehensive participation of all appropriate patients during the specified time period. Inclusion of participants was done in a systematic manner, reducing selection bias while remaining simplistic in a hospital-based environment. The study was granted approval by two ethical review boards: The College of Physicians and Surgeons Pakistan (CPSP), Reference No: CPSP/REU/OBG-2021-303-10565. This study was conducted according to the ethical standards of the National Bioethics Committee (NBC) in Pakistan regarding human subject's participation. All provided their written informed consent to participate in the study and their anonymity was preserved. Women who were diagnosed with PPD were referred for therapy. The study included women aged 15 to 40 years who were 2–6 weeks postpartum and had hypertensive disorders during pregnancy (gestational hypertension, preeclampsia, or eclampsia). The study excluded women with obstetric complications diabetes, epilepsy, or psychiatric illnesses before or during pregnancy. Women who delivered babies with congenital malformations, experienced stillbirth, or perinatal death. To minimize confounding variables, the study considered: Socioeconomic status, education level, age, and prior mental health history. Stratified analyses for variables like mode of delivery, neonatal admission, and birth weight to assess their independent impact on PPD. Exclusion of participants with known psychiatric disorders or unrelated obstetric complications. Chi-square tests and stratified subgroup analyses were performed to control confounders during statistical analysis. Data were collected via face-to-face interviews using a pre-designed questionnaire to document demographic details (age, residence, education, profession, and socioeconomic status). PPD was assessed using the Urdu version of the Edinburgh Postnatal Depression Scale (EPDS), where a score of >10 indicated depressions. This threshold aligns with validated cut-offs for PPD screening. Data were entered and analysed using IBM SPSS version 25. Quantitative variables (age, baby birth weight, depression score, BMI, haemoglobin levels) were tested for normality using the Kolmogorov-Smirnov test. Mean ± Standard Deviation (SD) was used for normally distributed variables, while median (IQR) was applied for skewed data. Categorical variables (marital status, education, hypertensive disorder type, neonatal admissions, EPDS scores) were expressed as frequencies and percentages. The association between hypertensive disorders and PPD was analysed using the Chi-square test or Fisher's exact test, with a p-value <0.05 considered statistically significant. The study divided participants into two groups based on their hypertensive status during pregnancy: women diagnosed with gestational hypertension, preeclampsia, or eclampsia were categorized as the hypertensive group, while those with normal blood pressure throughout pregnancy formed the normotensive group. This division aimed to assess the association between hypertensive disorders and the prevalence of

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postpartum depression (PPD) as well as adverse neonatal outcomes. The logic behind this grouping was to determine whether hypertensive pregnancies contribute to a higher risk of PPD, measured using the Edinburgh Postnatal Depression Scale (EPDS), and poor neonatal health, including low birth weight and increased neonatal admissions. By employing statistical analyses such as the Chi-square test and stratified subgroup analyses, the study ensured that confounding factors—such as socioeconomic status, education level, and prior mental health history—were accounted for. This structured comparison allowed for a clearer understanding of the psychological and neonatal risks associated with hypertensive disorders in pregnancy.

RESULTS

The study analysed 155 postpartum women, of whom 84 (54.2%) had hypertensive disorders during pregnancy, while 71 (45.8%) were normotensive. The demographic, clinical, psychological, and neonatal outcomes are detailed below. Table 1 presented the demographic and clinical characteristics of the participants. Women in the hypertensive group were significantly older, mean age = 35.12 ± 4.59 years compared to the normotensive group, mean = 30.51 ± 3.88 years, p = 0.001. They also had higher BMI levels, 30.04 ± 4.58 versus 25.17 ± 3.63, p = 0.001 and lower haemoglobin levels, 9.92 ± 1.5 versus 12.07 ± 0.93, p = 0.001.

Table 1: Demographic and Clinical Characteristics (n=155)

Variables	Hypertensive Group Mean ± SD/ Frequency (%)	Non-Hypertensive Group Mean ± SD/ Frequency (%)	p-value
Age (Years)	35.12 ± 4.59	30.51±3.88	0.001
Education			
Illiterate	27	17	0.427
Matriculate	27	25	
Graduate	23	18	
postgraduate	7	11	
Socioeconomic Status			
Poor (<20,000)	23	20	0.256
Lower (20,000 -50,000)	22	18	
Middle (60,000-80,000)	30	18	
Upper (>80,000)	9	15	
Marital Status			
currently Living with Spouse	67	63	0.09
Separated	14	4	
Widow	3	4	
Occupation			
Housewife	57	40	0.14
Employed	27	31	
Joint Family			
No	38	40	0.16
Yes	46	31	
Joint Family			
Gestational Hypertension,	42	0	0.001
Preeclampsia,	35	0	
N/A	0	71	
Eclampsia	7	0	
BMI	30.04 ± 4.58	25.17 ±3.63	0.001
Blood Pressure	150.28 ± 10.22	119.83 ± 5.35	0.001
Haemoglobin Level	9.92 ±1.5	12.07 ± 0.93	0.001
Depression Score	11.85 ±3.00	8.71 ±2.03	0.001

Table 2 highlighted the psychological and obstetric risk factors. PPD was significantly more prevalent among women with hypertensive disorders, with 59.5% of hypertensive women (50 out of 84) having an EPDS score ≥10, compared to 25.3% (18 out of 71) in the normotensive group (p = 0.001). Lack of emotional support (p = 0.001), history of depression (p = 0.001), and experience of domestic violence (p = 0.001) were significantly associated with PPD. Uneducated spouses and financial difficulties were also more common in the hypertensive group (p = 0.009 and p = 0.035, respectively).

Table 2: Psychological and Obstetrical Risk Factors (n=155)

Variables	Hypertensive Group Frequency (%)	Non-Hypertensive Group Frequency (%)	p-value
Unemployed Husband			
No	52	53	0.09
Yes	32	18	
Uneducated Husband			
No	38	47	0.009
Yes	46	24	
Husband with Psychiatric History			
No	63	63	0.029
Yes	21	8	
Lack of Emotional Support			
No	45	58	0.001
Yes	39	13	
Previous History of Depression			
No	54	62	0.001
Yes	30	9	
Dissatisfaction with Support			
No	54	53	0.164
Yes	30	18	
Domestic Violence			
No	53	65	0.001
Yes	31	6	
Financial Issues			
No	44	49	0.035
Yes	40	22	

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Dissatisfaction with Living Conditions			
No	51	61	0.001
Yes	33	10	
Stressful Life Events			
No	36	54	0.001
Yes	48	17	
Previous Loss of Baby			
No	71	65	0.18
Yes	13	6	
Chronic Disease History			
No	52	53	0.09
Yes	32	18	
History of Hypertension in Previous Pregnancy			
No	42	50	0.01
Yes	42	21	
Negative Attitude towards Pregnancy			
No	52	52	0.13
Yes	32	19	
Negative Attitude towards Mother Role			
No	50	47	0.39
Yes	34	24	
Lack of Childcare Knowledge			
No	43	54	0.001
Yes	41	17	
Absence of Breastfeeding			
No	55	56	0.65
Yes	29	15	

As shown in Table 3 neonates born to hypertensive mothers had lower birth weights, with 55% weighing <2.5 kg compared to 25% in the normotensive group (p = 0.001). Neonatal admissions were significantly higher in the hypertensive group (41% vs. 15%, p = 0.001). Operative delivery rates were also higher among hypertensive mothers (p = 0.002).

Table 3: Delivery and Neonatal Outcomes (n=155)

Variables	Hypertensive Group	Non-Hypertensive Group	p-value
Mode of Delivery			
NVD	43	12	0.002
Instrumental Delivery	26	55	
Operative	15	4	
Baby Gender			
Male	41	33	0.77
Female	43	38	
Neonatal Admission			
None	26	49	0.001
<7 Days	41	15	
>7 Days	17	7	
Birth Weight			
<2.5Kg	55	25	0.001
>2.5Kg	29	46	
EPDS Score			
<10	34	53	0.001
≥10	50	18	

Women with hypertensive disorders had significantly higher mean EPDS scores (11.85 ± 3.00) than normotensive women (8.71 ± 2.03, p = 0.001). Chi-square analysis confirmed a significant association between hypertensive disorders and PPD (p < 0.05). Stratified analysis showed that the risk of PPD remained significant even after adjusting for confounding factors such as mode of delivery, neonatal admission, and birth weight. The elevated prevalence of PPD among hypertensive women can be attributed to both physical and psychosocial stressors, complications during delivery, lack of emotional support, and adverse neonatal outcomes. The increased rates of neonatal admissions and low birth weight in hypertensive pregnancies likely add further stress, compounding maternal mental health challenges. These findings emphasise the need for comprehensive care that addresses both medical and psychological aspects in women with hypertensive disorders. Figure 1 showed that a higher proportion of hypertensive women had elevated depression scores (≥10) compared to the normotensive group.

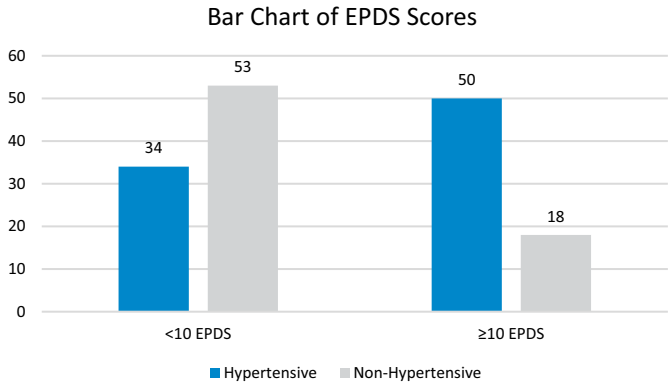

Figure 1: Illustrates the EPDS Score Distribution

DISCUSSION

This study highlighted the strong association between hypertensive disorders during pregnancy and an increased risk of PPD. These findings align with prior research suggesting that both physical complications and psychosocial stressors associated with hypertensive pregnancies contribute to heightened mental health risks [11, 12]. Women with hypertensive disorders had significantly higher EPDS scores (mean = 11.85 ± 3.00) than normotensive women (8.71 ± 2.03, p = 0.001), confirming a higher prevalence of PPD among hypertensive mothers. This association persisted even after adjusting for confounders such as socioeconomic status, mode of delivery, and neonatal admissions. The findings suggest that hypertensive conditions not only increase physical risks but also elevate psychological distress in postpartum women. The biological mechanisms linking hypertensive disorders and PPD remain an area of growing research. Several studies suggest that systemic inflammation,

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oxidative stress, and neuroendocrine dysregulation in hypertensive pregnancies may contribute to the onset of depressive symptoms. Elevated levels of pro-inflammatory cytokines such as interleukin-6 and tumour necrosis factor-alpha (TNF-α) have been associated with both hypertensive disorders and mood disturbances, providing a potential biological explanation for the observed link between hypertension and PPD [13, 14]. These results were consistent with previous studies emphasizing the strong correlation between hypertensive disorders and maternal mental health conditions [15]. The investigation of Rocha de Moura MD *et al.*, in 2021 documented that women suffering from preeclampsia had an almost twofold risk of encountering PPD compared to normotensive women, which aligns with these findings. Also, other studies by Lin YW *et al.*, in 2021 focused on the contribution of chronic stress during hypertensive pregnancies toward maternal depression [16, 17]. Alongside biological aspects, psychosocial stress was another important factor that explains the high prevalence of PPD in hypertensive mothers in this study. The lack of emotional support (p=0.001), financial challenges (p=0.035), and domestic violence (p=0.001) were linked to higher scores for EPDS. Mothers with complicated pregnancies, prolonged hospitalizations, and Neonatal Intensive Care Unit (NICU) admissions for their newborns showed a lot of anxiety and emotional distress. Such findings suggest that combined medical psychological and social support systems would be necessary in reducing the risk of PPD for women with high blood pressure complications. Similarly, this study found that babies born to hypertensive mothers were at greater risk of negative outcomes as they were more likely to be born underweight (<2.5 kg in 55% versus 25% of the normotensive group; p = 0.001) and need to be admitted to the neonatal unit (41% versus 15%; p = 0.001). These adverse neonatal outcomes add further emotional and psychological burdens on new mothers, increasing susceptibility to PPD.Previous research supports this association, as mothers of preterm or low-birth-weight infants experience heightened postpartum stress and depressive symptoms [18, 19]. This underscores the need for targeted postpartum interventions addressing both maternal mental health and neonatal well-being [20]. Despite these significant findings, this study has certain limitations: The use of a cross-sectional design prevents causal inference. Future longitudinal studies are needed to establish causality between hypertensive disorders and PPD. Non-probability consecutive sampling limits generalizability, as participants were selected from a single hospital setting. A larger, multi-center study would enhance external validity. Potential residual confounding remains, despite these efforts to adjust for key variables such as socioeconomic status and previous depression history. Future studies should explore the biological mechanisms linking hypertensive disorders and depression, focusing on inflammatory pathways, neuroendocrine dysregulation, and oxidative stress. Longitudinal analyses tracking PPD development over time in women with pregnancy-related hypertensive conditions. The effectiveness of integrated care models combining hypertensive disorder management with early mental health interventions.These findings highlighted the importance of integrating mental health screening into routine prenatal and postnatal care for hypertensive women. Healthcare providers should: Implement early PPD screening in hypertensive pregnancies to ensure timely psychological support. Address social determinants of maternal mental health, such as domestic violence, lack of emotional support, and financial strain.Encourage a multidisciplinary approach involving obstetricians, psychiatrists, and neonatologists to provide holistic care.

CONCLUSIONS

The research showed that women suffering from hypertensive complications throughout pregnancy were more likely to develop PPD. Particularly, women with severe hypertensive disorders such as preeclampsia and eclampsia were at risk of developing PPD. The findings emphasized the need for early identification and management of hypertensive disorders, not only to mitigate physical complications but also to reduce the risk of postpartum mental health issues. Improved outcomes can be attained for both mothers and children by integrating mental health checks and support in routine prenatal and postnatal care for women with hypertensive disorders.

Authors Contribution

Conceptualization: N
Methodology: RM, FB, NM, N
Formal analysis: FG, NM, NH
Writing, review and editing: FG, NM, NH, RM
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Maternal and Neonatal Health Outcomes in Placenta Accreta: Short-Term Morbidity and Long-Term Neurodevelopmental Impacts

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ABSTRACT

Placenta accreta (PA) is a serious maternal complication defined by abnormal attachment of the placental trophoblastic tissue to the myometrial wall of the uterus. **Objectives:** To evaluate the effect of placenta accreta on maternal morbidity and neonatal health outcomes, with an emphasis on long-term neurodevelopmental effects. **Methods:** This retrospective study was conducted at Social Security Teaching Hospital, Lahore, from October 2022 to March 2023. A total of 231 patient data was gathered for the study, comprising 77 infants delivered after third-trimester bleeding due to placenta accreta and 154 gestational age-matched controls. The maternal outcomes assessed included rates of postpartum hemorrhage, cesarean section, and peripartum hysterectomy. Neonatal outcomes were evaluated by Apgar scores, the incidence of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), and hypoglycemia. Long-term neurodevelopmental outcomes, including cerebral palsy (CP) and minor neurodevelopmental abnormalities, were followed up at 2 years. Statistical analyses were conducted using one-way ANOVA and Chi-square test using SPSS-26. **Results:** Infants born to mothers with PA had lower Apgar scores at 1 minute (24.7% vs. 5.2% in controls; adjusted OR-5.67), higher rates of RDS (40.3% vs. 7.8%; adjusted OR-7.42), and severe IVH (11.7% vs. 1.9%; adjusted OR-6.30). Hypoglycemia occurred in 18.2% of the PA group compared to 3.2% in controls (adjusted OR-6.41). At 24 months, 7.8% of infants with PA had cerebral palsy (adjusted OR-13.5) and 6.5% had severe developmental delays (adjusted OR-10.4). **Conclusions:** It was concluded that PA is a serious risk factor for maternal and neonatal morbidity and long-term neurodevelopmental impairment.

INTRODUCTION

The abnormally invasive placenta, often referred to as morbidly adherent placenta or placenta accreta (PA), is characterized by the invasion of trophoblast tissue into the myometrial tissue of the uterus. The rising incidence of PA is closely linked to the increased rate of cesarean births globally [1]. However, PA can also develop in the absence of prior uterine scars [2]. Massive intraoperative hemorrhages associated with placenta accreta can lead to hypovolemic shock, severe coagulopathy, and a significant rise in Intensive Care Unit (ICU) admissions following cesarean deliveries [3]. Consequently, managing morbidly adherent placenta presents ongoing challenges for obstetricians and gynecologists, resulting in increased maternal-fetal morbidity and mortality [4]. Proper management, involving multidisciplinary care teams and antenatal interventions, aims to improve maternal and neonatal outcomes, especially in low- and middle-income countries where healthcare resources may be limited [5]. Despite these efforts, PA is associated with several life-threatening complications. Pregnancy termination is frequently recommended in cases of unusual placental invasion up to the middle of the second trimester [6].

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Planned deliveries between 34 and 36 weeks of gestation have been linked to improved maternal outcomes following PA [7]. It is generally advised against extending pregnancies beyond 36 weeks due to the risk of emergency cesarean births arising from severe hemorrhage in approximately 50% of women with PA after this gestational age [6]. Notably, pregnancies complicated by PA are not associated with fetal growth restriction, as supported by various studies [5]. Furthermore, poor neonatal outcomes in emergency deliveries may result from a lack of corticosteroids for fetal lung maturation [8]. Recent findings by Del *et al.*, indicate that cesarean operations for PA are significantly associated with lower ≤5-min APGAR scores, reduced birth weights, and increased instances of preterm delivery compared to non-PA cesarean sections [9]. Given these complexities, it is crucial to diagnose PA before delivery. When deliveries occur at specialized hospitals with skilled obstetricians before the onset of labor, catastrophic hemorrhages and placental disruptions can be minimized, thereby maximizing maternal-fetal outcomes [10]. However, there was a notable gap in knowledge regarding the long-term neurodevelopmental outcomes of infants born to mothers with PA, despite evidence linking PA with immediate complications in high-risk pregnancies.

This study aims to examine the neurodevelopmental trajectories of infants born to mothers with PA at Social Security Teaching Hospital.

METHODS

This retrospective study was conducted at Social Security Teaching Hospital, Lahore, over six months from October 2022 to March 2023. The study aimed to analyzed short-term maternal and neonatal morbidity (postpartum haemorrhage, caesarean section, peripartum hysterectomy, neonatal respiratory distress syndrome, intraventricular haemorrhage, and hypoglycaemia) and long-term neurodevelopmental outcomes (cerebral palsy and minor neurodevelopmental abnormalities assessed at 2 years of age) in infants born to mothers with placenta accreta compared to those without the condition. Ethical approval was obtained from the Institutional Review Board, Social Security Teaching Hospital, Lahore (Reference number: 15/2022). The sample size was calculated using Open Epi version 3.01, considering postpartum hemorrhage as the primary outcome variable, based on a reported incidence of 41% in placenta accreta cases versus 5% in controls by taking 95% confidence interval and 5% level of significance [11]. The calculated sample size was too small so to increase sample size to 231 pregnant female among which 77 cases of placenta accreta (PA group) and 154 gestational age-matched controls (control group). Medical records of 231 pregnant women aged 18 to 45 years, who delivered between May, 2020, and October, 2020, were reviewed. A written informed consent was taken from each participant. The retrospective design was chosen because the required data were already available in hospital records, facilitating the identification of cases and controls. The study included all available patients meeting the inclusion and exclusion criteria during the specified timeframe. Inclusion criteria included pregnant women with complete medical records, follow-up of infants for 24 months, and gestational ages of 32 weeks or more at the time of delivery. Exclusion criteria included multiple gestations, incomplete records, pre-existing maternal conditions (e.g., preeclampsia, uncontrolled diabetes), congenital anomalies in infants, preterm deliveries before 32 weeks, and lack of follow-up care at the hospital. The control group consisted of 154 gestational age-matched controls, selected based on having delivered in the same timeframe but without placenta accreta. Controls were selected from their medical records available to match cases by gestational age within two weeks and had no history of third-trimester bleeding or placenta accreta. Characteristics of the control group were similar to the PA group regarding maternal age, parity, and antenatal care, ensuring comparability for outcome analysis. Adequate antenatal care was defined as having received at least four scheduled antenatal visits during the pregnancy, with proper routine screenings, including blood pressure, hemoglobin and blood sugar level monitoring. The patients with missing or incomplete medical history were excluded. Maternal outcomes assessed included rates of postpartum hemorrhage, cesarean section, and peripartum hysterectomy. Neonatal outcomes included Apgar scores, the incidence of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), and hypoglycemia. Long-term neurodevelopmental outcomes were assessed at 2 years, including cerebral palsy (CP) and minor neurodevelopmental abnormalities. Neurological assessments were performed at discharge and follow-up visits at 3, 6, 12, and 24 months. Cognitive development was measured using the Bayley Scales of Infant Development (Mental Development Index)[12]. The Bayley Scales assess cognitive, language, and motor development, with scores ranging from 49 to 155, where a score below 85 indicates developmental delay, 85–100 is considered low average, and above 100 is normal development. Statistical analyses were conducted using SPSS version 26.0. Descriptive statistics (mean ± SD for continuous variables and frequencies/percentages for categorical variables) were used to summarize baseline characteristics. Continuous variables were compared between groups using the independent t-test, while categorical variables were analyzed using the Chi-square test. Crude and adjusted

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odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for maternal and neonatal outcomes using logistic regression models to control for potential confounders. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 231 women, with 77 cases of placenta accreta (PA group) and 154 gestational age-matched controls (control group). The average age of the women in the PA group was 32.4 ± 4.8 years, compared to 31.9 ± 5.2 years in the control group. Most women in both groups had received adequate antenatal care. There were no significant differences in gestational age at delivery, which ranged from 32 to 40 weeks across both groups (Table 1).

Table 1: Basic Characteristics of Women in the Study

Characteristics	PA Group (n=77)	Control Group (n=154)
Age (years)	32.4 ± 4.8	31.9 ± 5.2
Gestational Age at Delivery (Weeks)	36.3 ± 1.8	36.7 ± 2.1
Adequate Antenatal Care	Yes	

Postpartum hemorrhage occurred in 58.4% of women in the PA group compared to just 14.3% in the control group. This suggests that women with placenta accreta are about 8 times more likely to experience severe bleeding after childbirth (OR-8.01), even after accounting for other factors (adjusted OR 7.65). A similar trend was seen in the case of Cesarean section rates and Peripartum hysterectomies (Table 2).

Table 2: Effect of Placenta Accreta on Maternal Morbidity

Maternal Outcome	PA Group (n=77)	Control Group (n=154)	Crude OR (95% CI)	p-value (Crude OR)	Adjusted OR (95% CI)	p-value (Adjusted OR)
Postpartum Hemorrhage	45 (58.4%)	22 (14.3%)	8.01 (4.4–14.6)*	<0.001	7.65 (4.2–13.9)*	<0.001
Caesarean Section	66 (85.7%)	79 (51.3%)	5.28 (2.8–10.0)*	<0.001	5.10 (2.7–9.8)*	<0.001
Peripartum Hysterectomy	12 (15.6%)	2 (1.3%)	14.7 (3.2–67.4)*	<0.001	13.9 (3.1–63.8)*	<0.001

All crude and adjusted odds ratios presented above are statistically significant at p<0.05. *means that the results are statistically significant.

Apgar scores at 1 minute were significantly lower in the PA group, with 24.7% of infants having a score of less than 7, compared to just 5.2% in the control group. Hypoglycemia was also associated with PA, it was observed in 18.2% of infants in the PA group, in contrast to only 3.2% in the control group. Infants born to mothers with placenta accreta were about 6 times more likely to develop hypoglycemia (adjusted OR 6.41), which can lead to serious complications if not managed. This means that infants born to mothers with placenta accreta are about 6 times more likely to have lower Apgar scores at birth (adjusted OR 5.67), indicating poor initial health status. RDS and IVH were much more common in the PA group when compared with the control group (Table 3).

Table 3: Effect of Placenta Accreta on Neonatal Outcomes

Neonatal Outcome	PA Group (n=77)	Control Group (n=154)	Crude OR (95% CI)	p-value (Crude OR)	Adjusted OR (95% CI)	p-value (Adjusted OR)
Apgar Score <7 at 1 Minute	19 (24.7%)	8 (5.2%)	5.89 (2.5–13.9)*	<0.001	5.67 (2.4–13.5)*	<0.001
Respiratory Distress Syndrome (RDS)	31 (40.3%)	12 (7.8%)	7.83 (3.8–16.2)*	<0.001	7.42 (3.6–15.5)*	<0.001
Intraventricular Hemorrhage (IVH)	9 (11.7%)	3 (1.9%)	6.86 (1.8–26.5)*	0.005	6.30 (1.6–24.4)*	0.008
Hypoglycemia	14 (18.2%)	5 (3.2%)	6.85 (2.4–19.1)*	0.002	6.41 (2.2–18.4)*	0.003

All crude and adjusted odds ratios presented above are statistically significant at p<0.05. *means that the results are statistically significant.

At 24 months of age, Cerebral palsy (CP) was diagnosed in 7.8% of infants in the PA group, in comparison to just 0.6% in control having adjusted OR (CI) as 5.67 (2.4–13.5). For the Bayley Mental Index, which measures cognitive development, 6.5% of infants in the PA group had a score below 71, indicating severe developmental delay. In contrast, only 0.6% of infants in the control group showed this level of delay. Additionally, 11.7% of infants in the PA group had borderline cognitive development, with Bayley Mental Index scores between 71 and 84, compared to just 1.3% in the control group (Table 4).

Table 4: Effect of Placenta Accreta on Long-Term Neurodevelopmental Outcomes

Neurodevelopmental Outcome	PA Group (n=77)	Control Group (n=154)	Crude OR (95% CI)	p-value (Crude OR)	Adjusted OR (95% CI)	p-value (Adjusted OR)
Cerebral Palsy (CP)	6 (7.8%)	1 (0.6%)	14.1 (1.7–116.0)*	0.012	13.5 (1.6–110.3)*	0.015
Bayley Mental Index < 71 (severe delay)	5 (6.5%)	1 (0.6%)	11.1 (1.3–91.3)*	0.018	10.4 (1.2–87.5)*	0.021
Bayley Mental Index 71–84 (borderline)	9 (11.7%)	2 (1.3%)	10.3 (2.2–48.1)*	<0.001	9.87 (2.1–45.7)*	<0.001

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All crude and adjusted odds ratios above are statistically significant at p<0.05. *means that the results are statistically significant.

DISCUSSION

The abnormal adhesion of the trophoblastic tissue to the myometrial wall is the hallmark of placenta accreta (PA), a serious maternal complication [13]. Despite PA prevalence historically being less than 1%, national data from 2015 to 2017 showed that PA increased by about 2% every three months in women with prior cesarean deliveries. By 2025, the incidence is expected to reach 1 in every 200 women undergoing cesarean deliveries [2, 14]. Early detection and management are crucial since PA increases the risk of severe complications such as catastrophic bleeding, hysterectomy, organ damage, coagulopathy, and even maternal death [15, 16]. Current study confirms that PA is associated with significant maternal morbidity. Women with PA experienced markedly higher rates of postpartum hemorrhage (58.4%) compared to controls (14.3%) (OR 7.65). This finding aligns with prior studies that identify PA as a major risk factor for hemorrhage, given the abnormal placental attachment and difficulty separating the placenta after delivery [17]. Additionally, cesarean section rates (85.7% in the PA group vs. 51.3% in controls) and peripartum hysterectomy (15.6% vs. 1.3%) were significantly elevated in the PA group. These results are consistent with Aryananda *et al.*, findings of increased blood loss and complications in PA patients undergoing cesarean hysterectomy [18]. Similarly, Nieto-Calvache *et al.*, reported prolonged operating times and higher blood transfusion rates in PA patients requiring hysterectomy [19]. Neonatal outcomes were also significantly impacted by PA, with lower 1-minute Apgar scores (24.7% of PA infants scoring below 7 compared to 5.2% in controls; adjusted OR 5.67). The PA group had higher rates of respiratory distress syndrome (RDS) (40.3% vs. 7.8%) and intraventricular hemorrhage (IVH) (11.7% vs. 1.9%). These findings align with prior studies reporting increased neonatal complications in PA pregnancies, particularly in relation to preterm deliveries and lower birthweights [20]. The odds of RDS (adjusted OR 7.42) and IVH (adjusted OR 6.30) were significantly elevated in the PA group, highlighting the association between PA and poor neonatal outcomes [21, 22]. Hypoglycemia rates were also higher in the PA group (18.2% vs. 3.2%, adjusted OR 6.41). Long-term neurodevelopmental outcomes were notably worse in infants born to mothers with PA. By 24 months, 7.8% of PA-exposed infants were diagnosed with cerebral palsy (CP) compared to 0.6% in the control group (adjusted OR 13.5). Moreover, 6.5% of infants in the PA group had severe cognitive delays (Bayley Mental Index scores <71) compared to 0.6% of controls (adjusted OR 10.4). Similar findings were reported by Moeini *et al.*, linking lower gestational ages and increased NICU admissions to higher morbidity rates in neonates exposed to PA [23]. Additionally, 11.7% of PA-exposed infants showed borderline cognitive development (scores 71-84), compared to 1.3% in controls (adjusted OR 9.87), further emphasizing the long-term developmental impact of PA [24, 25]. Clinical recommendations for PA management include antenatal diagnosis via imaging and planned cesarean delivery at 34-36 weeks in specialized centers to minimize risks for both mother and infant. While cesarean hysterectomy remains the standard for managing PA, uterine-sparing procedures may be considered in select cases to preserve fertility and reduce morbidity. Multidisciplinary care teams involving obstetricians, anesthesiologists, and neonatologists are critical for optimal outcomes [26].This study's retrospective design may introduce biases, especially concerning data completeness. Additionally, the study population was drawn from a specific demographic, limiting generalizability to other populations. Future prospective studies are needed to validate these findings and improve PA management strategies.

CONCLUSIONS

It was concluded that placenta accreta is associated with serious maternal morbidity, increasing hemorrhage, rate of cesareans, and hysterectomies. It also causes poor short-term neonatal outcomes in terms of having RDS, IVR hypoglycemia, and long-term neurodegenerative disorders from minor cognitive defects to major problems like CP.

Authors Contribution

Conceptualization: ZEH
Methodology: ZEH, UZ, AS[1]
Formal analysis: AS[2]
Writing review and editing: SN, AA
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Indications and Frequencies of Elective and Emergency Cesarean Section in Social Security Landhi Hospital Karachi, Pakistan

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ABSTRACT

The cesarean section rate is high in Pakistan as compared with WHO recommendations. It is quite high in the public sector hospitals due to high-risk pregnancies repeat cesarean sections and referrals from private sector hospitals. **Objectives:** To determine the proportions of indications of elective and emergency cesarean sections. **Methods:** This cross-sectional study was carried out in the Department of Obstetrics and Gynecology, Social Security Landhi Hospital, Karachi, from January 1st, 2023 to December 31st, 2023. A total of 1150 patients were enrolled with a convenient sampling technique. Performa was filled by patients who delivered by cesarean section and through vaginal delivery. Patients who attended the Obstetrics patient's department were marked as booked cases and those who were admitted for early labor and later cesarean-section was performed, were marked as un-booked. Cesarean sections through emergency were also included. Patients of ruptured uterus were excluded from this study. Data were entered in SPSS software version 24.0 and analyzed for frequencies and percentages. **Results:** A total of 770 cesarean sections were done. Overall frequency of cesarean-sections was 66.95%. Frequency of elective and emergency cesarean-section was 485 (62.98%) and 285 (37.01%). Booked cases were 658 (85.45%) while un-booked were 112 (14.54%). The commonest indication was repeat cesarean-section in 150 (19.48%), cervical dystocia in 105 (13.63%), fetal distress in 103 (13.37%), and antepartum hemorrhage were 94 (12.20%) patients. **Conclusions:** It was concluded that the Cesarean-sections rate was very high as compared to normal vaginal deliveries. The most common indication of cesarean section was repeat cesarean section.

INTRODUCTION

Cesarean section delivery is defined as the birth of a fetus through the abdomen after given incision in the abdominal and uterine wall [1]. According to documents, 1st cesarean section was done in 1610 and 1st modern cesarean section was performed by Dr. James Barry on July 25th, 1826. When delivery through the vagina is impossible or contraindicated, cesarean section is the only way to deliver a fetus although it has its risks and complications which may be long-term or short term such as maternal morbidity, mortality, increased need for blood transfusion, postpartum hemorrhage, postpartum infection, morbidly adherent placenta, and prolong stay in hospitals [2]. Birth of a newborn through cesarean section is a life-saving operation for the mother as well as for her fetus. When the rate of cesarean section is limited up to 10%, maternal and neonatal death decreases [3] and when the cesarean section rate rises above 15% there is an increased risk for maternal and perinatal morbidity [1]. The incidence of cesarean section is increasing in both developed and developing countries and worldwide it is the commonest operation performed by obstetricians. Mostly cesarean-sections are done safely but complications may be

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encountered in a few cases which may be immediate or late [4]. Recent literature reveals that the rate of cesarean-section increases with advanced maternal age, especially in nulliparous patients [5]. The highest rate of cesarean-section reported in Latin America i.e. 42.8% [6]. World Health Organization notified that the rate of cesarean-section should be 10-15%. The latest data from 150 countries shows that 18.6% of total births by cesarean-section range from 6% to 27.2% in the least developed to modern developed countries [7]. Nowadays cesarean sections have an active role in the obstetrics practice for improving clinical performance [8]. In South Asia trend of cesarean-section is increasing with indications such as fetal distress, repeat cesarean-section, antepartum hemorrhage (APH), placenta Previa, and abruption. The rising trend for C-sections in developing countries is influenced by different factors such as advanced maternal age, higher level of education, urban residence, and socio-economic status [9]. The rate of emergency cesarean section was higher among young women in prim gravida i.e. 54.4% and elective cesarean section was 45.6% [10]. There are many recognized reasons for performing a cesarean section such as fetal distress, failure to progress, arrest of descent of fetus in the pelvis, repeat C-section, and breech presentation. In Pakistan, the cesarean-section rate was doubled in private hospitals as compared with public sector hospitals due to maternal requests. [11]. The most common cause of death in developing countries is hemorrhage and obstructed labor which could be decreased by up to 92% when a timely decision was taken [12].

This study aims to provide proper knowledge regarding cesarean-section versus normal vaginal delivery to pregnant ladies for controlling cesarean-section rates and promoting vaginal delivery and avoiding unnecessary cesarean-sections.

METHODS

A cross-sectional study was carried out in the Department of Obstetrics and Gynecology, Sindh Employees Social Security, Landhi Hospital, Karachi, Pakistan from January, 2023 to December, 2023. The age range of patients was 16-45 years. Ethical approval was taken from the Institutional Review Board before conducting the study. IRB reference No. SS/LH/2022-23/IRB-45 and informed consent were also taken from patients who agreed to participate in the study. The sample size was calculated by Open EPI Software. A convenient Sampling Technique was used. All the pregnant women who attended the Obstetrics patient's department for their antenatal checkups were booked for deliveries, and those pregnant patients who were admitted in early labor and later on cesarean-sections were underwent, labelled as unbook cases, and all those pregnant women who had attended Obstetrics emergency for cesarean-section were also included in this study. The patients who had been diagnosed with ruptured uterus during emergency laparotomy were excluded from this study. A total of 1150 patients were enrolled during the specified period including booked or un-booked for their deliveries. A good design updated proforma was filled out for each patient separately about their relevant history and evidence of the cesarean-section delivery or normal vaginal delivery. Variables were maternal age, booked cases or un-booked cases, elective C-section or emergency C-section, cervical dystocia, fetal distress, antepartum hemorrhage, eclampsia, obstructed labor, bad obstetrical history, breech presentation, maternal wish, post maturity, twin pregnancy, cord prolapses, cord presentation, hydrops fetal is, socio-economic status and education. Data were analyzed by using SPSS software version 24.0 and frequency and percentage were calculated.

RESULTS

In the study period, there were 1150 pregnant women enrolled and underwent deliveries. Among them 770 underwent cesarean-section and 380 patients were delivered by normal vaginal delivery. The rate of cesarean-section and normal delivery were 66.95% and 33.04%. The cesarean-sections rate was very high as compared with normal vaginal deliveries. Out of 770 patients 658 were booked 112 were un-booked and they attended in Obstetrics Emergency Department. Elective cesarean sections were performed in 485 (62.98%) patients while emergency cesarean sections were in 285 (37.01%) patients (Table 1).

Table 1: Description Regarding C-Sections and Normal Delivery (n=1150)

Characteristics of the Patients	Frequency (%)
Cesarean-Sections	770 (66.95%)
Normal Delivery	380 (33.04%)
C-Sections	
Booked Cases	658 (85.45%)
Unbook Cases	112 (14.54)
Elective Cesarean Sections	485 (62.98%)
Emergency Cesarean Sections	285 (37.01%)

Patients who had delivered their babies by cesarean section. Total number of patients were 770 with different age groups. Most cesarean sections were done in the age group of 21-30 years. In multigravida, the cesarean-sections rate was high i.e. 425 (55.19%). The majority of patients were poor i.e. 575 (74.67%) and mostly patients were un-educated 565 (73.37%), (Table 2).

Table 2: Sociodemographic Pattern in C-Sections, (n=770)

Characteristics of the Patients	Frequency (%)
Age	
<21 Years	105 (13.63%)
21-30 Years	415 (53.89%)

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31-40 Years	165 (21.42%)
>40 Years	85 (11.03%)
Gravidity	
Primi Gravida	171 (22.20%)
Multi Gravida	425 (55.19%)
Grand Multi Gravida	174 (22,59%)
Socio-Economic Status	
Poor	575 (74.67%)
Middle Class	195 (25.325)
Education	
Educated	205 (26,62%)
Un-Educated	565 (73.37%)

Repeat cesarean-section was the most common indication for cesarean-section i.e. 19.48%. Other common indications of cesarean-sections were cervical dystocia 13.63%, fetal distress 13.37% and antepartum hemorrhage 12.20% (Table 3).

Table 3: Indications of Cesarean-Sections. (n=770)

Characteristics of the Patients	Frequency (%)
Repeat Cesarean Sections	150 (19.48%)
Among Repeat C-Sections	
Previous-1	65 (8.44%)
Previous-2	45 (5.84%)
Previous-3	30 (3.89%)
Previous-4	10 (1.29%)
Transverse/Oblique	35 (4.54%)
Maternal Wish	14 (1.81%)
Post Maturity	14 (1.81%)
Twin Pregnancy	14 (1.81%)
Cord Prolapses	12 (1.56%)
Cord Presentation	8 (1.03%)
Hydrops Fetalis	04 (0.5%)
Cervical Dystocia	105 (13.63%)
Fetal Distress	103 (13.37%)
Antepartum Hemorrhage	94 (12.20%)
Eclampsia	70 (9.09%)
Obstructed Labor	56 (7.27%)
Bad Obstetrical History	52 (6.75%)
Breech Presentation	39 (5.06%)

DISCUSSION

In our study rate of cesarean section was 66.95% and the rate of normal vaginal deliveries was 33.05%. Elective cesarean sections were performed in 485 (62.98%) patients and emergency cesarean sections were in 285 (37.01%) patients. In a study, the reported rate of cesarean section was 39.4% and the rate of normal vaginal delivery was 60.57% [13]. This is a little bit resemble to our study. In another study, 90.37% of patients were delivered by normal vaginal delivery and only 9.63% were undergoing emergency cesarean section. In that study, emergency cesarean sections were 67.2% due to fetal distress. Indication of cesarean section due to antepartum hemorrhage was 1.11%. [14]. While in our study antepartum hemorrhage was higher i.e. (12,20%) fetal distress was lower (13.37%) and the cesarean section rate was (66.95%) In another study, out of 1968 patients 40.95% patient were undergone cesarean section delivery. Maximum patients (57.69%) were undergone cesarean-section in the age group 25-30 years. Indications of cesarean section were fetal distress 22.21%, mal-presentation 18.26%, antepartum hemorrhage 7.21%, eclampsia 5.28%, obstructed labor 3.36%, bad obstetrical history 3.36%, post maturity 1.92% and twin pregnancy was 0.96% [15]. In our study rate of cesarean section was higher i.e. 66.95%, and cesarean section in the age group of 21-30 years was 53.89%, resembled with that study and fetal distress and mal-presentation was lower and antepartum hemorrhage, eclampsia, obstructed labor and bad obstetrical history was higher. Nair *et al.*, reported in a study that all patients were prim gravida and delivered by cesarean sections. Among them, 80% were booked and 20% were un-booked. The most common age group was 20-25 years. Elective cesarean was done in 18% of patients and emergency cesarean-section in 82% of patients.Indications of cesarean sections for breech presentation 5%, post maturity 3%, fetal distress 52%, cord presentation 2%, cervical dystocia 2% and antepartum hemorrhage 2% [16]. While in current study cesarean-sections were done only in 22.20% in prim gravida. Fetal distress was much higher in that study although antepartum hemorrhage and cervical dystocia were lower. Presnt study is quite different from that study. According to Mostafayi *et al.*, in their study illiterate patients were 6.6%, primary school education was higher 50%, diploma education was 39.8% and only 6.6% of patients got college education [17]. While in present study majority were illiterate (un-educated) 73.37%, poor were 74.67% and resided in industrial 63.63%. In a study, it was reported that the rate of cesarean section was 81% and 19% of patients were delivered normally. Among them 68% were delivered by emergency cesarean-section and 32% by elective-cesarean, book patients were 25%, prim gravida was 30.87% and multigravida was 69.13%. the most common indication for cesarean section was a failure to progress 31%, fetal distress was 22%, mal-presentation was 11.7%,obstructed labor was 0.47% and maternal request for cesarean section was 2.87% [18]. In presnt study rate of cesarean section and emergency cesarean section were lower, booked patients were more, multi gravida were higher, and common indications for C-section were repeat cesarean followed by cervical dystocia, fetal distress, antepartum hemorrhage, eclampsia, obstructed labor and bad obstetrical history. Current study is different from that study. Taj *et al.*, reported in a study that emergency cesarean section was 81.05% and elective cesarean was 18.94%. Cesarean section under the age of 20 years was 25% and between the age group 20-30 years 60% [19]. While in present study cesarean section under the age 21 years was 13.63% and between age group 21-30 years was 53.89%. In that study 41.70% of patients were

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delivered by cesarean section due to repeat C-section, twin pregnancy and breech presentation 8.3%, maternal wish 2.8% and bad obstetrical history was 8.3%, in that study indication for cesarean-section was more in repeat cesarean cases while in current study it was 19.48%. Coskun *et al.*, revealed in their study that 10.3% of patients delivered by emergency cesarean-section due to complete breech presentation. Elective cesarean-section was 9.7% due to breech presentation [20]. In a study 39% of women were nulliparous and among them, 14% had undergone emergency cesarean section [21]. In a study, 48.3% patients were prim gravida, and 12% of patients had a history of repeat cesarean section. Cesarean-section due to cord prolapse was 2.15%, Antepartum Hemorrhage 6.15% and Breech Presentation 9.23% [22]. Idrees *et al.*, reported in a study that rate of cesarean-section was 10.1% and indications for cesarean-section due to mal-presentation was 14.4%, obstructed labor 21.2%, Repeat-cesarean section 10.2% and fetal distress was 5.9% [23].

CONCLUSIONS

It was concluded that the cesarean-section rate was very high as compared to normal vaginal deliveries which is against WHO criteria. Elective cesarean sections were performed more as compared to emergency cesarean sections. The most common indication of cesarean section was found to be a previous cesarean section. The other common indications were cervical dystocia, fetal distress, and antepartum hemorrhage. Cesarean section rate should be controlled specially in prim gravidas with the help of proper antenatal care and management of its complications appropriately. So, that it will reduce the rate of cesarean section. For controlling cesarean section rate and enhanced maternal health outcome we are recommending proper antenatal checkup and care during labor.

Authors Contribution

Conceptualization: HT
Methodology: SA, SM
Formal analysis: ZB
Writing-review and editing: MS, AN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Perspective of Women in Neurosurgery: Quantitative Study Interpreting Journey of Professional Identity Formation in Female Doctors of Low Middle Income Country

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ABSTRACT

Globally, there is a shift towards choosing medical and allied specialities over neurosurgery. In Pakistan, where female medical students now outnumber males, this trend has led to a significant gap in the availability of qualified neurosurgeons. **Objectives:** To assess how the perception of neurosurgery evolves from final year medical school to house job among female doctors focusing on educational adequacy, socioeconomic factors and challenging career choices. **Methods:** This cross-sectional descriptive study was conducted through a validated questionnaire. This questionnaire encompassed demographic information, and a series of items designed to evaluate students' educational perceptions regarding neurosurgery, their socioeconomic viewpoints on neurosurgery, and their perspectives on neurosurgery training within Pakistan. **Results:** We received 216 responses from participants, with 115 (53.2%) being final-year students and 101 (46.8%) serving as house officers. 57.9% of participants disagreed to consider neurosurgery as a career option whereas 97.7% considered neurosurgical illnesses challenging and interesting. Neurosurgery involving long operating hours was the strongly agreed question among participants (97.2%). Final-year students were significantly more likely to perceive their neurosurgery education as inadequate (61.7%). Likewise, they reported greater concerns about limited job opportunities compared to house officers (20% vs 7.9%, p=0.012). **Conclusions:** It was concluded that although there is considerable interest in neurosurgery, enrollment among females remains low due to educational gaps, socioeconomic barriers and gender challenges. Limited teaching resources, the demanding nature of the field, and perceived negative impacts on personal life among female doctors contribute to this trend.

INTRODUCTION

The brain is one of the most fascinating organs of the body, making its study both intriguing and challenging for medical students. However, mastering the basic anatomy and clinical understanding of neurosurgery can be daunting in the early years of training. The critical question remains: Does this fascination translate into a willingness to pursue neurosurgery as a career, particularly among female medical students who often face additional family and socioeconomic challenges in developing countries like Pakistan? [1]. Globally, there is a paradigm shift in speciality preferences with a growing inclination towards internal medicine and allied fields due to various factors [2]. In Pakistan, only one-third of medical students show interest in surgery-related fields as a career, which is concerning given the country's large and growing population that requires a balanced distribution of specialists [3].

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Additionally, the proportion of female medical students has been gradually increasing, reversing the historical gender ratio from 30% to 70% female dominance. If this trend continues, Pakistan's healthcare system will require more female specialists in surgery, including neurosurgery to meet the needs of its 235.8 million people [4]. Neurosurgery is considered one of the most demanding surgical specialties requiring dedication, technical proficiency and long-term commitment. However, the interest in pursuing neurosurgery remains alarmingly low despite the rising global burden of neurosurgical diseases [5]. In Pakistan, neurosurgical diseases are currently catered by approximately 400 neurosurgeons and 700 postgraduate residents. While it has been estimated that around 22 million patients require neurosurgical interventions with a significant (5 million) proportion from third-world countries [6]. Given the current statistics and this stark gap between demand and availability of qualified neurosurgeons, there is an urgent need to address the factors influencing career choices in the speciality of neurosurgery [7]. Previous studies have explored medical students' hesitancy towards surgery. Existing research has identified several factors such as long training duration, the requirement of competence, and the impact on family life [8]. Along with these social factors, several other factors are related purely to the teaching deficiencies present in our education system. Taking female doctors, especially under consideration, the field as being male dominant as well as societal norms including gender roles can further halt women being entering the clinical field, not alone neurosurgery [9]. Moreover, policies like the Central Induction Policy (CIP) may play a pivotal role in career choices, as female doctors as role as they choose specialities based on social circumstances rather than professional aspirations [10, 11]. Instead of broadly examining neurosurgery as a career choice, our study is structured into three key domains to give a more comprehensive perspective: 1) Educational Adequacy in Neurosurgery – Assessing whether medical training sufficiently prepares students for neurosurgery, 2) Socioeconomic Aspects of Neurosurgery – Exploring financial stability, work-life balance and long term career outlook in demanding speciality and 3) Challenges and Barriers in Neurosurgery – Identifying gender-specific obstacles from pursuing neurosurgery.

This study aims to analyze the perception of neurosurgery as a career choice among final-year female medical students and female house officers in Pakistan. By examining their perspectives at two critical transition points, the last year of medical school to the first year of practical life, we seek to identify the factors influencing their interest, concern and decision-making regarding neurosurgery.

METHODS

This cross-sectional descriptive study was conducted at Allama Iqbal Medical College Jinnah Hospital Lahore from May 2024 to July 2024 following ethical approval from the Institutional Review Board (ERB164/8/16-05-2024/SI ERB). A pre-validated questionnaire, previously utilized in an international study was adapted for this research and transformed into Google Form [12]. The questionnaire comprised multiple sections to gather demographic data and assess participants' perceptions of neurosurgery. The questions from the questionnaire were grouped into three key domains: Educational Adequacy in Neurosurgery (Questions 1, 3 and 4), Socioeconomic Aspects of Neurosurgery (Questions 2, 11-15) and Challenges and Barriers in Neurosurgery (Questions 5-10). The study targets female final-year MBBS students and female house officers to examine their views on neurosurgery as a career choice. The sample size was calculated as 186 using a 95% confidence interval and 5% margin of error with 14 % of participants considering neurosurgery as an option for future careers [13]. However, due to logistical feasibility and accessibility to the target population, and to enhance study validity, 216 participants were employed through convenience sampling to recruit participants. An informed consent was taken from each participant. Data collection was conducted via online forms, ensuring informed consent. All data were anonymized before analysis. The anonymized data were stored securely with restricted assess and only aggregated results were reported to maintain privacy. Responses were analyzed using SPSS version 21. Descriptive statistics, including frequencies and percentages were used for categorical variables and the chi-square test was applied to study correlations. Likert scale responses (ranging from 1=disagree; 2=agree; 3=moderately agree; 4=strongly agree) were analyzed to assess trends in participants' perceptions regarding neurosurgery.

RESULTS

A total of 216 participants were included in the study, comprising final year study, comprising final-year students (n=115, 53.2%) and house officers (n=101, 46.8%). The majority of participants were single (n=185, 85.6%) (Table 1).

Table 1: Demographic Characteristics of Participants

Variables	n (%)
Single	185 (85.6%)
Engaged/ Married	31 (14.4%)
Final Year	115 (53.2%)
House Officer	101 (46.8%)

Results represent participants' responses to various questions regarding their perceptions of neurosurgery. Notably more than half of the participants (n=115, 53.2%)

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felt that their neurosurgery education was inadequate. Additionally, 57.9% (n=125) of the respondents did not consider neurosurgery as a career option. Conversely, a significant majority of respondents found neurological illnesses challenging and interesting (97.7%) and agreed that neurological illnesses are complicated (94.9%). Furthermore, 93.5% of respondents believed that neurosurgery could impede family life and 96.8% agreed that neurosurgery requires a long training period (Table 2).

Table 2: Participants' Perception of Neurosurgery

Sr. No.	Questions	Disagree n (%)	Agree (Likert 2-4) n (%)
1	My neurosurgery teaching is adequate	115 (53.2%)	101 (46.8%)
2	I consider neurosurgery as a career option	125 (57.9%)	91 (42.1%)
3	Neurosurgical history is difficult to obtain	27 (12.5%)	189 (87.5%)
4	Neurosurgical signs are difficult to elicit	54 (25.0%)	162 (75.0%)
5	Limited interventions are available in neurosurgery	39 (18.1%)	177 (81.9%)
6	Neurosurgical illnesses are complicated	11 (5.1%)	205 (94.9%)
7	Neurosurgical illnesses are challenging and interesting	5 (2.3%)	211 (97.7%)
8	Most Neurosurgical illnesses have poor outcomes	18 (8.3%)	198 (91.7%)
9	Neurosurgery requires a long training period	7 (3.2%)	209 (96.8%)
10	Neurosurgery involves long operating hours	6 (2.8%)	210 (97.2%)
11	Huge prestige and income are attached to neurosurgery	12 (5.6%)	204 (94.4%)
12	Neurosurgery can impede family life	14 (6.5%)	202 (93.5%)
13	Neurosurgery training in Pakistan is too prolonged	15 (6.9%)	201 (93.1%)
14	Neurosurgery training centers in Pakistan are few	10 (4.6%)	206 (95.4%)
15	Future job opportunities will be limited	31 (14.4%)	185 (85.6%)

Participants' overall satisfaction with neurological education was low with only 68.9% of final year students and 70.63% of house officers agreeing. Socioeconomic stability associated with neurosurgery was perceived positively by 83.63% of final year students and 84.49% of house officers. However, concerns regarding hurdles in the field were prevalent with 91.01% of final-year students and 96.04% of house officers agreeing that significant challenges exist (Table 3).

Table 3: Overall Perception of Neurosurgery among Final Year and House Job Participants

Domains	Disagree n (%) Total Questions		Agree n (%) Total Questions	
	Final Year	House Officers	Final Year	House Officers
Overall Satisfaction with the level of education in neurosurgery	107 (31.10%)	89 (29.37%)	238 (68.90%)	214 (70.63%)
Overall Socioeconomic stability associated with neurosurgery	113 (16.37%)	94 (15.51%)	577 (83.63%)	512 (84.49%)
Overall perception of hurdles associated with the neurosurgery field	62 (8.99%)	24 (3.96%)	628 (91.01%)	582 (96.04%)

A comparison between final year students and house officers showed significant differences in their perceptions. Final-year students were significantly more likely to disagree that their neurosurgery education was adequate (61.7% vs 23.6%, p=0.008). Similarly, final year students perceived more limitations in future job opportunities compared to house officers (20% vs 7.9%, p=0.012). However, house officers were more likely to find neurological illnesses complicated (98% vs 92.2%, p=0.051) though this difference was not statistically significant (Table 4).

Table 4: Comparison of Final Year and House Officers

Questions	Category	Disagree n (%)	Agree (Likert 2-4) n (%)	p-value
My neurosurgery teaching is adequate	Final Year	71 (61.7%)	44 (38.3%)	0.008*
	House Officer	44 (43.6%)	57 (56.4%)	
I consider neurosurgery as a career option	Final Year	60 (52.2%)	55 (47.8%)	0.070*
	House Officer	65 (64.4%)	36 (35.6%)	
Neurosurgical history is difficult to obtain	Final Year	13 (11.3%)	102 (88.7%)	0.571
	House Officer	14 (13.9%)	87 (86.1%)	
Neurosurgical signs are difficult to elicit	Final Year	23 (20.0%)	92 (80.0%)	0.070*
	House Officer	31 (30.7%)	70 (69.3%)	
Limited interventions are available in neurosurgery	Final Year	24 (20.9%)	91 (79.1%)	0.251
	House Officer	15 (14.9%)	86 (85.1%)	
Neurosurgical illnesses are complicated and difficult	Final Year	9 (7.8%)	106 (92.2%)	0.051*
	House Officer	2 (2.0%)	99 (98.0%)	
Neurosurgical illnesses are challenging and interesting	Final Year	4 (3.5%)	111 (96.5%)	0.225
	House Officer	1 (1.0%)	100 (99.0%)	
Most Neurosurgical illnesses have poor outcomes	Final Year	15 (13.0%)	100 (87.0%)	0.008*
	House Officer	3 (3.0%)	98 (97.0%)	

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Neurosurgery requires a long training period	Final Year	5 (4.3%)	110 (95.7%)	0.327
	House Officer	2 (2.0%)	99 (98.0%)	
Neurosurgery involves long operating hours	Final Year	5 (4.3%)	110 (95.7%)	0.134
	House Officer	1 (1.0%)	100 (99.0%)	
Huge prestige and income are attached to neurosurgery	Final Year	5 (4.3%)	110 (95.7%)	0.408
	House Officer	7 (6.9%)	94 (93.1%)	
Neurosurgery can impede family life	Final Year	9 (7.8%)	106 (92.2%)	0.392
	House Officer	5 (5.0%)	96 (95.0%)	
Neurosurgery training in Pakistan is too prolonged	Final Year	10 (8.7%)	105 (91.3%)	0.280
	House Officer	5 (5.0%)	96 (95.0%)	
Neurosurgery training centers in Pakistan are few	Final Year	6 (5.2%)	109 (94.8%)	0.661
	House Officer	4 (4.0%)	97 (96.0%)	
Future job opportunities will be limited	Final Year	23 (20.0%)	92 (80.0%)	0.012*
	House Officer	8 (7.9%)	93 (92.1%)	

DISCUSSION

During the last few years, there has been a paradigm shift in choosing the surgical and allied speciality as a future career which can be due to the high technical demands of surgical fiend along with long duty hours, but it can also be related to increasing the entry of women in the medical field and inclusion of information technology in medical horizon [14, 15]. Although a study conducted on medical students of Oman showed a negative perception of choosing neurosurgery almost 42.1% in our study viewed it as a career option, which is lower than a study conducted in Karachi, Pakistan, which reported 56.2% of participants' interest in neurosurgery [11, 16]. However, this percentage remains significantly lower than in a study in Saudi Arabia, where 86% of participants showed enthusiasm for neurosurgery as a career option [13]. According to our study, 46.8% of participants considered neurosurgery teaching to be adequate, which is lower than the Saudian study [13]. Despite this, many participants found neurosurgery teaching, history-taking, and examination techniques challenging. A significant proportion (94.9%) agreed that neurological illnesses are complicated and 97.7% found them challenging and interesting. In our study, 93.5% believed neurosurgery could impede family life. Various studies have highlighted neurosurgery as a demanding and strenuous field due to poor patient outcomes, lengthy training periods, and extensive operating hours [7, 9]. While there is a desire to pursue neurosurgery, concerns about its impact on social and family life persist due to limited training centers in Pakistan (95.4%) and constrained future job prospects (85.6%). The study conducted in Saudi Arabia reported that 81.7% of participants perceive an adequate number of training centers in their country, possibly contributing to higher interest levels in neurosurgery surprisingly 93.9% of our participants perceive that training centers in Pakistan are few which may be one of the leading cause of lack of interest [13]. Economic survival has become a global issue which impacts the choice of future professional field same is the case with doctors, the concept of eternal service and humanitarian welfare is gradually being overshadowed by high-salary speciality choices [17]. Nowadays bread and butter earning is influencing young lads of the medical profession to think again before choosing their future speciality, Akhigbe and Sattar, registered in their study that most medical lads considered neurosurgery a high take-home pay field with a well-sophisticated reputation among the medical fraternity, and similar perception was observed in our study [12]. Around 30% of study participants in both groups were dissatisfied with neurosurgery education, indicating the need for curriculum improvement, the recently introduced integrated curriculum might enhance satisfaction and encourage female doctors to pursue neurosurgery/ Similar results were reported by Balasubramanian *et al.*, who suggested that apart from curriculum, mentorship opportunities play a crucial role [18]. Despite high salaries, work-life balance remains a major barrier for female doctors, especially in low-middle-income countries where family responsibilities impact career choice. The central induction policy has further influenced specialty selection with location often prioritized over passion. Interest in neurosurgery declined from 42.5% among final-year students to 39.6% among house officers warranting further exploration. In a study on Saudi female doctors, 50.3% reported that family responsibilities affected their career choices [19]. The inherent challenges of neurosurgery, largely due to the complexity of neurosurgery largely due to the complexity of brain structures. Managing neurosurgical conditions demands precision and a steep learning curve with only 6.78% disagreeing with this challenge reinforcing the intense nature of the field. Ahmed *et al* found that 48.6% acknowledged the complexity of neurological diseases which discouraged them from entering the field [20]. The findings align with Krumboltz's Social Learning Theory, which suggests that career choices are influenced by prior experiences and external conditions. Participating in this study demonstrated a decision-making process shaped by

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exposure to clinical settings and, mentorship, reinforcing the impact of learning experiences on career pathway [21]. Improving socioeconomic support and teaching facilities can make neurosurgery more attractive to medical graduates. Introducing comprehensive teaching methods at the medical student level can build confidence in theoretical knowledge, increasing interest in the field as students enter professional life. While creating new training centers in less populated areas may be difficult, enhancing support and resources for residents in existing centers can make the speciality more appealing and less socially challenging.

CONCLUSIONS

It was concluded that deficiencies in neurological education, socioeconomic concerns and gender-based challenges were observed in career choices. While most of the participants found neurological illness stimulating, significant dissatisfaction exists regarding career prospects, training duration and work-life balance. House officers perceived greater challenges associated with neurosurgery compared to final year students, potentially reflecting an increased exposure to clinical exposure.

Authors Contribution

Conceptualization: UAK, AS
Methodology: UAK, AS, HK, MM
Formal analysis: MM, MAA
Writing review and editing: GA, AN, MAA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Comparison of Fracture Resistance of Conventional Composite Veneers with Novel Veneer Preparation Design- In Vitro Study

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ABSTRACT

The patient's primary concern or need for good and pleasing esthetics of anterior teeth has increased. With the progression in the restorative field, multiple treatment options exist for patients' complaints. Composite veneering is one of the suitable and an appropriate treatment option with classic properties that is a good mechanical property, bend strength, abrasion resistance, and longevity of direct anterior restoration. **Objectives:** To compare fracture resistance of conventional and novel veneer preparation (a modified form of feather edge preparation) design in the indirect composite veneer method. **Methods:** In Vitro, a comparative study was conducted at the Department of Operative Dentistry and Endodontics Dr. Ishrat Ul Ebad Khan Institute of Oral Health Sciences, Dow University of Health Sciences Karachi time duration of six months by using a non-probability consecutive sampling technique. Data analysis was performed using SPSS version 26.0. The independent sample T-test was applied to compare the fracture resistance between the two procedures. **Results:** In terms of fracture load performance, the Conventional Veneer group had an average fracture load of 309.7 ± 126.3 N, compared to 335.5 ± 136.14 N in the Novel Veneer group. Although the Novel Veneer group showed a higher mean fracture load, this difference was statistically significant (p=0.005). **Conclusion:** It was concluded that increasing fracture resistance of the prepared materials with new preparation designs trends in the present study, however, the obtained data were statistically significant (p-value 0.005).

INTRODUCTION

The fracture resistance of composite veneers is one of the significant parameters that affect the effectiveness and durability of rehabilitative dental interventions [1]. As the need for cosmetic dental treatments grows, there is a consequent trend towards composite veneers as an option for restoring anterior teeth [2]. However, the ideal bond strength as well as resistance to fracture is crucial for the longevity of these veneers. The various preparation designs of the tooth have been investigated to establish if they improve or alter the composite veneer's fracture resistance – conventional and novel designs [3, 4]. These preparation designs can substantially alter the biomechanical functionalities of the veneers and consequently distinguish the degree of the fracture. Among properties, fracture resistance is considered to be critical for defining the stability of the dental veneers [5].

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There is a strong relation between a patient's dental appearance and psycho-social status, hence choosing the appropriate restoration to upgrade the patient's esthetics, likewise, it emphatically affects the patient's self-confidence and lifestyle [6, 7]. Naturally malformed teeth such as enamel hypoplasia, peg-shaped lateral incisors, sensitivity due to hypo-mineralization, abrasion, and erosion in all these cases composite veneer gives good results [8-10]. A veneer is a shell with a fine and shiny surface. Composite veneers can be used directly and indirectly called direct composite veneer and indirect composite veneer, respectively. Direct composite veneer requires minimal preparation of tooth surface and composite material is directly used on the prepared tooth surface and cured by composite curing light (LED). Indirect composite veneer on the other hand is fabricated in the laboratory on a die prepared on the silicone impression taken from the patient's mouth and then bonded to the prepared tooth structure with the help of different resin cements [11-13]. The properly performed composite veneer gives the patient satisfactory results [14-16]. Composite veneers have a common and significant problem of debonding and fracture of veneer. In this study, a novel veneer preparation was used and compared with conventional veneer preparation to overcome major issues of deboning and fracture strength.

This study aims to introduce novel methodologies or preparation designs that haven't been explored previously. This could include differences in material composition, preparation techniques, or testing protocols. While this study might address the long-term durability and performance of the veneers.

METHODS

In Vitro Comparative Study was conducted at the Department of Operative Dentistry and Endodontics Dr. Ishrat Ul Ebad Khan Institute of Oral Health Sciences, Dow University of Health Sciences Karachi and the duration of the study was six months (18th January to 17th July 2023) after approval from the research ethics committee of Dow university of health sciences (IRB-2791/DUHS/EXEMPTION/2022/16). Samples were collected from the Oral and Maxillofacial Surgery Department. Veneer preparation was done at the Department of Operative Dentistry and Endodontics, while a strength testing test was performed at the Pakistan Council of Scientific and Industrial Research (PCSIR)Laboratory Complex, Karachi, Pakistan. Patient selection was made at the time of extraction of teeth for study purposes, based on patients having ages of 20 to 60 years, periodontal compromised anterior teeth, and extraction due to trauma, staining, and RCT failure of anterior teeth. Veneer includes properly cured and without defect, marginal or surface discrepancy were included and patients having developmental defects, hypoplastic tooth, carious tooth, and worn out tooth were excluded and veneer excludes teeth not able to lute properly and broken during luting. Inclusion criteria were based on anterior teeth, premolars were included and the study excluded individuals with developmental defects, hypo-plastic teeth, and grossly carious teeth. The sample size was calculated from an online calculator open Epi using pass version 15 based on a 95% confidence interval and 96% power of the test.Mean $\pm$ SD of fracture load [1] unconventional preparation (100.6 $\pm$ 7.956) fracture load in slot preparation (107.4 $\pm$ 6.804) https://eprints.ugd.edu.mk/id/eprint/16325. The sample size was 16 per group, but now it has increased to 30 per group for strong study results and non-responders, etc. Non-probability sampling technique was applied for the selection of patients. A total number of 60 anterior teeth extraction patients attending the Oral and Maxillofacial Surgery Department of Dr. Ishrat Ul Ebad Khan Institute of Oral Health Science, fulfilling inclusion criteria were included in this study Written informed consent was taken from all the patients included in this study. Demographic details like name, age, gender, and address were noted. Extracted teeth were placed in a normal saline solution at room temperature until use. Teeth were randomly divided into two groups (n=30) with different veneer preparation designs. Conventional preparation and novel preparation (modified form of feather edge preparation by adding 2 slots 2x2 in diameter at the mesial and distal side of the tooth) Impression of prepared veneer was taken with light body and heavy body (hydrophilic vinyl poly-siloxane material, ISO 4823 TYPE 0) impression material and models made. Composite (light cure, radiopaque Nano-hybrid, IvoclarvivadentAG9494 Schaan) material was used for preparing veneer designs for restoration, according to the instructions of manufacturers. The polymerization of material was taken by curing unit (light emitting diode LED) in the wavelength range 400-500nm for 30 sec. Resin-based luting cements were used for bonding of veneer to prepare tooth structure. Thereafter, all specimens were arranged vertically. The fracture strength test was carried out at a constant speed of 5mm/min. Force was applied at the 45° angle to the long axis of the tooth. Fracture strength of all the teeth was noted at the given fracture load and data were statistically analyzed.The collected data were analyzed in the statistical program SPSS version 26. Mean ± standard deviation was evaluated for quantitative variables like the age of the patient. Frequency and percentage were calculated for qualitative variables like the patient's gender and the success of the veneers in terms of fracture. The independent sample T-test was applied to compare the fracture resistance between the two procedures.A

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surgical instrument was used to analyze the tooth. a) Novel veneer preparation (black arrows show slots on mesial & distal walls). b) the Depth of the slot is 2mm (using the Williams probe), c) the Depth of the prepared tooth is 0.5 mm (using the Williams probe) and d) Direct composite veneer preparation and cementation (Figure 1).

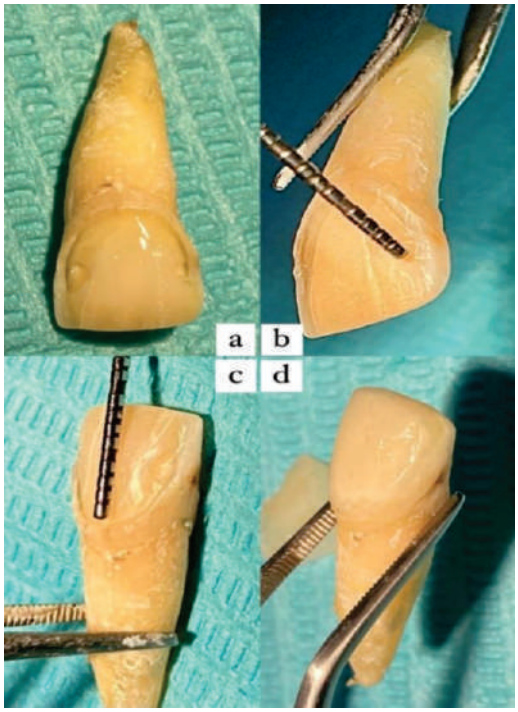

Figure 1: Analysis of Tooth

A fracture load was applied (cyclic/stress path triaxial system) in a testing machine (universal testing machine Instron 4301)(Figure 2).

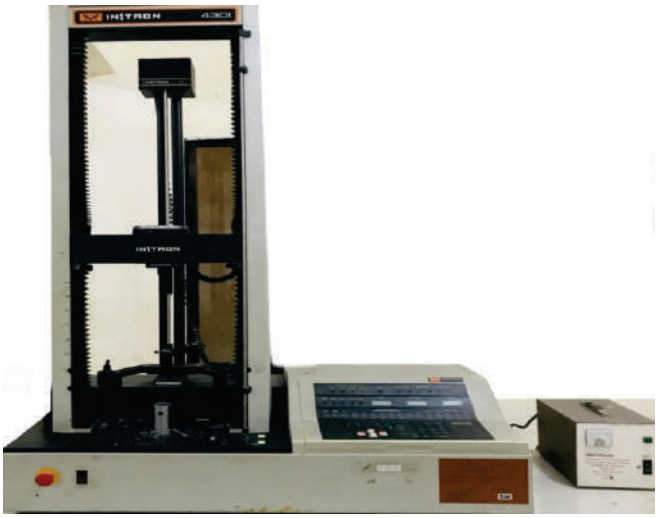

Figure 2: Instron 4301 Universal Testing Machine (Used for Tensile, Compression, Shear, Fatigue, Friction, and Flex Tests)

Novel prepared tooth cemented with indirect composite veneer by placing under Universal Testing Machine (Instron 4301)(Figure 3).

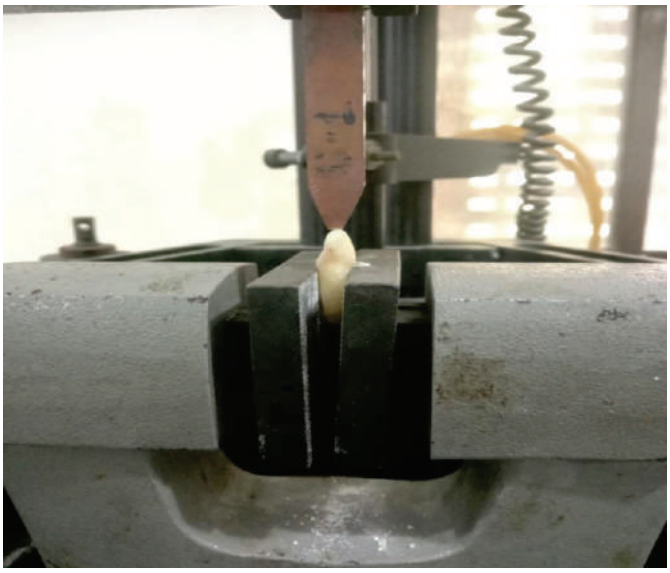

Figure 3: Novel Prepared Tooth Cemented with Indirect Composite Veneer Placed Under Universal Testing Machine (Instron 4301).

RESULTS

Results show the demographic parameters of the study participants. In this study, a total of 60 patients were divided equally between the two groups (n=30 for each). In this study, the demographic characteristics and fracture resistance of composite veneers with different preparation designs were compared between two groups of participants. The average age of participants in the Conventional Veneer group (n=30) was 52.46 ± 15.05 years, while the Novel Veneer group (n=30) had a slightly younger mean age of 46.03 ± 17.9 years. Regarding gender distribution, the Conventional Veneer group consisted of 13 males (43%) and 17 females (57%), whereas the Novel Veneer group included 14 males (46%) and 16 females (54%) as presented in table 1.

Table 1: Demographic Parameters of the Study Participants

Parameters	Conventional Veneer	Novel Veneer
Age	52.46 ± 15.05	46.03 ± 17.9
Gender		
Male	13 (43%)	14 (46%)
Female	17 (57%)	16 (54%)

Results show a comparison of fracture load between the two groups. In terms of fracture load performance, the Conventional Veneer group had an average fracture load of 309.7 ± 126.3 N, compared to 335.5 ± 136.14 N in the Novel Veneer group. Although the Novel Veneer group showed a higher mean fracture load, this difference was statistically significant (P=0.005) as presented in table 2.

Table 2: Comparison of Fracture Load between Two Groups

Parameters	Conventional Veneer (n=30)	Novel Veneer (n=30)	p-Value
Fracture Load	309.7 ± 126.3	335.5 ± 136.14	0.005

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DISCUSSION

Different research works have examined the effect of preparation design on composite veneers' fracture strength. For example, Huang *et al.*, concluded that a veneer preparation with a chamfered design provided significantly higher fracture resistance than that of a beveled edge design [17]. As well, other researchers have examined the factors influencing the fracture strength of veneered teeth such as the depth of tooth preparation and the design of the veneering margin [18]. A recent study by Nabil *et al.*, highlighted that the new preparation methods including slot and groove can increase the bonding between the composite material and the tooth as the effect was on the fracture resistance [19].They mentioned the mean fracture load was about 100 N for the conventional preparations but the novel slot preparations were 107 N or more.These results indicate that it is possible to alter the mechanical properties of the composite veneer through changes in the preparation design. In another study, Tribst *et al.*, established that other factors that enhance the fracture resistance include; veneer thickness and also the right curing process [20].This is in line with information from other studies, which showed that veneer failure load dependency is determined by the preparation design, the choice of composite material,and bonding techniques. The study contributes to the existing knowledge about the effects of preparation design on the fracture toughness of the composite veneer.This study did not find any difference in the fracture load between the Conventional and Novel Veneer preparation groups, although the resulting trend supports the outcomes of prior studies. For instance, Bommanagoudar *et al.*,concluded from their study published in 2019 that preparation designs which they concluded as novel preparations including slot and groove configurations offered improved fracture resistance than the conventional chamfer preparations [21]. In their study they compare the mean fracture load of conventional designs being 320 N with novel preparations of 345 N, the latter was significantly different from the former at $p<0.05$. This indicated that although integration of new designs may increase fracture resistance, the actual value added cannot be measured easily due to sweeping elements of material, depth of preparation, adhesive methods, etc. Likewise, Zlatanovska *et al.*, compared the role of various preparation geometry on the fracture load of the composite veneer and noted that a chamfer preparation had significantly less fracture resistance of about 295 ± 110 N than that of slot preparation that was 355 ± 120 N ($p<0.05$) [22].The results of these analyses imply that in some cases, new geometries may reduce stress concentrations and distribute forces evenly across the veneer which could likely enhance the material's longevity. However, the present study in terms of mean Fracture load is at conventional preparations=309.7 ± 126.3 N and novel preparations=335.5 ± 136.14 N, in which the difference is statistically significant p-value=0005. Since the data obtained in this study displayed a high standard deviation, it might be the variability inherent to the samples that has affected the significance of the results compared to the specific design used in the study Thus, the effect of this novel design may be less pronounced or specific to certain circumstances than was previously described in other articles. Additional research also shows that the fracture toughness of veneers may be sensitive to bonding methods and curing duration.The study of Nagi *et al.*, revealed that better curing and higher bonding enhanced the fracture resistance with values higher than 360 N in the optimized methodologies irrespective of the preparation modality [23].Their results also suggest that the design of preparation might not always be sufficient to produce enhanced fractural toughness disregarding procedural effects. Further individual specific parameters, like prognosis in tooth shape and biting force, probably may affect the veneer preparation as demonstrated by Juncar *et al.*, [24]. In their work, they stated that design novelty described better patient outcomes inasmuch younger patients and patients with high force generation capacity attained means of 350N of fracture loads instead of 310 N in their counterparts; Old patients and low force generation patients as evidenced by the patient demographics and variability.

CONCLUSIONS

It was concluded that increasing fracture resistance of the prepared materials with new preparation designs trends in the present study, however, the obtained data was statistically significant between two groups (p-value0.005).The study has revealed Novel veneer preparation to be more reliable and consistent the Conventional Veneer.

Authors Contribution

Conceptualization: FURQ
Methodology: RZ, SH, SA, JM
Formal analysis: RZ,
Writing review and editing: FURQ, GR, NK, SA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

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Patient Satisfaction Level and its Various Determinants in a Tertiary Care Hospital of Peshawar, Pakistan: A Cross-Sectional Study

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ABSTRACT

Patient satisfaction is a surrogate metric for quality of services provided by healthcare system. **Objective:** To assess patient satisfaction and associated factors in a major tertiary care hospital. **Methods:** This cross-sectional study was conducted at the Lady Reading Hospital (LRH), Peshawar, Pakistan. All patients admitted for indoor treatment for at least 2 days were enrolled through multistage sampling technique. Patients admitted to ICU, CCU, psychiatry or oncology wards and COVID-19 positivity were excluded. Patient satisfaction level was assessed with the Patient Satisfaction Questionnaire (PSQ)-18. Likert scale was utilized to evaluate patients' response, where the scale ranged from 1 (complete dissatisfaction) to 5 (complete satisfaction). Patients with cumulative score of ≥ 50 were classified as satisfied. **Results:** Of the total 384 patients enrolled, 199 (~52%) patients were older than 45 years of age, while the female to male ratio was 1.25:1. The number of satisfied patients was significantly higher than dissatisfied patients (313 vs. 71: $p < 0.01$). Highest number of patients were satisfied with the domain D7 (i.e., accessibility and convenience: 72%), followed by domain D6 (i.e., time spent with the doctor: 69%). A minimum number of patients were satisfied with the domain D2 (i.e., technical quality: 53%). Moreover, higher number of patients with age ≥45 years (~86%), female gender (~86%), with bachelor education (~100%) and patient admitted to medical and allied wards (~86%) expressed satisfaction. **Conclusion:** Overall, the study showed a high patient satisfaction at LRH, Peshawar.

INTRODUCTION

Patient satisfaction is a vital metric in evaluating services of healthcare system and eliminating claims of malpractice. Studies focused on evaluating patient satisfaction are increasing worldwide [1]. Healthcare providers are always interested in providing cost-effective facilities that can deliver superior and efficient medical services [2]. While a patient is in the hospital, the workflow coordinates both the safety of hospital staff and patients, and the quality of care they receive [3, 4]. To move forward, hospital administrators and healthcare professionals should consider key factors including the quality of patient care and specialty practices that create competency and capacity. Achieving such goals requires the inclusion of several categories [5]. For example, by analyzing patient data, hospital management can find deeper correlations and data patterns that can lead to improvements in medical procedures and practices [6]. With the pioneering work started in 1950s, patient satisfaction (and improving quality of patient care) is still an ongoing process, and comprise of a combination of technical, interpersonal and organizational aspects [7, 8]. The following six areas have been identified to cover the entire structure of the

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healthcare system: Healthcare and medical care should be knowledge-based, safe, patient-centered, effective, equitable and timely [9]. Moreover, many parameters have been related to patient satisfaction, including physician's knowledge, attitudes, and responsiveness, wait times, patient privacy, infrastructure, cleanliness, cost-effectiveness, length of visit, access to medication, counseling and clinical procedures [10]. Patients also differ in their satisfaction with various aspects of the healthcare system, depending on their personal quality of life is influenced by the environmental, social, and informational aspects that affect patient satisfaction with the services availed [11]. Recently, the focus of healthcare system has shifted to the quality of services. In this regard, a simple and direct approach is to ask patients themselves to rate the healthcare system [12]. As a result, the notion of patient satisfaction surveys with questionnaires on the quality of care was established [13]. Patient satisfaction being a key indicator for characterizing the healthcare system and the services it provides to the public, this cross-sectional study was designed to evaluate patient satisfaction and related factors at the Lady Reading Hospital (LRH) Peshawar, Pakistan [14].

It is hypothesized that this study will identify areas of improvement and provide suggestions to elevate the level of patient satisfaction.

METHODS

This study was designed as a cross-sectional, single hospital-based study for a duration of 6 months (Jan-June, 2024), was carried at the LRH Peshawar, Khyber Pakhtunkhwa. Patients admitted for indoor treatment at all departments of LRH, Peshawar for at least 2 days were eligible for enrollment in this study. The terms "ward admission" and "indoor treatment" were used interchangeably. All indoor patients were categorized based on their admission into either Surgical and Allied Wards or Medical and Allied Wards. Patients admitted for indoor treatment were included in the study; however, those with specific conditions were excluded to maintain the study's focus on general inpatient satisfaction. Exclusion criteria included patients admitted to the Intensive Care Unit (ICU) or Coronary Care Unit (CCU), as well as those in psychiatry and oncology wards. Additionally, patients who tested positive for COVID-19 or Congo virus were not enrolled. Pediatric and nursery ward patients were also excluded to ensure the study targeted adult inpatients capable of independently assessing their satisfaction with healthcare services. The OpenEpi Calculator- an open-source statistical tool- was used to estimate the sample size for this study. It was assumed that the data collected in this study will follow the Chi square statistics. Keeping a 50% patients proportion in MTI, statistical significance at 0.05 and a 95% confidence level, the required sample size was estimated, which came out to be 384. After ensuring the eligibility, patients were enrolled through multistage consecutive sampling technique. The Patient Satisfaction Questionnaire (PSQ)-18 was utilized to quantify the level of patient satisfaction [15]. The PSQ-18 consisted of 18 questions, pertaining to the following seven domains: general satisfaction (2 items), interpersonal manner (2 items), time spent with the doctor (2 items), technical excellence (4 items), economical aspects (2 items), accessibility and convenience (4 items). Many items of the PSQ-18 use the term health screening, which is indicative of the particular diagnostic and/or therapeutic services availed at the hospital. The patient response to each of these question was recorded on the Likert scale, ranging from 1 (completely unsatisfied) to 5 (completely satisfied). The Likert scale is a psychometric scale is widely involved in research that employs questionnaires [16]. Thus, the satisfaction level of each patient was reflected by a cumulative score of 18-90. The patient was regarded as dissatisfied if PSQ-18 cumulative score < 50 and satisfied if PSQ-18 cumulative score ≥ 50 [17]. The SPSS (version 21) was used for data storing, sorting, manipulation and analysis. Statistical significance was determined using chi-square test. The study was approved by the Ethical Board of Khyber Medical University, Peshawar (Reference No. KMU/IPHSS/Ethics/2023/PS/0171). Patients were enrolled up on agreement for participation, and signing a written consent.

RESULTS

The PSQ-18 consists of two major parts, including patient demographics and patient satisfaction regarding different domains of the healthcare system. Table 1 presented a summary of patient demographics. Of the total 384 patients enrolled, 214 (~ 55.7 %) were female patients. The majority of patients were of old age. Specifically, 199 (~ 51.82%) patients belonged to the age of more than 45 years. There were 58 (~ 15.1 %) patients younger than 25 years. The number of patients in 26-25 years and 36-45 years were 63 (16.41 %) and 64 (16.67%), respectively. Education level assessment of the patients revealed that maximum number of patients did not studied at all, followed by the school education (up to grade 10). The number of patients with intermediate, bachelor and graduate level education were 36 (9.4%), 16 (4.2%) and 02 (0.5%), respectively. The distribution of patients in the medical and allied and surgical and allied was 81.5 and 18.5%, respectively.

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Table 1: Demographics of Patients included in this Study

Variables	Category	Frequency (%)
Gender	Male	170 (44%)
	Female	214 (56%)
Age (Years)	< 25	58 (15%)
	26-35	63 (16%)
	36-45	64 (17%)
	>45	199 (52%)
Education	No Education	283 (74%)
	School	47 (12%)
	Intermediate	36 (9.5%)
	Bachelor	16 (04%)
	Master	02 (0.5%)
Ward of Admission	Medical and Allied	313 (81.5%)
	Surgical and Allied	71 (18.5%)

Overall, 82.81% (313/384) of the patients were satisfied with the services and facilities at the hospital, while a relatively small number of patients (71/384: 17.19%) were not satisfied. Table 2 showed stratified data on patient satisfaction in each of the seven domains of PSQ-18. The highest number of patients (277: 72%) were satisfied with domain D7 (Accessibility and Convenience), followed by 264 (69%) in the D6 (Time Spent with Doctors). Likewise, 257 (67%) and 248 (65%) patients were satisfied with D5 (Financial Aspects) and D3 (Interpersonal Manner), respectively. The lowest patient satisfaction was observed D2 (202: 53%).

Table 2: Satisfaction and Dissatisfaction Frequencies in Various Domains of PSQ-18

Domain of PSQ-18	Satisfaction Frequency (%)	Dissatisfaction Frequency (%)
D1: General Satisfaction	207 (54%)	177 (46%)
D2: Technical Quality	202 (53%)	182 (47%)
D3: Interpersonal Manner	248 (65%)	136 (35%)
D4: Communication	233 (61%)	151 (39%)
D5: Financial Aspects	257 (67%)	127 (33%)
D6: Time Spent with Doctors	264 (69%)	120 (31%)
D7: Accessibility and Convenience	277 (72%)	107 (28%)

Table 3 presented the minimum, maximum, median and mean Likert score for each of the 18 items of the PSQ-18. Majority of the median and mean scores are equal to or above 3, suggested that majority of the patients were satisfied.

Table 3: Satisfaction and Dissatisfaction Frequencies against Each Item of PSQ -18

Questions	Mini Score	Max Score	Median Score	Mean Score	Standard Deviation
Screening received was perfect	1.00	5.00	3	3.21	1.34
Dissatisfied with the screening received	1.00	5.00	3	2.71	1.14
Screening station provided appropriate medical care	1.00	5.00	4	3.77	1.03
I wonder about the correctness of diagnosis	1.00	5.00	3	3.03	1.37
During screening, the staff carefully examined everything	1.00	5.00	4	3.78	1.15
Doubts about the capability of my doctor	1.00	5.00	3	2.89	1.29
Staff acted busy and impersonal	1.00	5.00	3	2.66	0.98
Screening staff was very friendly and courteous	1.00	5.00	4	3.83	1.10
Staff explained the health screening	1.00	5.00	2	2.17	1.16
Doctor sometime ignored me	1.00	5.00	3	3.00	1.31
Screening availed without financial set back	1.00	5.00	3	3.25	1.05
Affordability of health screenings	1.00	5.00	3	2.74	1.13
The screening staff was in too much hurry	1.00	5.00	3	3.08	1.27
Time spent on screening was adequate	1.00	5.00	2	2.27	1.18
Ease in access to the health screenings	1.00	5.00	4	3.59	1.10
Waiting period for the health screening	1.00	5.00	3	2.79	1.14
Getting appointment for health screenings was hard	1.00	5.00	3	2.96	1.05
Health screenings is offered whenever needed	1.00	5.00	3	3.06	1.27

The gender-wise data stratification for patient satisfaction showed significantly higher satisfaction level for female patients compared to male patients (86.5% vs. 78.2%, $p < 0.05$: Figure 1a). Age stratification (Figure 1b) illustrated highest satisfaction rate of 86.4% for older patients of age > 45 years. Focusing on the younger patients, differences in satisfaction rate were seen (<25, 26-35, 36-45 years: 87.9%, 77.8%, 71.9%, $p > 0.05$). However, these differences were not statistically significant ($p > 0.05$). Moreover, it was found that the patients admitted to the medical and allied wards were more satisfied than those admitted to the surgical and allied wards (86.26% vs. 67.61%, $p < 0.01$: Figure 1c). Moreover, the impact of patients' education levels on satisfaction levels was also evaluated (Figures 1d and 2b). Educational attainment was categorized into five levels: No Education, School, Intermediate, Bachelor, and Master. The correlation between education level and satisfaction was analyzed, with results further stratified by gender to assess variations between male and female patients. Overall, satisfaction among patients with no, school, intermediate, bachelor and master education was 82.69% (234/283), 85.11% (40/47), 75% (27/36), 100% (16/16) and 50% (1/2), respectively (Figure 1d).

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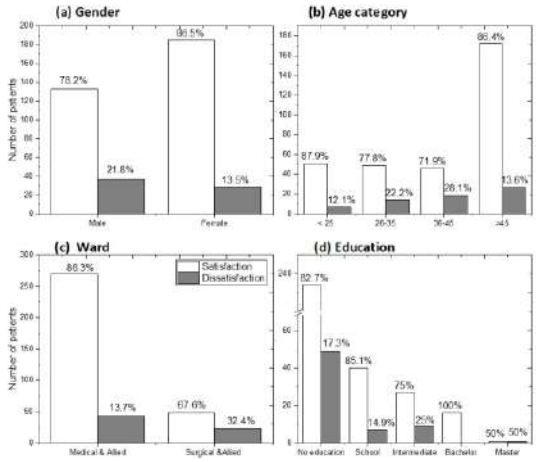

Figure 1: Patient satisfaction evaluated using PSQ-18. The number of satisfied patient (x-axis) were stratified on the basis of (a) gender, (b) age, (c) ward admission, and (d) education. White and gray bars represent satisfied and dissatisfied patients, respectively.

Patient satisfaction was further carried out in sub-groups. Results for satisfaction of male and female patients with respect to their age, level of education and ward admission are shown in Figure 2. For the male group, patients older than 45 years of age (87.37%) (Figure 2a), with no or school education (83.3% and 100%) (Figure 2b) and those admitted to medical and allied wards (90.21%) (Figure 2c) showed higher satisfaction. This trend was slightly different in the female patient group. Specifically, the satisfaction rate in female patients older than 45 years of age was 85.58% (Figure 2a), in patients with no or bachelor education was 100% and 82.29% (Figure 2b) while 82.94% in female patients admitted to medical and allied wards (Figure 2c).

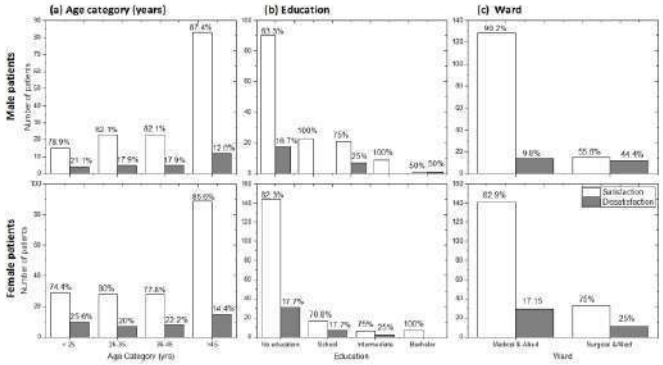

Figure 2: Patient satisfaction stratified for male (top row) and female (bottom row) patients. Sub-stratification of male and female patient groups was performed with respect to their age (a), education (b), and ward admission (c). White and gray bars represent satisfied and dissatisfied patients, respectively.

DISCUSSION

The PSQ-18 is a valuable tool that allows to measure patients' satisfaction in a variety of domains [15]. This analyses revealed that the number of satisfied patient was significantly higher than the number of dissatisfied patients (318 vs. 66: $p < 0.01$). Expanding the analysis to each question of PSQ-18 showed that mean satisfaction score in 16/18 question was 60% or above. Nonetheless, the results presented herein may be viewed in the light of their inherent shortcomings. First, a cross-sectional study only provides a snapshot of the prevailing situation. Due to the design of the PSQ-18, the responses may seem subjective. Moreover, although this study enrolled the required number of eligible participants, a multicenter study would provide better understanding of the factors related to patient satisfaction. Such analyses can potentially reveal more heterogeneity and other substructures in the patient experience, leading to a deeper understanding of patient satisfaction and related factors. The quality of care has been divided into the professional quality of the service providers and the functional quality perceived by the patients [18]. Professional quality refers to the level of competence in providing professional medical skills and making accurate diagnoses. On the other hand, patient-perceived quality means not only medical competence but also functional quality, which indicates how well the patient's needs (equipment, facilities, physical environment, communication, etc.) are met [19]. Based on this, it was found that patients with poor medical outcomes were satisfied. In addition, poor quality of care has been reported when patients feel they have not received an accurate diagnosis and treatment [20]. The quality of medical services depends heavily on the criteria that patients use to make their own assessments. As patient needs become more diverse and demanding, subjective assessment from the patient's perspective is considered more important for assessing the quality of medical care [21]. Previous studies investigating patient satisfaction have concluded that the attitude of the medical staff (i.e., doctors, nurses, paramedics) had the highest satisfaction value, while other studies emphasized the importance of trust in the competence and attention of doctors on the quality of care [22]. The existing literature also suggests that the interpersonal communication, soft skills and behaviors of the healthcare provider towards patients are directly related to patient satisfaction [23]. Meanwhile, hospital facilities seemed to be the area that should be given more attention to improve inpatient satisfaction, in line with other findings [24]. Moreover, longer waiting times are negatively correlated with patient satisfaction of the service provider. Studies have also shown that elderly patients, low-income patients, female patients, patients with only primary education and patients in rural areas have high levels of satisfaction [25]. Interestingly, the results of this study are consistent with previous studies on age and educational level in several developed countries. Beside international studies, several authors have investigated and evaluated patient satisfaction in Pakistan [26]. These studies have assessed patient satisfaction from various angles, such as the provision of free medicine in public hospitals, comparing satisfaction between public and

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private hospitals, patient satisfaction at the medical, surgical, outdoor, registration departments, etc. For example, Farid *et al.*, studied the correlation between provision of free medicines to the patients in public hospitals and patient satisfaction in a cohort of 384 patients.The results showed that 59.4% of the respondents agreed that prices of medicines in Pakistan are low, 49.7% denied the availability of free medicines, 58.3% responded lack of proper information about drug utilization, while 63.3% respondents agreed that non-registration of pharmacies leads to substandard medicines [27]. Farooq *et al.*, compared patient satisfaction attending the Combined Military Hospital (CMH), Lahore and Jinnah Hospital, Lahore.The results revealed that patient satisfaction was significantly better ($p = 0.03$) at CMH in six (out of seven) domains studied [28]. Likewise, the patient satisfaction among private and public hospitals of Islamabad have also been compared in a multi-center cross-sectional study. The score of time spent by the doctor with the patient, communication, and convenience was significantly higher ($p < 0.05$) in private hospitals [29]. A recent study assessed patient satisfaction in tertiary care hospitals of Peshawar, with the use of PSQ-18. The results showed a higher patients satisfaction level for private hospitals compared to public hospitals (i.e., 96% vs. 86%) [30]. Similar comparison of patient satisfaction for public and private hospitals of Lahore has also been reported [31]. Moreover, patients' satisfaction with the utilization of different ambulance services at LRH Peshawar has been evaluated.

CONCLUSIONS

This study assessed the satisfaction of admitted patients and associated factors using PSQ-18 at the LRH, Peshawar, Pakistan. Overall, majority of the patients expressed satisfaction. Data stratification demonstrated that the highest number of patients were satisfied with the domain D7, followed by domain D6, while minimum number of patients were satisfied with the domain D2. Moreover, higher number of patients older than 45 years, patients of female gender, patients with bachelor education and patient admitted to medical and allied ward expressed satisfaction. The same trend of patient satisfaction was found among male patients and female patients separately.

Authors Contribution

Conceptualization: MW, KR, MP
Methodology: MP, JS, SMN
Formal analysis: MP, JS
Writing, review and editing: MW, KR, MP, JS, SMN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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Case Study

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A Rare Case of Metachromatic Leukodystrophy (MLD)

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ABSTRACT

Metachromatic Leukodystrophy (MLD) is a rare hereditary lysosomal storage disorder affecting white matter, often leading to progressive motor and cognitive decline. This case presents a 30-month-old child from a consanguineous family who was in good health four months prior but initially exhibited mild symptoms of diarrhea and a chest infection before rapidly deteriorating neurologically. The delayed diagnosis highlights the challenges of early recognition in resource-limited settings. MRI findings, coupled with genetic testing, confirmed the diagnosis, emphasizing the importance of integrating neuroimaging with molecular diagnostics. This case underscores the critical need for prenatal and newborn genetic screening, particularly in populations with a high prevalence of consanguinity, to facilitate timely interventions and improve disease management. Early recognition and a multidisciplinary approach, including genetic counseling, can enhance outcomes and inform future preventive strategies for at-risk families.

INTRODUCTION

Metachromatic leukodystrophy (MLD) is an unusual medical condition that results in the decline of myelin owing to the genetic alterations in the arylsulfatase A (ARSA) gene located on chromosome 22q13.33 [1]. Additionally, the PSAP (Prosaposin) gene plays a crucial role in sphingolipid metabolism by encoding saposin proteins, which are necessary for ARSA activation, further highlighting the genetic complexity of MLD pathogenesis in this case. Mutations in the ARSA gene, such as point mutations, deletions, and splice site alterations, can lead to reduced or absent arylsulfatase A enzyme activity, resulting in metachromatic leukodystrophy (MLD). Several mutations in the ARSA gene, such as c.465+1G>A and c.1283C>T, have been identified to cause severe phenotypic expressions of MLD. These mutations interfere with proper enzyme folding and activity, leading to a significant buildup of sulfatides. Additionally, genes like SUMF1 have been shown to modulate ARSA enzyme functionality, offering insights into the broader genetic mechanisms influencing disease progression [2]. In the central nervous system this conglomeration leads to continuous myelin damage [3]. MLD leads to demyelination, resulting in symptoms namely

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reduced motor function, spastic tetraparesis, ataxia, muscle spasms, optic atrophy, and cognitive decline [4]. Motor diminution is a primary attribute in metachromatic leukodystrophy (MLD) [5]. The global incidence of metachromatic leukodystrophy (MLD) is estimated to range from approximately 1 in 40,000 to 1 in 160,000 live births, with prevalence varying across different regions [6]. In Pakistan, the cultural tradition of consanguineous marriages contributes to a higher incidence of inherited metabolic disorders like MLD compared to other regions globally [7]. The precise prevalence of MLD in Pakistan remains unclear; however, research indicates a significant association between consanguinity and genetic disorders, underscoring the importance of genetic counseling and screening in managing these conditions [8].

This case study of a thirty months old boy explained the clinical manifestation, diagnostic issues, and management strategies.

Case Presentation

This was a case of a thirty months old boy of a consanguineous parent. The case was presented at Saidu Group of Teaching Hospital, Swat, Khyber Pakhtunkhwa, in the Pediatric/Neurology Department for detailed evaluation and management. His parents explained that he was living a normal life for first four months of his life. The child was admitted to the hospital with diarrhea and chest infection. During his stay in the hospital, the child also experienced regression of developmental milestones and myoclonic jerks. Initially, gross motor movement impacted. With time, the child was unable to sit and eventually, head control compromised. The child admitted to the pediatric neurology ward on basis of aforementioned complaints for further investigation. An Electroencephalogram (EEG) conducted on the patient showed a burst suppression pattern, which is a sign of abnormal brain activity. Additionally, the Magnetic Resonance Imaging (MRI) scan revealed abnormal signals in the cerebral periventricular and deep white matter, which were symmetric and confluent on both sides (Figure 1). Based on these findings, genetic testing was recommended, which revealed a homozygous variant in the ARSA gene. In addition to palliative care, the patient was encouraged to carry on with physiotherapy sessions to maintain as much mobility as possible. The physician informed the parents of the child that the prognosis suggests a continued decline, and existing treatments have proven unsatisfactory. The patient was observed from January 2022 to June 2022. The patient was under observation for three months, followed by a confirmed diagnosis of MLD. Over the next three months, the child's condition progressively worsened, leading to recurrent episodes of aspiration pneumonia. Ultimately, the child passed away due to complications arising from the disease.

MRI and Genetic Analysis Findings

There is confluent bilateral symmetrical homogenous intermediate high T2 and FLAIR abnormal signal in the cerebral periventricular and deep white matter predominantly in the frontal, parietal, and occipital lobes. Relatively faint T2/FLAIR high signal is also noted in the splenium of the corpus callosum which otherwise appears unremarkable. The subcortical white matter and basal ganglia including internal capsule are spared. Normal gray matter signal is demonstrated. No overt brain parenchymal hypertrophic or atrophic changes are seen. Bilateral cerebellopontine angles are grossly unremarkable. Orbits, optic nerves, and chiasm appear unremarkable. There is no evidence of acute intracranial hemorrhage or infarct. No intracranial space-occupying lesion or radiological signs of raised intracranial pressure are seen. There is no evidence of hydrocephalus. The basal cisterns are unremarkable. There is no radiological evidence of cortical migration anomalies or cortical dysplasia. Medial temporal morphology is also bilaterally grossly symmetrical and unremarkable. No gross cranial vault lesion is demonstrated. Metachromatic leukodystrophy (MLD) was confirmed to follow an autosomal recessive inheritance pattern in this case. Genetic analysis identified a homozygous pathogenic variant in the ARSA gene in the affected child. Both parents were initially advised to undergo genetic screening, which would have confirmed them as heterozygous carriers of the same ARSA mutation. However, they declined the screening. The consanguineous nature of the family likely contributed to the inheritance of this genetic disorder, highlighting how such familial connections can increase the risk of autosomal recessive diseases like MLD.

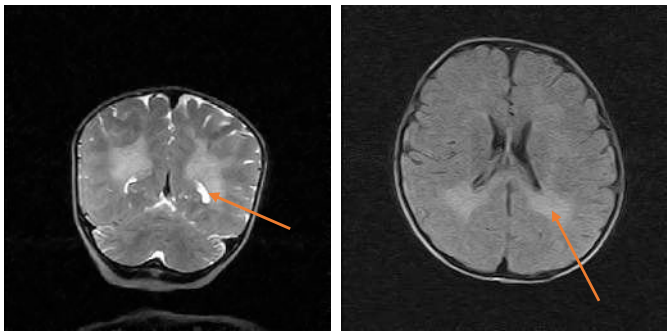

Figure 1: Arrows Showed Symmetrical Confluent Bilateral Abnormal Cerebral Periventricular White Matter

DISCUSSION

Metachromatic Leukodystrophy (MLD) is an uncommon neural degeneration disorder owing to lack of an enzyme called arylsulfatase A. This case study highlighted several critical aspects of MLD that demand further exploration. Firstly, the clinical presentation of our patient harmonized

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with typical features of MLD that reinforced the importance of recognizing nuanced neurological symptoms early in the disease course. The consanguinity of the parents in this case served as a vital factor in the hereditary basis of MLD. This highlighted the importance of extra vigilance in clinical assessments, particularly in cases with a family history of consanguinity. This experience highlighted the call for a multidisciplinary strategy by integrating medical examination, neuroimaging studies, and genetic testing to achieve accurate and timely diagnosis. Other cases from the literature review are presented below. This case aligned typical MLD features, emphasized the importance of early recognition of neurological symptoms. The consanguinity of the parents was crucial in the hereditary basis of MLD, highlighted the need for extra vigilance in such families. This experience underscored the value of a multidisciplinary approach, combining medical examination, neuroimaging, and genetic testing for an accurate diagnosis. Patil SA and Maegawa GH studied 18 MLD patients similarly found a high incidence of consanguinity and abnormal electromyography, supported the importance of genetic assessment in MLD diagnosis [9]. The MRI findings in this case, showed bilateral symmetrical T2 and FLAIR hyperintensities in the periventricular and deep white matter with sparing of subcortical U-fibers, aligned with those reported in the study of an adult Chinese MLD patient with ARSA mutations. Both cases highlighted the characteristics white matter changes in MLD, though our case also notes involvement of the splenium of the corpus callosum [10]. These findings reinforced the importance of genetic analysis in diagnosing MLD and the need for counseling in consanguineous families. The MRI findings demonstrated symmetrical periventricular and deep white matter hyperintensities on T2 and FLAIR imaging, align with the patterns used in the "Metachromatic Leukodystrophy: A Scoring System for Brain MR Imaging Severity" study to assess disease severity [11]. While this case did not employ a formal scoring system, the characteristic distribution of white matter changes highlighted the utility of MRI in evaluating and potentially monitoring disease progression. Incorporating such scoring systems could enhance the objective assessment and tracking of MLD in future cases. A study conducted by Kubaski *et al.*, investigated the quantification of sulfatides levels in the amniotic fluid supernatant. This study highlighted the significance of timely assessment for detecting MLD. This study proved that sulfatide quantification in amniotic fluid can facilitate in a rapid and correct identification of MLD patients [12]. Rastogi *et al.*, emphasized the critical role of MRI in diagnosing MLD, highlighting classical features such as gait and psychiatric disturbances alongside characteristic brain MRI findings, including the tigroid pattern. The case aligned with these clinical features and underscored the importance of MRI in identifying the characteristic white matter changes associated with MLD [13]. Kehrer *et al.*, describe the intrinsic pathway of gross motor regression in late-stage infantile MLD, noting that all patients exhibit severe impairment of gross motor coordination. This aligned with this case study findings, as the patient in this case also experienced a complete loss of gross motor functions, highlighted the progressive nature of motor deterioration in MLD and its impact on quality of life [5]. There are no approved treatments for MLD; however, Shaimardanova *et al.*, discussed in diagnosis, modeling and treatment approached for MLD that the majority of patients treated with symptomatic therapies, included antiepileptic drugs for seizures, muscle relaxants, physiotherapy, and anti-inflammatory treatments like prednisolone or IVIg. Symptomatic treatment given in this case to the patient [4]. While these treatments provide symptom relief, they do not address the underlying cause or pathogenesis of the disease and have no impact on the progression rate. Gene therapy and integrated gene and cell interventions are emerging as promising approaches for treating MLD. Biffi *et al.*, in 2008 highlighted the limitations of HSCT in MLD treatment and discussed emerging gene therapy approaches using autologous hematopoietic stem/progenitor cells to enhance arylsulfatase-A expression, potentially overcoming HSCT-related challenges [14]. Mallikarjun *et al.*, in 2011 presented a rare case of Metachromatic Leukodystrophy (MLD), emphasizing its clinical variability and diagnostic challenges [15]. This aligned with Politi *et al.*, in 2018, who highlighted the frequent misdiagnosis of MLD, underlining the need for improved diagnostic accuracy [16]. In support of this, Borges *et al.*, in 2020 discussed the difficulties in early pediatric diagnosis, which is crucial for timely intervention [17]. Fumagalli *et al.*, in 2021 provided a longitudinal perspective on 45 patients, offering insights into disease progression and treatment outcomes [18]. Gieselmann and Krägeloh-Mann in 2010 further updated the understanding of MLD pathophysiology and therapeutic advancements, which are critical for evolving treatment strategies [19]. Historically, MacFaul *et al.*, in 1982 reviewed 38 cases, laying the foundation for contemporary studies by detailing early clinical presentations and disease trajectories. Together, these studies contribute to a comprehensive understanding of MLD, reinforcing the importance of early detection and advancing therapeutic approaches [20].

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CONCLUSIONS

Pakistan has a low incidence of Metachromatic Leukodystrophy (MLD), highlighting the need for improved diagnostic and management strategies. This case underscores the importance of early screening, particularly in consanguineous families, for timely diagnosis and intervention. The rapid neurological decline of a 30-month-old child emphasizes the necessity of genetic counseling, targeted screening, and proactive management. MRI and genetic analysis confirmed the diagnosis, demonstrating the value of integrating neuroimaging with molecular techniques. Strengthening diagnostic capabilities, multidisciplinary care, and genetic counseling in Pakistan can improve patient outcomes and contribute to the literature on MLD in low-incidence regions.

Authors Contribution

Conceptualization: BK, SK, HBM, AQ
Methodology: BK, SK, HBM, AQ
Formal analysis: IA, AN, BK, SK, HBM, AQ
Writing, review and editing: IA, AN, BK, SK, HBM, AQ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

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Systematic Review

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Role of Serum and Dietary Vitamins A and E in Pulmonary Function and Chronic Obstructive Pulmonary Disease: A Systematic Review

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern, significantly affecting quality of life and healthcare systems. Oxidative stress plays a critical role in COPD pathogenesis. Vitamins A and E, as fat-soluble antioxidants, are believed to support pulmonary health, but studies report conflicting findings. **Objectives:** To evaluate associations between serum and dietary concentrations of vitamins A and E with pulmonary function parameters and COPD risk or severity, this systematic review was conducted. **Methods:** A systematic search was conducted in PubMed, EMBASE, Scopus, and the Cochrane Library. Of 150 screened studies, 22 met the inclusion criteria, comprising cross-sectional, cohort, case-control, and interventional designs. Studies assessing serum or dietary levels of vitamins A and E and their relationships with pulmonary function parameters (FEV_1, FVC, FEV_1/FVC) were included. **Results:** Higher serum and dietary vitamin A levels were linked to improved FEV_1 and FVC and reduced COPD prevalence. Vitamin E intake was associated with a lower risk of COPD, though its effects on lung function varied. Supplementation studies showed mixed results, with vitamin E benefits observed mainly when combined with other antioxidants. Effects were more pronounced in smokers and individuals with systemic inflammation. **Conclusions:** Vitamins A and E, particularly vitamin A, may support pulmonary health and slow COPD progression. However, inconsistencies highlighted the need for well-designed trials to confirm their role in COPD management.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent respiratory symptoms and airflow limitation due to structural changes in the airways and alveoli. It is a leading cause of morbidity and mortality worldwide, contributing significantly to healthcare costs and reducing patient quality of life. According to the World Health Organization (WHO), COPD accounted for approximately 3.5 million deaths in 2021, representing 5% of all global fatalities [1]. A key driver of COPD pathogenesis is oxidative stress, which arises from an imbalance between pro-oxidants and antioxidants [2]. This imbalance leads to heightened inflammation, airway remodelling, and progressive deterioration in pulmonary function. Highly Reactive Oxygen Species (ROS), either directly or through lipid peroxidation by-products, amplify inflammatory responses, exacerbating COPD progression [3, 4]. Given the central role of oxidative stress, antioxidant

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micronutrients such as vitamins A and E have been proposed as potential protective factors for lung function. Vitamins A and E are essential fat-soluble antioxidants involved in pulmonary health. Vitamin A plays a crucial role in maintaining epithelial integrity, immune defense, and tissue repair, while vitamin E protects cell membranes from oxidative damage and inflammatory processes [5]. Several studies suggest that these vitamins may mitigate oxidative damage, reduce inflammation, and improve pulmonary function. However, evidence regarding their role in COPD remains inconsistent, with conflicting findings from observational and interventional studies [6]. Prior research has examined the associations between serum concentrations and dietary intake of these vitamins with pulmonary function markers (FEV_1, FVC, FEV_1/FVC ratio) and COPD outcomes. Some studies report significant benefits, showing that higher serum and dietary vitamin A levels correlate with improved lung function and lower COPD prevalence [7, 8]. Conversely, others fail to establish significant associations, particularly for vitamin E [9, 10]. These discrepancies may arise due to variations in study design, population characteristics, and adjustments for confounding factors such as smoking and inflammation. Despite these findings, major gaps remain in the literature [11, 12]. While prior systematic reviews have explored the impact of individual micronutrients on COPD, there has been no comprehensive review assessing both serum and dietary levels of vitamins A and E together in relation to pulmonary function and COPD risk [13, 14]. Furthermore, the potential role of these vitamins in COPD prevention and disease progression remains unclear. To address these gaps, this systematic review aims to synthesize available evidence on the associations between serum and dietary levels of vitamins A and E with pulmonary function and COPD severity.

By consolidating findings from observational and interventional studies, this review seeks to clarify the role of these micronutrients in pulmonary health and provide evidence-based guidance for future research and clinical practice.

METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews PRISMA) figure 1 guideline. A comprehensive literature search was performed in PubMed, EMBASE, Scopus, and the Cochrane Library to identify relevant studies investigating the association between serum and dietary concentrations of vitamins A and E with pulmonary function and COPD. Observational studies, including cross-sectional, cohort, and case-control designs, as well as interventional studies, were included if they evaluated the relationship between serum or dietary concentrations of vitamins A and E with pulmonary function parameters such as forced expiratory volume in one second (FEV_1), Forced Vital Capacity (FVC), and FEV_1/FVC ratio. The review considered studies involving adults aged 18 years and above, irrespective of smoking status or comorbidities, with or without a COPD diagnosis. The primary outcomes assessed included pulmonary function parameters (FEV_1, FVC, and FEV_1/FVC ratio). Secondary outcomes included COPD prevalence, incidence, severity, exacerbation rates, and all-cause or disease-specific mortality. Only studies published in English between 2001 and 2024 were included to ensure a comprehensive analysis of recent and relevant literature. Studies from all geographical regions were considered to enhance the generalizability of findings across diverse populations and healthcare settings. A systematic search strategy was employed using Medical Subject Headings (MeSH) terms and Boolean operators to combine keywords related to vitamins A and E, pulmonary function, and COPD. References were imported into EndNote for duplicate removal. Titles and abstracts were screened based on predefined eligibility criteria, followed by a full-text review of relevant studies. Two independent reviewers conducted the screening and data extraction. Any discrepancies were resolved through discussion, and a third reviewer was consulted when consensus could not be reached. A tracking log was maintained to document all disagreements and their resolutions. A standardized data extraction form was used to collect information on study characteristics, including publication year, study design, sample size, population demographics, exposure assessment (serum or dietary vitamin levels), and lung function parameters. Data on potential confounders, such as smoking, dietary intake, and systemic inflammation (e.g., Hs-CRP), were also extracted. The Newcastle-Ottawa Scale (NOS) was used to assess the quality and risk of bias in observational studies, focusing on sample selection, comparability of study groups, and outcome assessment. Two independent reviewers evaluated each study for bias, and any disagreements were resolved through discussion or consultation with a third reviewer. A narrative synthesis was performed to summarize key findings, study quality, and methodological limitations. Findings were reported in accordance with PRISMA guidelines, and a PRISMA flow diagram (figure 1) was included to illustrate the study selection process. This PRISMA flow diagram outlines the systematic process of study identification, screening, eligibility assessment, and final inclusion in the review. The diagram details the number of records retrieved from multiple databases (PubMed, EMBASE, Scopus, and Cochrane), the removal of duplicates, the exclusion criteria applied during screening, and the final number of studies included in the review (n = 22). In figure 1 the PRISMA flow diagram outlined the study selection process, detailing the identification, screening, eligibility, and inclusion phases.

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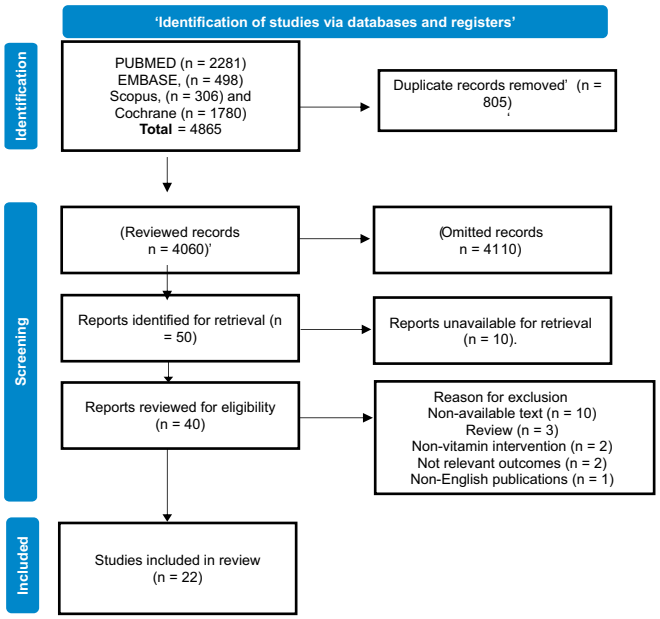

Figure 1: Flow Diagram: PRISMA Flow Diagram for Study Selection Process

RESULTS

Overview of Included Studies

This systematic review analysed 22 studies, comprising observational (cross-sectional, cohort, case-control) and interventional research designs. These studies examined the relationships between serum and dietary concentrations of vitamins A and E with lung function parameters and COPD prevalence or severity. Sample sizes ranged from 30 to over 7,000 participants, primarily including adults aged 40 years and older. While several studies focused specifically on smokers and individuals with COPD, others assessed general populations.

Associations between Vitamins A and E and Pulmonary Parameters

FEV_1: Several studies identified a significant correlation between higher circulating vitamin A levels and improved FEV_1 measurements. Individuals in the highest quartile of vitamin A intake consistently demonstrated better FEV_1 values compared to those in the lowest quartile. One study reported a 15% increase in FEV_1 among participants with optimal vitamin A levels. Findings on vitamin E were inconsistent. While some studies suggested a protective role, particularly in smokers, others found no significant association between vitamin E intake and FEV_1.

Forced Vital Capacity (FVC): Serum retinol concentrations were strongly associated with FVC in several studies. Underweight COPD patients exhibited notable FVC improvements following dietary interventions involving vitamin A.While higher vitamin E intake was linked to modest improvements in FVC, the evidence was less robust compared to vitamin A.

FEV_1/FVC Ratio: The FEV_1/FVC ratio, a key diagnostic marker for obstructive lung diseases, was positively associated with higher dietary intake of vitamins A and E. One cross-sectional study reported a 0.05-point increase in the FEV_1/FVC ratio among individuals with the highest antioxidant vitamin consumption.

Residual Volume (RV) and Total Lung Capacity (TLC): Studies evaluating vitamin E supplementation, either alone or in combination with antioxidants such as vitamins C and D, showed improvements in RV and TLC. One study found a 10% increase in TLC after three months of supplementation.

Inspiratory Reserve Volume (IRV): IRV significantly improved in studies where COPD patients supplemented with vitamins A and E, alongside other antioxidants. These findings suggest potential benefits for respiratory muscle strength.

Peak Expiratory Flow Rate (PEFR): Smokers and COPD patients with higher oxidative stress tended to have lower PEFR values. However, increased dietary intake of vitamins A and E was linked to enhanced PEFR outcomes, suggesting a possible role in mitigating oxidative stress-induced lung impairment.

COPD Prevalence and Severity

Several studies reported that higher dietary intake of vitamins A and E was associated with a lower risk of developing COPD. Individuals in the highest quintile of vitamin E intake had a significantly reduced COPD risk compared to those with the lowest intake. Vitamin A intake also showed potential benefits in reducing COPD-related mortality and slowing disease progression, as observed in long-term dietary studies.

Findings from Supplementation Studies

Interventional studies examining vitamin E supplementation produced mixed results. While some studies reported a protective effect against lung function decline, others found no significant improvements in spirometric measures or disease progression.

Heterogeneity and Variability

The included studies displayed variability in methodologies, including differences in:

Vitamin level measurements (serum vs. dietary intake).

COPD definitions and diagnostic criteria.

Adjustment for confounding factors such as smoking history, dietary patterns, and inflammation markers.

Subgroup Analyses

Subgroup analyses revealed that the benefits of higher vitamin intake were more pronounced in smokers and individuals with high levels of systemic inflammation. These findings suggest that certain populations may derive greater benefits from antioxidant-rich diets.

Summary of Findings

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Overall, higher levels of vitamins A and E, whether through serum concentrations or dietary intake, were associated with improved pulmonary function and a lower prevalence of COPD. However, the variability in study findings and methodological differences highlight the need for further research to confirm these associations and establish clear clinical guidelines.

The table 1 summarized key studies that have examined the effects of vitamins A and E on pulmonary function parameters, COPD prevalence, and related mortality, highlighting study design, population, key findings, and reported effect types.

Table 1: Studies Investigating the Role of Vitamins A and E in Pulmonary Health and COPD Outcomes

S.No.	Study	Year	Design	Sample Size	Study Location	Study Setting	Key Findings
1	Noh and Baik [13]	2024	Cross-Sectional	2,005 adults aged ≥40 years	South Korea	Population-based survey	Higher serum vitamin A levels were positively correlated with improved FEV_1 and a lower prevalence of COPD,particularly among individuals with reduced hs-CRP levels. In contrast, no significant association was observed for vitamin E.
2	Salo *et al.* [15]	2022	Prospective Cohort Study	29,133 adults	Multiple European countries	National health survey	Higher serum concentrations of vitamins A and E were linked to a lower risk of respiratory disease incidence and mortality. Specifically, participants in the highest quartile of serum vitamin A had a 33% lower risk of respiratory disease-related mortality compared to those in the lowest quartile. Likewise, higher serum vitamin E levels were associated with a 20% reduction in respiratory disease mortality.
3	Førli *et al.* [16]	2002	Cross-Sectional	71 patients with advanced pulmonary disease (42 underweight, 29 normal-weight)	Norway	Hospital-based study	Serum retinol (vitamin A) concentrations were significantly associated with BMI and weight gain following dietary intervention. Baseline serum retinol levels demonstrated a positive correlation with FVC and FEV_1. Among COPD patients, tocopherol (vitamin E) levels were higher in underweight individuals compared to those with normal weight. Additionally, tocopherols were linked to improved lung gas exchange in individuals with respiratory disorders other than COPD.
4	Ng-Blichfeldt *et al.* [17]	2017	Experimental study	Human lung tissue samples	Netherlands	Laboratory experiment	A deficiency in vitamin A impairs angiogenesis, contributing to the failure of lung regeneration in emphysema.
5	McKeever *et al.* [18]	2002	Cross-sectional	NHANES III participants	United States	National health database	Elevated serum levels of vitamins A and E were independently associated with higher FEV_1 levels, suggesting a potential beneficial effect on lung health.
6	Russo K *et al.* [19]	2006	Cross-sectional	38 patients with stable cystic fibrosis	United States	Clinical setting	Serum vitamin A concentrations showed a significant correlation with various aspects of lung function, while no notable associations were observed for vitamins D and E.

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7	Hong *et al.* [20]	2018	Cross-sectional	1,002 adults, taking (A, C, and E) supplements for two months improved pulmonary functions in smokers.	South Korea	Community-based study	Dietary antioxidant vitamins A and E were positively associated with lung performance, with variations observed based on gender and smoking status.
8	Tian *et al.* [21]	2024	1,261 COPD patients	1,261 COPD patients	China	Hospital setting	Higher dietary intake of vitamin E was linked to reduced mortality rates from all causes and chronic lower respiratory diseases in individuals with COPD.
9	Liu *et al.* [22]	2023	Cross-sectional	4,706 adults	United States	Population-based survey	A higher dietary intake of vitamin E was significantly associated with a lower risk of developing COPD.
10	Christensen *et al.* [23]	2016	quasi-experimental study	33 patients. Participants received supplements of (E, C, and D) A dosage regimen of (200 IU daily), (250 mg on alternate days), and (50,000 IU weekly) was administered. for a duration of 12 weeks.	Iran	Clinical trial	In pulmonary fibrosis, supplementation with vitamins D, C, and E significantly improved lung function parameters, including increases in FEV_1, IRV, RV, and TLC. However, in the context of COPD, supplementation with vitamin C and E alone did not show a notable impact on respiratory performance.
11	Cassano *et al.* [24]	2015	Randomized Controlled Trial	1,641 men	Iran	Clinical trial	Long-term supplementation with selenium and/or vitamin E had no significant impact on lung function, as measured by FEV_1 and FEF_{30-70}. However, selenium supplementation helped slow the decline in FEF_{30-70} among current smokers.
12	Schünemann *et al.* [25]	2001	Cross-sectional	'1,616 aged 35 to 79 years	United States	Community-based intervention	Individuals in the lowest quartile of serum antioxidants, including vitamins C and E, retinol, and carotenoids, consistently had lower FEV_1% and FVC% compared to those with higher antioxidant levels. Multiple linear regression analysis revealed significant associations between FEV_1% and the concentrations of vitamin C, vitamin E, β-cryptoxanthin, lutein/zeaxanthin, β-carotene, and retinol,even after adjusting for relevant covariates.
13	Prasad, R.R. and M.I. Sushil [26]	2021	Cross-sectional comparative study	30 smokers and COPD patients, 30 non-smoker controls	India	Hospital-based study	Pulmonary function test parameters, including FVC, FEV_1, FEV_1/FVC ratio, and PEFR, were significantly lower in smokers and COPD patients compared to non-smoker controls. Additionally, serum malondialdehyde (MDA) levels, a marker of oxidative stress,were notably higher in smokers and COPD patients. The decline in lung function correlated with elevated MDA levels, emphasizing the detrimental impact of oxidative stress and cellular imbalance caused by excess reactive oxygen species on respiratory performance.

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14	Baybutt R.C. and A. Molteni [27]	2007	Randomized Controlled Trial	617 elderly nursing home residents	United States	Elderly care facility	A daily dose of 200 IU of vitamin E supplementation had no significant effect on reducing the overall occurrence of respiratory tract infections. However, participants receiving vitamin E supplementation experienced a lower incidence of common colds compared to those given a placebo.
15	Caram *et al.* [28]	2015	Cross-sectional	50 COPD patients and 50 controls	Brazil	Hospital-based study	COPD patients had lower serum vitamin A levels compared to controls. However, no significant association was found between serum vitamin A levels and systemic inflammatory markers. Additionally, sputum vitamin A levels showed a negative correlation with neutrophil counts.
16	Tug *et al.* [29]	2004	Prospective Study	24 COPD patients during acute exacerbation and stable periods, 23 healthy controls	Turkey	Hospital-based study	During acute exacerbations, COPD patients had significantly lower serum vitamin A and E levels compared to controls. Although vitamin A levels increased during stable periods, they remained lower than those of the controls. Malondialdehyde (MDA) levels, an indicator of oxidative stress, were elevated in COPD patients during both acute and stable periods.These findings suggest that supplementation with vitamins A and E may provide potential benefits for COPD patients.
17	Wu *et al.* [30]	2007	Randomized, placebo-controlled trial	35 patients with stable COPD	China	Clinical trial	Supplementation with vitamin E (200 mg/day and 400 mg/day) or vitamin C (250 mg/day) for 12 weeks had no significant effect on the average level of endogenous DNA breakages. However, H_2O_2-induced DNA breakages were reduced by 45%, 59%, and 52% in the groups receiving 400 mg of vitamin E, 200 mg of vitamin E, and vitamin C, respectively.
18	Kim *et al.* [31]	2020	Cross-sectional	4,060 participants from the Korea (KNHANES)	South Korea	Population-based study	The study examined the relationship between dietary nutrient intake and COPD prevalence. Findings indicated that higher consumption of certain nutrients, including vitamins A and E, was associated with a lower prevalence of COPD. Specifically, adequate intake of these vitamins may have a protective role in reducing the risk of developing COPD.
19	Cai W *et al.* [32]	2016	Cross-sectional	20 COPD patients and 20 healthy controls	France	Clinical setting	COPD patients had significantly lower physical activity levels, higher depression scores, and a reduced Fat-Free Mass Index (FFMI) compared to healthy controls. Nutritional analysis showed that COPD patients had lower total caloric intake and reduced vitamin E consumption. Additionally, individuals with lower FFMI had significantly lower vitamin E intake than those with normal FFMI. These findings suggest that nutritional

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							deficiencies, particularly in antioxidants, may play a role in the pathophysiology of COPD.
20	Li H *et al.* [33]	2017	Cross-sectional	20 patients with COPD, 20 with asthma-COPD overlap syndrome (ACOS), 20 with bronchial asthma, and 20 healthy controls	Japan	Hospital-based study	Plasma levels of antioxidant nutrients, including vitamins A and E, were significantly lower in individuals with COPD and ACOS compared to healthy controls. Additionally, lung function parameters such as FEV_1 and FVC were reduced in these patients, indicating impaired pulmonary function.These findings suggest that decreased antioxidant nutrient levels may contribute to the pathophysiology of COPD and ACOS.
21	Rodríguez *et al.* [34]	2016	Case-control	50 institutionalized elderly individuals (25 with COPD and 25 healthy controls)	Spain	Institutionalized elderly care	COPD patients consumed fewer fruits and had a lower dietary antioxidant capacity compared to healthy controls. They also exhibited significantly lower serum levels ofvitamin C and vitamin E. Individuals with serum α-tocopherol levels below 14.1 µmol/L had a **6.43-fold higher** risk of developing COPD compared to those with higher levels. These findings suggest that diets deficient in antioxidants, particularly vitamins C and E, may be associated with an increased risk of COPD in the elderly.
22	Joshi *et al.* [35]	2015	Prospective cohort	7,106 participants '(325 COPD patients and 6,781 at-risk individuals) from the KoGES cohort	South Korea	Cohort study	Higher dietary intake of vitamins C and E was associated with a reduced risk of developing COPD. Individuals with the highest vitamin C intake had a **34% lower risk** (OR = 0.66, Ptrend = 0.03), while those with the highest vitamin E intake had a **44% lower risk** (OR = 0.56,Ptrend = 0.05) compared to those with the lowest intake levels. Additionally, increased consumption of these vitamins was significantly linked to improved lung function, as reflected in higher FEV_1 and FVC values. The protective effects were more pronounced in men. Although the study also assessed vitamin A (retinol) intake, no significant association was found with COPD risk.

In figure 1, Heatmap illustrating the relationships between vitamins A and E with pulmonary function parameters (FEV_1, FVC, FEV_1/FVC ratio), COPD prevalence, and mortality across 22 studies. The color intensity represents the number of studies supporting each effect type (positive, mixed, or no effect) for each vitamin. The evaluation of vitamins A and E highlights a direct connection between these micronutrients and pulmonary health indicators, including FEV_1, FVC, FEV_1/FVC ratio, COPD prevalence, and mortality rates. An analysis of 22 studies indicates that vitamin A positively influences lung function, with **9 studies reporting improvements in FEV_1, 7 studies showing benefits for FVC, and 5 studies demonstrating enhancements in the FEV_1/FVC ratio. While most findings support the role of vitamin A in maintaining pulmonary health, some studies present conflicting results. Similarly, research on vitamin E suggests beneficial effects, with **8 studies reporting improvements in FEV_1, 6 studies showing progress in FVC, and 4 studies indicating positive changes in the FEV_1/FVC ratio. Furthermore, vitamin E demonstrated a stronger association with a lower prevalence of COPD, as **5 studies found a reduced risk compared to 4 studies for vitamin A. Regarding mortality, vitamin E was linked to reduced deaths in three studies, whereas vitamin A showed a mortality reduction in two studies. Overall, evidence suggests that vitamins A and E

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contribute to respiratory health by potentially lowering COPD risk and supporting lung function. However, conflicting findings indicate that individual factors, dietary habits, and environmental influences may shape their effects. Further research, particularly well-designed long-term studies, is necessary to establish the precise role of these vitamins in pulmonary health and COPD prevention.

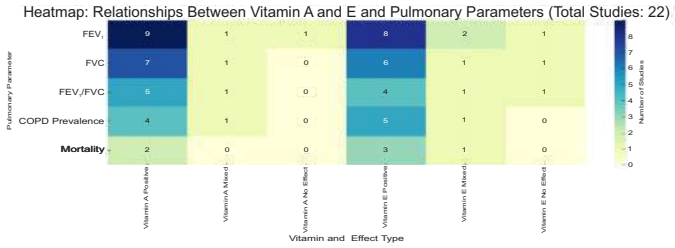

Figure 1: Heatmap of Vitamin A and E Effects on Pulmonary Function and COPD

DISCUSSION

The studies analyzed in this review provide valuable insights into the potential roles of vitamins A and E in pulmonary health. However, several methodological limitations must be considered when interpreting these findings. Many studies employed cross-sectional designs, which capture a snapshot in time but do not establish causality. Noh and Baik in (2024) demonstrated an association between serum vitamin A levels and improved FEV_1, yet the cross-sectional nature of the study precludes conclusions about causality [13]. According to Pinto *et al.*, in (2022) intermittent fasting has been shown to influence gut microbiota and body composition, which may have implications for pulmonary health [14]. In contrast, longitudinal studies, such as the prospective cohort by Salo *et al.*, in (2022), offer stronger evidence by tracking changes over time; however, they remain susceptible to confounding factors that could influence both vitamin levels and pulmonary outcomes [15]. The methods used to assess vitamin intake and serum concentrations varied across studies, leading to inconsistencies. Dietary intake assessments often relied on self-reported food frequency questionnaires, which are subject to recall bias and may not accurately reflect true intake. Additionally, serum vitamin levels can be influenced by factors such as recent dietary intake, absorption rates, and individual metabolism, contributing to variability. For example, the study by Kim *et al.*, in (2021) investigated dietary vitamin intake and COPD prevalence, but its reliance on self-reported dietary data introduces a risk of measurement bias [11]. According to Førli *et al.*, in (2002), serum levels of vitamins A and E have been linked to weight and lung function in patients with advanced pulmonary disease, suggesting a potential role in respiratory health [16]. This is further supported by findings that inadequate retinoid-driven angiogenesis may contribute to impaired lung regeneration in emphysema, highlighting the importance of vitamin A in lung repair mechanisms by Ng-Blichfeldt *et al.*, in (2017) [17]. Several studies did not adequately control for confounding variables, such as smoking status, environmental exposures, socioeconomic status, and comorbidities, all of which significantly impact pulmonary function and disease prevalence. While McKeever *et al.*, in (2002) found that higher serum levels of vitamins A and E were linked with better lung function, their study design does not exclude potential unmeasured confounders [18]. Segregation in healthcare settings has been explored from the perspectives of young patients and their parents, shedding light on its psychological and social impacts. In parallel, dietary antioxidant vitamins have been found to influence lung function, with variations observed based on gender and smoking status, emphasizing the need for targeted nutritional interventions in respiratory health [19, 20]. Similarly, Tian *et al.*, (2024) reported an association between dietary vitamin E intake and lower mortality in COPD patients, but smoking history and comorbid conditions were not fully accounted for, potentially biasing the results [21]. Dietary intake of vitamin E has been associated with chronic obstructive pulmonary disease (COPD) events, highlighting its potential role in disease management. Additionally, COPD outpatients face risks of both unplanned weight loss and obesity, further emphasizing the importance of nutritional assessment and intervention in this patient population [22, 23]. Distinguishing between the effects of dietary intake and supplementation of vitamins presents another challenge. Some studies focused on dietary sources, while others examined the impact of supplementation, leading to potential differences in bioavailability and physiological effects. For example, the randomized controlled trial by Cassano *et al.*, in (2015) investigated long-term supplementation with selenium and/or vitamin E and found no significant improvement in lung function, suggesting that supplementation may not mirror the benefits observed with dietary intake [24]. Similarly, the study by Christensen *et al.*, in (2022) showed that supplementation with vitamins D, C, and E improved lung function in pulmonary fibrosis but failed to show significant benefits in COPD patients [23]. Serum levels of antioxidant vitamins, including vitamins C and E, retinol, and carotenoids, have been linked to pulmonary function in the general population, emphasizing the role of oxidative stress in lung health [25-27]. Comparisons of spirometric parameters and serum malondialdehyde levels further support the impact of oxidative stress in actively smoking COPD patients [28, 29]. The association between vitamin A and emphysema underscores the importance of adequate vitamin intake in preventing lung deterioration [30-32].

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Additionally, inflammatory markers and antioxidant vitamin levels in COPD patients highlight the interplay between oxidative stress and inflammation. Studies also reveal variations in antioxidant levels during acute exacerbations and stable periods, reinforcing the importance of nutritional support in disease management [33, 34]. Supplementation with vitamins C and E has shown potential benefits, while nationwide population-based studies confirm the link between dietary nutrient intake and COPD severity. Further investigations into antioxidant biomarkers and dietary interventions continue to shape the understanding of COPD progression and management [35]. Previous systematic reviews and meta-analyses have explored the relationship between antioxidant vitamins and pulmonary health, yielding mixed results. A systematic review by Tsiligianni IG and van der Molen T in (2010) concluded that higher intakes of vitamins A, C, D, and E were associated with improved COPD outcomes, including reduced symptoms and exacerbations [36]. However, this review also highlighted the lack of robust Randomized Controlled Trials (RCTs) to confirm these associations [37-40]. In contrast, the large randomized Women's Health Study investigated vitamin E supplementation (600 IU every other day) and found a modest 10% reduction in chronic lung disease risk, suggesting a potential protective effect of vitamin E Yousaf N *et al.*, in (2010) [41]. However, the generalizability of these findings remains uncertain, as the study population was limited to women. A meta-analysis by Varraso *et al.*, in (2007) emphasized the benefits of a diet rich in antioxidants, including vitamins A and E, in reducing COPD risk [42]. The review suggested that while observational studies support this association, there is a pressing need for well-designed RCTs to establish causality. Similarly, Seyedrezazadeh E *et al.*, in (2019) reported that low dietary intake of antioxidants was linked to increased COPD risk in elderly patients [43]. Despite some consistency across these studies, the lack of standardized methodologies and differences in participant characteristics contribute to conflicting findings. While many observational studies suggest a protective effect of vitamins A and E, supplementation trials have produced inconsistent results, highlighting the complexity of vitamin metabolism, absorption, and interaction with other dietary components. This systematic review integrates findings from both observational and interventional studies, providing a comprehensive overview of the potential impact of vitamins A and E on pulmonary health. However, several limitations should be acknowledged. The inclusion of both cross-sectional and cohort studies introduces variability in study quality and strength of evidence. Differences in how dietary intake and serum vitamin levels were measured across studies may contribute to inconsistencies. Studies reporting positive effects may be more likely to be published, whereas negative findings may be underreported. Many studies did not fully control for critical factors such as smoking, inflammation markers, and dietary patterns, which may influence results. While current evidence suggests a potential beneficial relationship between vitamins A and E and pulmonary health, significant methodological limitations and inconsistencies exist among studies. The variability in study designs, measurement techniques, and confounder adjustments complicates the ability to draw definitive conclusions. Comparisons with previous systematic reviews and meta-analyses reinforce the need for more rigorous, large-scale RCTs to clarify the precise roles of these vitamins in respiratory health. Future research should: Standardize measurement methods for vitamin intake and serum levels. Implement well-controlled longitudinal studies to establish causality. Explore the differential effects of dietary intake versus supplementation. And investigate the influence of genetic and environmental factors on vitamin metabolism and lung function.

CONCLUSIONS

This systematic review underscored the crucial roles of vitamins A and E in enhancing pulmonary function and reducing COPD prevalence and severity. While vitamin A consistently demonstrated benefits, the evidence for vitamin E remained variable, warranting further investigation. These findings support incorporating antioxidant-rich foods into dietary recommendations to promote respiratory health. However, further research is needed to establish clear clinical and public health guidelines.

Authors Contribution

Conceptualization: AI[1]
Methodology: SS, AI[1]
Formal analysis: SS
Writing, review and editing: SS, AI[1], SHAS, AI[2], MHAK, NP

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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