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Smog Exposure and Its Consequences for Human Health in Lahore

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Lahore is a metropolitan city and the capital of Punjab province, which is acclaimed due to historical sites, cultural diversity, and economic involvement. It is under this vibrant city atmosphere that there is a serious environmental and health concern of smog. Smog can be defined as a continuous presence of smoke, dust, and chemical contaminations suspended in humid air, which are very dangerous to human health. Research has reported its influence on respiratory and cardiovascular outcomes in residents, and thus an urgent need to intervene. [1-3]

The smog is a complex of various pollutants, among which are: particulate matter (PM_{2.5} and PM₁₀), nitrogen oxides (NO_x), sulfur dioxide (SO₂), ozone (O₃), and volatile organic compounds. These are due to motor vehicle emissions, industrial operation, construction, brick kiln, crop burning and burning of solid waste. Lahore has a high traffic density with intersections like Kalma Chowk, Liberty Roundabout, and Thokar Niaz Baig showing the level of vehicular pollution, and the industrial estates significantly add to the ambient pollutant concentrations. The issue is aggravated by winter months when the meteorological conditions promote the accumulation of smog. [4]

The long-term effects of being exposed to smog are health-threatening. Fine particulate matter is very deep-seated and aggravates asthma, chronic obstructive pulmonary disease (COPD), and pneumonia. There is also epidemiological evidence that smog contributes to cardiovascular risks (such as ischemic heart disease and stroke) with systemic inflammation and oxidative stress. The children, the elderly and socioeconomically disadvantaged populations are more affected at the expense of the rest of the population and this is part of greater environmental health disparities. The hospital surveys in Lahore verify that residents regularly cough, wheeze, have eye irritation, and shortness of breath at the time of high pollution, and the effects of this on daily living and well-being can be measured. [5,6]

The smog crisis in Lahore needs a well-coordinated, evidence-based approach. Although the health risks are well documented, the lack of appropriate interventions is due to the ineffective regulation enforcement, industrial lobby, and poor awareness among the population. The main actions that should be taken are the strong air quality monitoring, the tightening of the industrial emission regulations, the propagation of cleaner transportation use, the development of the urban green areas, and the educational campaigns among people to make them more aware and precondition the protective behavior. [2,5]

Smog is a critical health crisis affecting respiratory and cardiovascular well-being. Policymakers, industry, and citizens must take urgent measures to reduce emissions, improve air quality, and protect vulnerable populations. While actions like stricter emission controls, cleaner transportation, and public awareness are essential, extensive urban plantation and afforestation should be central to the strategy. Planting trees along roads, industrial zones, and residential areas can trap pollutants, absorb harmful gases, and enhance air circulation. Prioritizing green belts and urban forests alongside other interventions will help Lahore effectively combat smog, improve ecological resilience, and safeguard the health of its citizens.

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Original Article



Comparison of Intralesional Triamcinolone and Intralesional Verapamil in the Treatment of Keloids

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ABSTRACT

An imbalance between synthesis and degradation of collagen and the extracellular matrix leads to keloid formation. Inadequately treated keloids lead to significant physical and emotional distress. **Objectives:** To compare the mean reduction of the Vancouver Scar score in patients with keloids after 3 months of treatment with intralesional triamcinolone versus intralesional verapamil. **Methods:** This parallel group, single blind randomized controlled trial was performed at the dermatology department, Nishtar Hospital, Multan, from April 2025 to September 2025. Sixty patients aged 10–50 years with keloids (1–5 cm, duration <5 years, baseline Vancouver score ≥ 5) were enrolled. Exclusion criteria were pregnant and lactating women, positive family history of keloids, conditions of acromegaly, and congestive heart illnesses. Group A (n=30) received intralesional verapamil monthly, and Group B (n=30) received intralesional triamcinolone acetate (40 mg) monthly until keloid flattening or for three months. Vancouver scores were assessed at 16 weeks (four weeks post-treatment), and data were analyzed using SPSS version 23.0. Mean $\pm$ SD was recorded for quantitative and frequencies and percentages for categorical data. An independent sample t-test was used for numerical comparison at 5% significance level. **Results:** The mean age was 28.6 ± 7.9 years with 58.3% males. The baseline Vancouver score was 8.7 ± 1.7 , improving to 4.9 ± 1.5 after treatment. The triamcinolone group had a lower score (4.0 ± 0.7) and greater reduction (4.6 ± 1.2) than the verapamil group (5.9 ± 1.5 ; reduction 2.9 ± 0.8 ; $p < 0.001$). **Conclusions:** Overall, intralesional triamcinolone acetate is clearly more effective than verapamil in reducing keloid severity.

INTRODUCTION

A keloid is an aberrant growth of scar tissue that extends beyond the initial scar boundaries, usually at the place of skin distortion. After excision, it has a high chance of recurring and rarely regresses on its own [1]. Although keloids can develop anywhere on the body, they most frequently appear on the cheeks, shoulders, earlobes, and sternum. Minor skin injuries like ear piercing, abrasions, tattoo making, burns, and injection injury can cause keloids [2, 3]. Acne formation or chickenpox infection can also be the reasons, and sometimes keloids spontaneously appear in the sternal area in individuals who are prone to develop this condition [4]. Because of their high likelihood of recurrence, keloids are difficult to treat. Keloids can be prevented and treated with compression bandages,

silicone gel, intralesional corticosteroids, cryotherapy, radiation, intralesional interferon injection, bleomycin, and laser therapy [5, 6]. The most widely used corticosteroid for treating keloids is intralesional triamcinolone acetate, which promotes collagen and fibroblast degeneration while inhibiting fibroblast growth factors and the inflammatory process in the wound [7]. Another anti-hypertensive medication used to treat keloids is verapamil. When applied intralesionally, it promotes the breakdown of collagen by decreasing the production of extracellular collagen and increasing the synthesis of collagenases [8]. The rationale of current research is to compare the effect of intralesional triamcinolone and verapamil in patients presenting with keloid in our local setting. The local results



will direct us towards the most appropriate treatment of keloids by selecting the suitable drug. Adequate treatment will reduce significant emotional and physical distress in patients. We hypothesized that the mean reduction in Vancouver Scar Score will be higher in the triamcinolone acetanide group compared to verapamil after three months of treatment. This study aimed to compare the mean reduction of the Vancouver Scar score in patients with keloids after 3 months of treatment with intralesional triamcinolone versus intralesional verapamil.

METHODS

This parallel group, single blind (outcome assessor) randomized controlled trial (Registry No. NCT06897969) was conducted at the dermatology department, Nishtar Hospital, Multan, after approval from the institutional ethical review board of Nishtar Medical University, Multan (Ref. No. 21467/NMU) over a period of six months from April 2025 to September 2025. Patients of either sex, 10 - 50 years of age, keloid size of 1-5 cm on any site of the body, duration < 5 years, and a Vancouver scar score of ≥ 5 at enrolment were consecutively included in the study after informed consent. Pregnant or lactating mothers, with a family history of keloids, acromegaly, and congestive cardiac diseases, were excluded from the study. Patient characteristics like age, gender, obesity, diabetes mellitus, and duration of keloid (months) were recorded. The baseline Vancouver Scar Score was recorded for all the participants before starting treatment. The Vancouver Scar scale assesses four parameters of vascularity, pigmentation, pliability, and height (mm). The total score ranges from 0–13. The patients were randomly divided into group A and group B. The random sequences were generated manually using the lottery method, and allocation concealment was ensured through the use of sequentially numbered, sealed, opaque envelopes prepared by a person not involved in recruitment or data collection. Patients in group A were administered intralesional verapamil. One ml (2.5 mg) of intralesional verapamil injection was administered once a month. Patients in group B were given Intralesional Triamcinolone acetanide (40mg) monthly. The injections were administered with an insulin syringe with a 27-gauge needle. Patients and doctors administering the injections were not blinded due to the different colors of the injections. Treatment continued till the keloids were flattened or total duration of three months. Vancouver score was assessed at 16 weeks after randomization (4 weeks after completion of treatment) by the consultant dermatologist who was not aware of the assigned treatment. A minimum sample size of 60 participants was calculated using online OpenEpi software, taking a mean Vancouver scar score reduction of 2.50 ± 0.72 in verapamil

and 4.35 ± 0.70 in triamcinolone treatment groups [9] at 80% power, 5% significance level and 1.85 mean difference of Vancouver scar score between the treatments. SPSS version 23.0 was utilized for data analysis. Descriptive statistics in the form of mean $\pm$ SD for numerical data and frequency and percentages for categorical data were measured. Independent sample t-test and chi-square test were used for numerical and categorical comparisons between the groups, respectively. P-value < 0.05 was taken as significant.

RESULTS

In the overall group of 60 participants treated for keloids, the mean age was 28.6 ± 7.9 years, with a slight male predominance (58.3% male and 41.7% female). Approximately 31.7% (n=19) of the patients were classified as obese, and 25% (n=15) had diabetes mellitus. The keloids had been present for an average of 14.6 ± 5.9 months before treatment, and the baseline severity as measured by the Vancouver Score was 8.7 ± 1.7 . Following a three-month treatment period, the overall Vancouver Score improved significantly, decreasing to 4.9 ± 1.5 . The mean reduction in Vancouver scar score was 3.7 ± 1.3 . The demographic characteristics and baseline Vancouver score were comparable between the Verapamil and Triamcinolone treatment groups. After three months, the mean Vancouver score was significantly lower in Triamcinolone compared to the Verapamil treatment group (4.0 ± 0.7 vs. 5.9 ± 1.5 , $p < 0.001$). The mean reduction in Vancouver scar score was remarkably high in the Triamcinolone compared to Verapamil treatment group (4.6 ± 1.2 vs. 2.9 ± 0.8 , $p < 0.001$) (Table 1).

Table 1: Characteristics of patients undergoing treatment for Keloid (N=60)

Characteristics	Overall (N=60)	Verapamil Group (N=30)	Triamcinolone Group (N=30)	p-Value*
Age (years)	28.6 ± 7.9	28.8 ± 7.3	28.3 ± 8.5	0.808
Gender, N (%)				
Male	35 (58.3)	19 (63.3)	16 (53.3)	0.432
Female	25 (41.7)	11 (36.7)	14 (46.7)	
Obesity, N (%)				
Yes	19 (31.7)	10 (33.3)	9 (30.0)	0.781
No	41 (68.3)	20 (66.7)	21 (70.0)	
Diabetes Mellitus, N (%)				
Yes	15 (25.0)	9 (30.0)	6 (20.0)	0.371
No	45 (75.0)	21 (70.0)	24 (80.0)	
Duration of Keloid (months)	14.6 ± 5.9	15.3 ± 5.8	14.0 ± 6.0	0.402
Baseline Vancouver Scar Score	8.7 ± 1.7	8.8 ± 1.8	8.6 ± 1.6	0.707
Vancouver Scar Score after 3 months	4.9 ± 1.5	5.9 ± 1.5	4.0 ± 0.7	<0.001
Reduction in Vancouver Scar Score	3.7 ± 1.3	2.9 ± 0.8	4.6 ± 1.2	<0.001

*Independent sample t-test for numerical comparison and chi-

square test for categorical comparison

After stratification on demographic characteristics, the reduction in Vancouver scar score after three months of treatment remained significantly higher in triamcinolone compared to verapamil ($p < 0.005$) (Table 2).

Table 2: Effect of demographic characteristics on reduction of Vancouver scar score between the treatment groups (N=60)

Demographic Characteristics	Verapamil	Triamcinolone	Cohen's d (95% CI)	p-Value*
Age (years)	< 30-years	2.9 ± 0.8	-1.7 (-2.5 - -0.89)	<0.001
	≥ 30-years	2.8 ± 0.8	-1.7 (-2.6 - -0.85)	<0.001
Gender	Male	2.9 ± 0.7	-1.6 (-2.3 - -0.81)	<0.001
	Female	2.8 ± 0.9	-1.8 (-2.8 - -0.87)	<0.001
Duration of Keloids	≤ 12-month	2.9 ± 0.7	-1.5 (-2.4 - -0.66)	<0.001
	> 12-month	2.8 ± 0.8	-1.8 (-2.6 - -0.98)	<0.001
Obesity	Yes	3.0 ± 0.6	-1.7 (-2.8 - -0.65)	0.002
	No	2.8 ± 0.8	-1.7 (-2.5 - -1.00)	<0.001
Diabetes mellitus	Yes	3.1 ± 0.9	-1.6 (-2.8 - -0.38)	0.009
	No	2.7 ± 0.7	-1.7 (-2.5 - -1.1)	<0.001

*Independent sample t-test

DISCUSSIONS

Keloids most frequently affect those under 30 years of age, peaking between 10 and 20. Raised body hormone levels, particularly during puberty and pregnancy, also contribute to its incidence. The distribution of sexes is nearly equal. The higher rate of earlobe piercing may be associated with a slight female predominance. Keloid management is both demanding and difficult. Although many therapies have been promoted and asserted to be successful, cures are rarely seen. Keloids have been treated and prevented using a variety of methods. In our study, the mean age of patients was 28.6 ± 7.9 years, with a slight male predominance (58.3% male and 41.7% female). Similar to our results, previous studies showed that 47% of patients were female and 52% of patients were male. In contrast to our data, the occurrence of keloids is distributed approximately equally by sex on a global scale [9, 10]. The socioeconomic structure of our country, where fewer women with keloids visit hospitals, could be the cause of this. The dearth of epidemiologic research on keloids in Pakistan could be another factor; there might be variations in the sex distribution of keloids in this region of the world. According to previous study, the majority of the patients were under 30, with a peak age of 20 to 30 years. This is consistent with our findings and research conducted globally. More than 57% of the patients were under 30 years old. Earlier researchers discovered that the age range of 18 to 25 accounted for 40.9% of cases. In the present study, we observed that after three months, the mean Vancouver score was markedly lower in the Triamcinolone group in contrast to the Verapamil treatment group, and the mean reduction in Vancouver scar score was predominantly high in the

Triamcinolone group, in contrast to the Verapamil treatment group. Similar to our results, triamcinolone was reported to be more successful, since it totally eliminated pain and itching in six and twelve weeks, respectively, whereas Verapamil-treated patients did not experience a complete resolution [10, 11]. Previous studies enrolled 80 patients, divided equally into two groups (Group A - Intralesional Verapamil injection and Group B - Intralesional Triamcinolone acetone). After the completion of the study (3 months), a 58% decrease in the initial score was observed in the steroid group, in contrast to 36.7% in group A. The mean reduction in score was 2.5 ± 0.72 in Group A and 4.35 ± 0.70 in Group B [9]. Earlier studies enrolled 15 patients (30 scars) to compare the intralesional triamcinolone effect with that of verapamil. Better improvement in height (0.2 ± 0.5 vs. 3.1 ± 1.8) and pliability (0.20 ± 0.41 vs. 2.07 ± 0.26) was observed with steroids in contrast to verapamil at the 24th week of follow-up. In previous findings, 160 patients were divided into four groups, with 40 cases in each category. Group B received intralesional verapamil, Group C received intralesional 5-fluorouracil, Group D received intralesional platelet-rich plasma, and Group A (control) received intralesional triamcinolone. The most successful treatment was found to be intralesional verapamil, whereas intralesional triamcinolone acetone was found to be as effective as platelet-rich plasma [12]. Similar comparative research was done by Saki et al. who found that both study groups showed a decrease in height and pliability at the conclusion of the investigation. Compared to verapamil, triamcinolone showed a greater improvement in height and pliability [13]. In a prospective study, Shanthi et al. randomly assigned 54 patients to groups receiving verapamil and triamcinolone. They discovered that the length had not changed significantly [14]. Current findings were different from theirs. Their study's smaller sample size may have been the likely cause. Group A received intralesional 5-fluorouracil (5 FU), Group B received intralesional triamcinolone acetone (TAC), and Group C received intralesional triamcinolone acetone 40 mg/dl (0.1 ml) along with 5-fluorouracil 50 mg/ml (0.9 ml) every month for six months. There was a statistically significant difference between the 5 FU Vs 5 FU+TAC group ($p=0.04$) and the TAC Vs 5 FU+TAC group ($p=0.02$). TAC and 5FU together were more effective at treating keloids [15]. Verapamil hydrochloride may be less effective than corticosteroids because corticosteroids limit the production of collagen and glycosaminoglycans, degenerate fibroblasts and collagen, and have an extra anti-inflammatory impact on scar tissue [16]. Earlier studies investigated how calcium antagonists affected the synthesis of extracellular matrix. They proposed that calcium channel blockers change the

morphology of fibroblast cells from bipolar to spherical and depolymerise actin filaments, which could lead to an increase in the production of procollagenase [17]. Verapamil's reduced anti-inflammatory effect is most likely caused by its capacity to suppress the synthesis of proinflammatory mediators as well as the activity of enzymes phospholipase A2 and phospholipase C [18]. Eicosanoids and leukotrienes are produced, the mast cell membrane is stabilized by preventing calcium ions from entering, platelet aggregation is inhibited, granules are released, and neutrophil activity is reduced, all of which lessen pain and pruritus symptoms [19]. When verapamil is given, calcium channel blocking in excitable tissues, such as nerve fibers, decreases excitability by delaying the action potential, which alleviates pain and itch symptoms [20, 21]. Current results provide a well-researched comparison between intralesional triamcinolone acetonide and verapamil for keloid treatment. The findings strongly support the superior efficacy of triamcinolone acetonide in reducing keloid severity. The study's findings are backed by clear clinical evidence, making it a valuable reference for dermatologists. The strength of this study was its randomized controlled study design.

The limitations of our study were that firstly, it had small sample size. Secondly, we could not measure the side effects of the drugs. The follow-up duration was short (three months post-treatment), so long-term recurrence rates and sustained scar improvement could not be assessed. The study did not assess patient-reported outcomes such as pain, pruritus, or satisfaction, which are important measures of therapeutic success. Future studies should include larger samples with longer follow-up, systematic assessment of adverse effects, and incorporation of patient-reported outcomes to better evaluate long-term efficacy and tolerability of keloid treatments.

CONCLUSIONS

Treatment of keloids is very challenging, and management options are still evolving. Intralesional verapamil is a better option to treat keloids, but intralesional administration of triamcinolone acetonide is more efficacious. More randomized controlled studies on a larger scale are required to prove the efficacy of intralesional verapamil and steroids in managing keloids.

Authors' Contribution

Conceptualization: AB¹

Methodology: AB¹, ST, ZA, AB², SI

Formal analysis: ST

Writing and Drafting: AB¹, AA, ST, ZA, AB², SI

Review and Editing: AB¹, AA, ST, ZA, AB², SI

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Anatomical Variation in Sigmoid Sinus and Its Impact on Mastoid Exploration in Atticoantral Chronic Suppurative Otitis Media Surgery: A Prospective Study at Khyber Teaching Hospital, Peshawar

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ABSTRACT

Atticoantral Chronic Suppurative Otitis Media (CSOM) with cholesteatoma frequently causes intraoperative complications. Anatomical variations of the sigmoid sinus (SS) can increase surgical risk. This study correlates CT-identified SS variations with operative challenges and outcomes, addressing the limited literature on their specific impact. **Objectives:** To evaluate the anatomical variations of the sigmoid sinus on preoperative CT scans and determine their impact on intraoperative challenges and postoperative outcomes during mastoid exploration for atticoantral chronic suppurative otitis media. **Methods:** This analytical cross-sectional study of 300 patients undergoing radical mastoidectomy at a tertiary care hospital from January to December 2024. Temporal bone CT scans assessed variation in SS position and bony plate integrity. Intraoperative and postoperative complications were recorded. Categorical data were analyzed using chi chi-square test ($p < 0.05$). **Results:** CT evaluation demonstrated intact bony plates in 77.3% of cases, with 12.3% showing erosion and 11.3% exhibiting exposure; sinus position was posterior in 63%, anterior in 25%, and normotopic in 12%. Intraoperative observations matched CT findings. Anterior displacement was significantly associated with increased surgeon fatigue ($p = 0.014$), Dural injury ($p < 0.001$), significant hemorrhage ($p = 0.032$), facial nerve palsy ($p = 0.006$), and incomplete disease clearance ($p < 0.001$). Eroded or exposed plates also correlated with higher complication rates ($p < 0.01$). No postoperative meningitis occurred. **Conclusions:** Preoperative CT accurately predicts sigmoid sinus variations in atticoantral CSOM, aiding surgical planning and reducing intraoperative complications.

INTRODUCTION

CSOM is a chronic inflammation and infection of the middle ear and mastoid air cell system, characterized by persistent or intermittent ear discharge through a perforated tympanic membrane [1]. CSOM constitutes a significant global health problem affecting an estimated 65–330 million individuals [2]. CSOM is classified into two main types: the mucosal variant, frequently considered benign or 'safe', and the squamous (atticoantral) variant,

categorized as 'unsafe' due to its more destructive nature. The latter subtype essentially affects the posterosuperior part of the middle ear cleft and often shows association with cholesteatoma formation. Cholesteatoma constitutes a well-circumscribed nonneoplastic pathological entity characterized by the accumulation of keratinizing squamous epithelium within a connective tissue stroma, causing localized bone erosion [3]. Tympano-



mastoidectomy serves as a standard surgical procedure for the definitive management of atticofacial type of CSOM [4]. For a safe and effective tympanomastoidectomy procedure, definitive recognition of anatomical landmarks and their potential variations are essential; otherwise, the likelihood of intraoperative complications is considerably high [5]. The Sigmoid Sinus (SS), a dural venous sinus, traverses along the interface between the endosteal lining of the occipital bone and the inner meningeal layer of dura mater [6]. The substantial anatomical variability in the position of SS within the mastoid cavity profoundly affects the dimensions of Trautmann's triangle, carrying significant considerations for surgical planning and intraoperative exposure [7]. The spatial orientation of SS serves as a significant predictor of surgical accessibility during translabyrinthine and retrosigmoid procedures for inner ear structures. A posterosuperiorly positioned sinus reduces the available surgical space, necessitating increased cerebellar retraction during retrosigmoid surgical procedures, thereby potentially elevating the risk of complications [8]. An anteriorly and inferiorly positioned SS poses a challenge to the translabyrinthine approach by substantially restricting the operative window and limiting exposure to the middle and inner ear structures [9]. Computed tomography (CT) scan has shown robust diagnostic accuracy, evidenced by a pooled sensitivity of 79% and a pooled specificity of 90% [10, 11]. Marked interindividual variability in the anatomical positioning of SS enhances the risk of surgical trauma. Consequently, the integration of image-guided technologies is recommended for accurate identification of these alterations and to avoid adverse outcomes [12]. In atticofacial disease, where cholesteatoma has disrupted the conventional surgical landmarks, SS serves as a consistent anatomical reference point. A thorough understanding of the anatomical variations of SS and their clinical significance is essential for effective preoperative planning to minimize the risk of inadvertent sinus injury and related surgical complications [7, 13].

Although the variability in SS positioning is well documented in the literature, a comprehensive parametric analysis of its impact on mastoid exploration in atticofacial CSOM surgery remains lacking. This study aims to assess both preoperative and intraoperative anatomical variations of the sigmoid sinus during mastoid exploration for atticofacial CSOM. These findings will contribute to enhanced surgical planning and the intraoperative prevention of serious complications.

METHODS

This analytical cross-sectional study was conducted in the Department of Otolaryngology at Khyber Teaching Hospital, Peshawar, over the period from January to

December 2024. Ethical approval for the study was granted by the Institutional Research and Ethical Review Board of Khyber Medical College, Peshawar (Ref. No 764/DME/KMC). All participants provided written informed consent. A consecutive sampling technique was employed for recruitment. The study included patients undergoing Modified Radical Mastoidectomy (MRM) for clinically diagnosed atticofacial CSOM with cholesteatoma and extensive granulation tissue formation, and the age range was from 18 to 60 years. Informed consent was taken from all participants. Patients having the diagnosis of cerebral venous sinus thrombosis, congenital or acquired intracranial abnormalities, intracranial space-occupying lesions, prior mastoid surgery, or any abnormal findings on brain imaging were excluded. Sample size was calculated using the formula: $n = Z^2 \cdot P(1-P)/d^2$, where $Z=1.96$ (for 95% confidence), $P=25.93\%$. The required sample size was estimated based on the reported prevalence of anatomical variations of the sigmoid sinus (25.93%), with a 95% confidence interval (CI) and a 5% margin of error [6]. The sample size came out to be 296, but it was rounded up to 300. A detailed history, including the age, gender, and previous medical and surgical history, was obtained. The preoperative and postoperative CT scans of the patients were reviewed to evaluate the anatomical location of SS. Imaging was performed using a standardized high-resolution temporal bone CT protocol with a rotation time of 0.5 s, pitch factor of 0.637, and collimation of 0.5×80 mm (50 mm total). These acquisition parameters were adopted in accordance with previously validated high-resolution CT protocols for temporal bone and sigmoid sinus evaluation described in the literature [10-11]. Such imaging settings ensure optimal delineation of bony anatomy and venous sinus variations, facilitating accurate preoperative assessment. These findings were compared with intraoperative observations, including the anatomical position of SS, the presence or absence of bony plate covering the SS or its exposure, its influence on the extent of disease clearance during surgery, the occurrence of Dural injury or massive intraoperative haemorrhage, and the overall complexity of the surgical procedure. CT scan source images were meticulously analysed in sagittal planes to identify anatomical variations of the SS. The primary variables assessed included the anatomical classification of the SS as anterior (forward), posterior, superior, or inferior types. Emphasis was placed on the accuracy of source image interpretation to minimize diagnostic errors. Postoperative outcomes were systematically recorded for all participants, including the incidence of complications such as facial nerve palsy, meningitis, encephalitis, and postoperative CT findings documenting residual disease and SS positioning. Data

were analysed using the Statistical Package for the Social Sciences (SPSS) version 20.0. Continuous variables were presented as mean and standard deviation. "Chi-square tests were applied to evaluate the impact of preoperative anatomical variations of the sigmoid sinus (position and bony plate status) on intraoperative challenges and postoperative outcomes. A p-value ≤ 0.05 was considered statistically significant."

RESULTS

This analytical cross-sectional study evaluated 300 participants, consisting of 125 males and 175 females. The age of the participants ranged from 18 to 55 years, with a mean age of 28.89 years (± 8.05). The majority of the participants lie within the 18–30-year age group. Most of the patients presented with active CSOM, and ear discharge is the most common symptom. Almost all patients undergo Modified Radical Mastoidectomy (MRM) as the main surgical treatment (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants (N=300)

Characteristics	Category	Frequency (%)
Age Group (years)	18–30	182 (60.7%)
	31–40	99 (33.0%)
	41–50	12 (4.0%)
	51–60	7 (2.3%)
Sex	Male	125 (41.7%)
	Female	175 (58.3%)
Type of Mastoid Exploration	MRM	294 (98.0%)
	RM	6 (2.0%)

MRM: Modified Radical Mastoidectomy, RM: Radical Mastoidectomy

Preoperative CT scan of the temporal bone in 300 patients showed that the majority exhibited an intact sigmoid plate, showing the SS has a normal bony coverage. A smaller proportion demonstrated sigmoid plate dehiscence (12.3%), characterized by thinning or erosion of the bony plate, while 10.3% revealed the sigmoid sinus completely exposed due to absent bony coverage. Anatomic variations in SS position were also noted on CT scans preoperatively. The sinus was posteriorly displaced in 62.7% of cases, anteriorly displaced in 25.3%, and in a standard anatomical location, it is only 12.0%. Intraoperative findings demonstrated identical distribution patterns showing strong correlation with preoperative CT imaging regarding SS position (Table 2).

Table 2: Preoperative CT Findings and Intraoperative Observations of Sigmoid Sinus Anatomy in 300 Cases

Assessment Phase	Category	Findings	Frequency (%)	Assessment Phase
Pre-op CT Findings	Bony Sigmoid Plate	Well-defined	232 (77.3)	Pre-op CT Findings
		Eroded	37 (12.3)	

CT Anatomical Variation	Sigmoid Sinus Position	Exposed	31 (10.3)	CT Anatomical Variation
		Posterior	188 (62.7)	
		Forward	76 (25.3)	
Intraoperative Findings	Bony Sigmoid Plate	Normal	36 (12.0)	Intraoperative Findings
		Well-defined	232 (77.3)	
		Thin plate	37 (10.3)	
	Sigmoid Sinus Position	Exposed	31 (12.3)	
		Posterior	188 (62.7)	
		Forward	76 (25.3)	
		Normal	36 (12.0)	

A statistically significant association was found between forward-lying SS on CT scan and increased intraoperative challenges. Surgeon-reported fatigue due to procedural complexity, Intraoperative Dural injury, and massive hemorrhage was notably higher in patients with forward-positioned SS compared to posterior-lying and no variation groups ($p=0.014$, $p<0.001$, and $p=0.032$, respectively). Forward-lying SS was also associated with higher rates of postoperative facial nerve palsy ($p=0.006$). Poor disease clearance (51.3%) and residual disease on postoperative CT (50.0%) were significantly more common in the forward-lying group ($p < 0.001$ for both). No statistically significant association was observed between anatomical variation and postoperative meningitis or encephalitis ($p=0.399$) (Table 3).

Table 3: Association of Preoperative CT Scan and Intraoperative Anatomical Variations of SS With Surgical Challenges and Postoperative Outcomes (N=300)

Outcome Variables	Forward (Anterior) SS (N=76)	Posterior SS (N=188)	No Variation (N=36)	P-Value
Surgeon-reported fatigue	18 (10.5)	27 (14.3)	1 (2.8)	0.014*
Dural injury during surgery	8 (10.5)	0 (0.0)	0 (0.0)	<0.001*
Massive hemorrhage during surgery	6 (7.9)	2 (1.1)	0 (0.0)	0.032*
Facial palsy (post-op)	9 (11.8)	4 (2.1)	0 (0.0)	0.006*
Post-op meningitis/encephalitis	1 (1.3)	3 (1.6)	1 (2.8)	0.399
Incomplete disease clearance	39 (51.3)	12 (6.4)	0 (0.0)	<0.001*
Residual disease on post-op CT	38 (50.0)	6 (3.2)	0 (0.0)	<0.001*

* Indicates statistical significance at $p \leq 0.05$

Further analysis of preoperative CT and intraoperative findings revealed that patients with eroded bony plates or exposed sigmoid sinuses experienced significantly more surgical complications. Surgeon fatigue was reported in 51.3% of cases with eroded plates and 41.9% of cases with exposed sinuses ($p<0.001$). Dural injuries and massive hemorrhage occurred more frequently in cases with eroded plates and exposed sinuses ($p<0.001$ and $p=0.007$, respectively). Postoperative facial palsy was more prevalent in the eroded and exposed sinus groups ($p=0.004$). Disease clearance was significantly lower in patients with compromised bony structures (eroded plate and exposed sinus) compared to the well-defined plate

group ($p < 0.001$). Residual disease on postoperative CT was highest in the exposed sinus group (61.3%), followed by the eroded plate group (35.1%), compared to 5.2% in the well-defined plate group ($p < 0.001$). Again, no significant correlation was observed between bony sigmoid plate status and postoperative central nervous system infections ($p = 0.726$) (Table 4).

Table 4: Association of Preoperative CT scan and intraoperative Bony Plate Status with Surgical Challenges and Postoperative Outcomes (N=300)

Outcome Variables	Well-Defined Plate (N= 232)	Eroded Plate (N= 37)	Exposed SS (N= 31)	P-Value
Surgeon-reported fatigue	14 (6.0)	19 (51.3)	13 (41.9)	<0.001*
Dural injury during surgery	0 (0.0)	4 (10.8)	4 (12.9)	<0.001*
Massive hemorrhage during surgery	3 (1.3)	3 (8.1)	3 (9.7)	0.007*
Facial palsy (post-op)	6 (2.6)	5 (13.5)	3 (9.7)	0.004*
Post-op meningitis/encephalitis	4 (1.7)	1 (3.2)	0 (0.0)	0.726
Incomplete disease clearance	19 (8.2)	13 (35.1)	19 (61.3)	<0.001*
Residual disease on post-op CT	12 (5.2)	13 (35.1)	19 (61.3)	<0.001*

* Indicates statistical significance at $p \leq 0.05$

"The impact of anterior (forward) or posterior displacement of the sigmoid sinus, as well as variations in bony plate coverage, on surgical complexity and postoperative outcomes was assessed using Chi-square tests. Forward-lying or exposed sigmoid sinuses were significantly associated with increased intraoperative challenges, higher rates of dural injury, massive hemorrhage, facial nerve palsy, incomplete disease clearance, and residual disease on postoperative CT ($p \leq 0.05$ for all comparisons)."

DISCUSSIONS

This cross-sectional study analyzed 300 patients diagnosed with atticointral CSOM, with a predominance of females and a mean age of 28.89 (± 8.05) years. This is in agreement with a previous study, where the mean age was reported to be 27.5 (± 10) years [14]. As the SS anatomy is variable, on pre-op CT sigmoid sinus with an intact bony plate was the most common variation, followed by a thin bony plate and exposed SS, respectively [9]. These are likewise to previous findings [15, 16]. Considering the position of the SS, on pre-op CT scan, a posteriorly displaced sigmoid sinus was the most prevalent. These positions showed a strong correlation with intraoperative observations. The higher rate of surgeon fatigue with the forward (anteriorly) lying SS was associated with a narrow surgical window, reduced instrument mobility, and limited visibility of anatomic landmarks, making the surgery more complex and lengthier. However, previous studies reported no association between the location of the SS and difficulty in mastoidectomy. This contradiction is because of different procedures; in cholesteatoma surgery, a wide cavity is required as compared to cochlear implant surgery [9, 17]. Dural injury was found to be highly associated with

forward lying SS ($p < 0.001$); the association can be justified by the fact that forward lying sigmoid sinus restricts the exposure of presigmoidal Dural plate [18, 19]. Moreover, forward displacement was significantly linked to massive intraoperative hemorrhage ($p = 0.032$), potentially resulting from limited access via the post-aural approach, which increases the risk of sinus injury [20]. Facial nerve palsy was also more frequent postoperatively in cases with a forward-lying sinus. This association is likely attributable to the facial nerve lying closely to the semicircular canals, making it more vulnerable to injury during mastoid drilling [21, 22]. Furthermore, the disease was not cleared completely in half of the cases of forward lying SS, which was confirmed by CT scan postoperatively. This may be attributed to restricted access to the middle ear due to narrowing of Trautmann's triangle, thereby limiting the surgical field [7]. Different complications were reported due to variation in the SS bony plate. Bony plate variations were also associated with complications. Surgeon experienced fatigue was more in eroded bony plate cases, which was not reported in previous studies. Partially or completely erosion of the bony plate by cholesteatoma typically reflects more extensive spreads of the disease, making it more time-consuming. In the case of an eroded and exposed sinus, the dual injury and hemorrhage were found to be statistically significant, supported by data from a study in Nepal. The wall of the SS being eroded or exposed makes its injury more likely. Complete diseased clearance was not achieved in patients with exposed sinus and eroded bone plate. The possible reason for residual disease is the extensive spread, making its complete removal a dilemma for the surgeon. Facial nerve palsy was also more common postoperatively, potentially due to dehiscence of the facial canal in advanced disease stages, increasing the risk of intraoperative injury. Interestingly, no case of postoperative meningitis and encephalitis was noted in our study. This can be attributed to the use of aseptic protocols and, use of prophylactic antibiotics. In other studies, meningitis had a low prevalence of 2% [14, 19, 23, 24]. Based on our study, it is recommended that a patient with atticointral CSOM should be evaluated with a high-resolution contrast-enhanced CT scan in order to determine the anatomy of the sigmoid sinus. Patients with anteriorly displaced or exposed sinuses should be considered high-risk. Surgeons should be prepared in such cases, as there can be a massive hemorrhage during the surgery. Hemostatic preparedness should be done in case of an exposed sinus. Post-operative follow-ups must be considered in case of forward lying and exposed sinus, as there are high chances of residual disease. To reduce intraoperative complications, surgical training workshops should educate the surgeons about sigmoid sinus

variations and their impact on surgical complications. This study has limitations. The sample size was modest, and all patients were from a single center, limiting generalizability. Although HRCT provides high-resolution images, very subtle microanatomical variations may not be captured, potentially underestimating surgical risks. Future research with larger, multi-center cohorts and adjunct imaging modalities such as MR venography could provide a more comprehensive understanding of sigmoid sinus variations and their impact on surgical planning.

CONCLUSIONS

Preoperative high-resolution CT reliably identifies anatomical variations of the sigmoid sinus in atticofacial CSOM, and these variations significantly impact intraoperative challenges, surgical complexity, and postoperative outcomes; recognizing anterior, posterior, or bony plate alterations allows surgeons to anticipate difficulties, minimize complications, and optimize disease clearance during tympanomastoidectomy.

Authors' Contribution

Conceptualization: WS, MAI, AZ

Methodology: WS, FI

Formal analysis: MAI, HDK, HHM

Writing and Drafting: WS, MAI, HDK, AZ, FI, HHM, RUK

Review and Editing: WS, MAI, HDK, AZ, FI, HHM, RUK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Diagnostic Accuracy of Ottawa Ankle Rules in Acute Ankle Injuries in Patients Above Five Years of Age

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ABSTRACT

Ankle injuries are a common reason for emergency visits, but only 15% have fractures. The Ottawa Ankle Rules were introduced to reduce unnecessary imaging. **Objective:** To assess the diagnostic accuracy of Ottawa ankle rules in predicting ankle fractures and identify the main clinical predictors. **Methods:** This analytical cross-sectional study was conducted in the emergency department of Ghurki Trust and Teaching Hospital, Lahore, from July 2024 and March 2025 on consecutive patients with acute ankle trauma. OAR was used to evaluate patients, followed by radiography. Calculations were done on sensitivity, specificity, PPV, and NPV. Data were analyzed using frequencies and percentages for categorical variables and means with standard deviation for continuous variables. **Results:** In this cohort of 71 patients (66.2% male; mean age 36.6 ± 15.3 years), falls and road traffic accidents were the primary injury mechanisms. X-rays revealed fractures in 69.0% of the cases. The Ottawa Ankle Rules (OAR) achieved a sensitivity and negative predictive value of 100%, although the specificity was low at 13.6%, leading to 19 false-positive results. Notably, medial malleolus pain ($p < 0.001$) and inability to bear weight ($p = 0.003$) were the strongest predictors of fracture. **Conclusion:** Our study demonstrated 100% sensitivity and negative predictive value for detecting fractures and no false negatives, but specificity was low at 13.6%, resulting in 19 false positives. Fractures were present in 69.0% of cases and were found mostly to be bimalleolar (25.4%) and tri-malleolar (18.3%). Medial malleolus pain and inability to bear weight had the strongest capability to predict fractures clinically.

INTRODUCTION

There is a high incidence of ankle injuries, with ankle fractures occurring at a rate of 122 per year per 100,000 people. Acute trauma to the ankle joint constitutes one of the top reasons patients present to the emergency department (ED). Only around 15% of these patients actually turn out to have a fracture. X-rays are almost routinely prescribed for all, even though apparently 85% are negative for fracture. The individual cost per X-ray is cheap, but the total cost becomes substantial due to so many being performed. The Ottawa ankle rules were thus designed to limit unnecessary radiographs. These were introduced in 1992 [1-3]. These rules are included in guidelines in multiple countries around the world [4, 5]. The

Ottawa ankle rules are constructed on the basis of objective criteria with the intention of making it as clear as possible while reducing the subjective aspects of clinical evaluation. These rules very clearly describe the indications for which radiographs must be taken leading to hospital cost savings, decreased ionizing radiation exposure, and waiting times in emergency departments. Based on the criteria, ankle films are only indicated when there is pain in the malleolar area and at least one of the following: bony tenderness along the distal 6 cm of the posterior edge of either malleolus (tibia or fibula), or inability to bear weight for four steps both immediately after the injury and in the emergency department. [1].



Various studies have shown that OAR has a 93-100% sensitivity [6, 7]. A prospective study showed that the OARs have shown a sensitivity of 100% (95% confidence interval, 39.76-100.00) and specificity of 23.33% (95% CI, 15.06-33.43) with a negative predictive value of 100%. [8-10] Another study at a single hospital showed that OAR implementation significantly reduced unnecessary ankle radiographs without compromising patient care. Also, it can effectively decrease emergency department stay time and overcrowding in the ED [11, 12]. Ankle injuries are frequent in adults and children, often leading to emergency visits. However, many of these cases do not involve fractures, resulting in unnecessary X-rays, increased healthcare costs, and longer wait times. The Ottawa Ankle Rules (OAR) are a clinical tool developed to reduce unnecessary imaging by identifying low-risk patients. While the OAR has shown high sensitivity in adult populations, its effectiveness in patients over five years of age, especially children and adolescents, requires further validation. The study conducted by MacLellan et al. [13] was an assessment of OAR accuracy within the pediatric population. The authors determined that the foot rule used by NPPs was 100% sensitive (56-100% CI) and 17% specific (9-29% CI) to clinically important fractures. NPPs used the ankle component of the rule to have a sensitivity of 88% (47-99% CI) and specificity of 31% (23-40% CI) in the clinically significant fractures. Evaluation of the diagnostic performance of the OAR in this age bracket is critical in safe and cost-effective care without over-radiating or missing a fracture.

This research will be used to test the reliability of the OAR in patients with acute ankle injury of more than five years and aid in improved resource utilization and clinical decision-making. This study hypothesizes that the OAR is highly sensitive for detecting ankle fractures in patients over five years and aims to evaluate its diagnostic accuracy and identify key clinical predictors, including medial malleolus pain, lateral malleolus pain, and inability to bear weight. This study aimed to assess the diagnostic accuracy of Ottawa ankle rules in predicting ankle fractures and identify the main clinical predictors

METHODS

This analytical cross-sectional study was conducted in the Emergency Department of Ghurki Trust and Teaching Hospital, Lahore. Ethical approval was obtained from the ethical review board of Ghurki Trust and Teaching Hospital (Ref. No. 2024/07/R-51), and the study followed the Helsinki regulations. Informed consent was obtained from all patients included in this study. Patients were assured that their participation was voluntary, their confidentiality would be maintained, and no identifying information would be disclosed in any publication or presentation. The paper

used a non-probability convenience sampling method to include 71 patients who were presented to the ED between July 2024 and March 2025 using a convenience sampling technique. Inclusion criteria were: patients who had ankle trauma within the last 24 hours and were aged more than 5 years. Exclusion criteria were: polytrauma, pregnant females, patients with altered consciousness or suspected drug intoxication, open fractures, those with reduced or absent lower-limb sensations (due to any cause), and patients who refused radiography. An orthopedic surgeon examined all patients, and the questionnaire recorded the date. Biodata, address, and mechanism of injury were captured in the data. The presence of pain and localized tenderness over the tip or the distal 5cm of the medial and lateral malleolus, as well as the patient's ability to bear weight on the injured ankle, were noted. X-ray ankle anteroposterior, lateral, and mortise views were recommended in all subjects and analyzed by an examining and a senior orthopedic surgeon. The X-ray examinations in the study were conducted using a Toshiba Multix Impact X-ray machine, ensuring high-quality radiographic imaging for accurate fracture assessment. The interpretation of the X-ray was recorded. Diagnostic outcomes were defined as follows: True positives (TP) were cases where OAR indicated a fracture, and X-ray confirmed its presence. True negatives (TN) were cases where OAR correctly excluded a fracture, confirmed by a negative X-ray. False positives (FP) were cases where OAR suggested a fracture, but X-ray showed no fracture. False negatives (FN) were cases where OAR did not indicate a fracture, but X-ray confirmed one. The collected data were analyzed in SPSS version 28.0. Categorical variables (e.g., gender, residence, diabetes status, fracture presence) were reported as frequencies and percentages, while continuous variables (e.g., age) were summarized as mean $\pm$ standard deviation. The chi-square test or Fisher's Exact Test was used to assess associations, with $p \leq 0.05$ considered significant. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using a 2x2 contingency table, with confidence intervals (95% CI) computed for diagnostic accuracy measures [9]. Sensitivity % = $(TP / (TP + FN)) * 100$, Specificity % = $(TN / (TN + FP)) * 100$, Positive predictive value (PPV) % = $(TP / (TP + FP)) * 100$, Negative predictive value (NPV) % = $(TN / (TN + FN)) * 100$, False positive rate (FPR) % = $(FP / (FP + TN)) * 100 = 100 - \text{Specificity}$, False negative rate (FNR) % = $(FN / (FN + TP)) * 100 = 100 - \text{Sensitivity}$.

RESULTS

Our sample (N=71) demonstrated a male predominance (66.2%) with a mean age of 36.6 ± 15.3 years (range: 9-85), consistent with global trauma demographics. While most patients presented from Lahore (77.5%), 22.5% traveled

from other districts. Diabetes prevalence (12.7%) mirrored national estimates, supporting metabolic generalizability. Mechanism of injury analysis showed falls as the leading cause of injury (53.5%), followed by RTAs (39.4%). The remaining 7.0% comprised miscellaneous mechanisms (Table 1).

Table 1: Characteristics of Patients(N=71)

Variable	N (%)
Gender (%)	
Male	47 (66.2%)
Female	24 (33.8%)
Age (Years)	
5-15	4 (5.6%)
16-30	25 (35.2%)
31-45	24 (33.8%)
>45	18 (25.4%)
Residence (%)	
Lahore	55 (77.5%)
Others	16 (22.5%)
Diabetes (%)	
Present	9 (12.7%)
Absent	62 (87.3%)
Mechanism of Injury (%)	
Fall	38 (63.5%)
RTA	28 (39.4%)
Others	5 (7.0%)

Fracture distribution revealed bimalleolar (25.4%) and tri-malleolar (18.3%) patterns most frequently, while 31.0% had no radiographic fracture. Talus involvement (5.6%) was uncommon but clinically significant due to the risk of osteonecrosis(Figure 1).

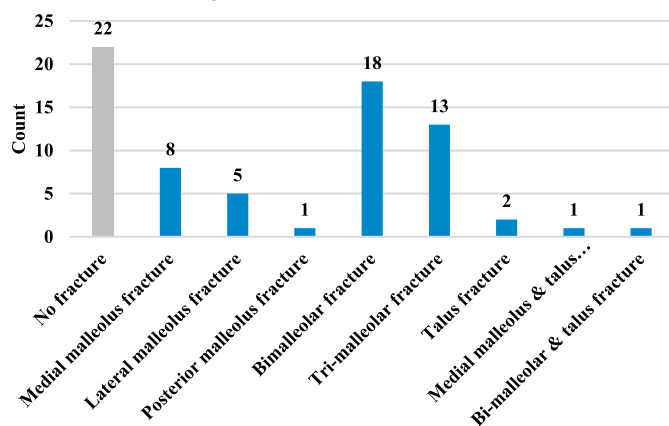


Figure 1: Frequency Distribution of Different Ankle Fracture Types Among the Study Participants(N=71)

The 2×2 contingency table presents the diagnostic performance of the Ottawa Ankle Rules (OAR) for 71 patients, comparing OAR predictions (OAR+ for positive, OAR- for negative) with radiographic outcomes (fracture confirmed or no fracture). Of the 68 patients with a positive OAR result, 49 were true positives with confirmed

fractures, while 19 were false positives with no fractures. Among the 3 patients with a negative OAR result, all were true negatives with no fractures, and there were no false negatives. This data indicates a perfect sensitivity, as all 49 fractures were correctly identified by OAR, and a perfect negative predictive value, as no fractures were missed when OAR suggested their absence. However, the specificity was notably low at 13.6%, reflecting the 19 false positives out of 22 non-fracture cases, which suggests that OAR has limited utility for confirming fractures but significant value in ruling them out (Table 2).

Table 2: Diagnostic Accuracy of the Ottawa Ankle Rules(OAR)

Ottawa Ankle Rules (OAR)	Fracture confirmed on X-ray	No Fracture on X-ray	Total
OAR+	49	19	68
OAR -	0	3	3
Total	49	22	71

The perfect sensitivity and negative predictive value underscore OAR's reliability in ensuring no fractures are missed, making it an effective screening tool. However, the low specificity and moderate positive predictive value highlight a high false positive rate, leading to unnecessary X-rays for 19 patients, which necessitates supplementary clinical judgment to enhance fracture confirmation and optimize resource use (Table 3).

Table 3: Performance Metrics of the Ottawa Ankle Rules(OAR)

Parameters	Value (95% CI)
Sensitivity	100% (92.75% to 100%)
Specificity	13.64% (2.91% to 34.91%)
Positive Predicted Value	72.06% (68.60% to 75.28%)
Negative Predicted Value	100.0% (29.24% to 100%)
Accuracy	73.24% (61.41% to 83.06%)

The study revealed significant associations between clinical findings and ankle fractures in 71 patients, with medial malleolus pain ($p<0.001$) showing the strongest link (38 with fractures vs. 3 without), followed by inability to bear weight ($p=0.003$, 38 with fractures vs. 9 without), and lateral malleolus pain ($p=0.009$, 34 with fractures vs. 9 without). These findings, discussed in the context of the Ottawa Ankle Rules (OAR), highlight their role as key predictors, supporting OAR's perfect sensitivity in ruling out fractures. However, the low specificity (13.6%), leading to 19 false positives, suggests these signs may also trigger unnecessary X-rays, possibly due to subjective pain assessment or high fracture prevalence (69.0%) (Table 4).

Table 4: Association Between Clinical Findings and Fracture Diagnosis

Radiograph	Fracture	No Fracture	p-Value
Medial Malleolus pain			
Yes	38	3	* <0.001

No	11	19	
Lateral Malleolus pain			
Yes	34	9	*0.009
No	15	14	
Unable to bear weight			
Yes	38	9	*0.003
No	11	13	

*Statistically significant at 0.05 level of significance

DISCUSSIONS

Acute ankle injuries are frequent and represent 6-12 % of emergency department visits. Radiography was generally requested on every patient presenting with trauma to the ankle, resulting in 85 percent of unnecessary radiographs. This results in increased emergency department stays, costs, and radiation exposure [14]. Our study confirmed that OAR has perfect sensitivity and NPV (100%) for detecting ankle fractures in patients above five; however, the low specificity led to 19 of 22 non-fracture patients classified as OAR+. This low specificity suggests that while OAR is highly effective for ruling out fractures, it may lead to over-referral for radiographs, increasing healthcare costs, radiation exposure, and ED wait times, particularly in resource-constrained settings. The diagnostic accuracy of OAR has been evaluated in many studies. A survey conducted by Morais et al showed a sensitivity of 100% and 26% specificity. This study included 148 patients. They also concluded that adding pain grading and the context of the accident to the criteria can increase its diagnostic accuracy [15]. In line with this research, Gomes et al. have found that the information on the diagnostic accuracy of the OAR could be extracted from all 15 studies involved. The sensitivity and specificity that were calculated in 15 studies were presented as data. Sensitivity and specificity point estimates ranged between 59-100 and 2-69, respectively, and were highly heterogeneous between studies (sensitivity: $I^2=94.3$, $p<0.01$; specificity: $I^2=99.2$, $p<0.01$) [16]. Earlier studies provided an excellent systematic review of the available material. The outcome of using the OAR is a 30-40% decrease in the number of needless radiography exams. There is proof that the OAR is a reliable clinical technique for ruling out ankle fractures. The OAR has a modest specificity and nearly 100% sensitivity. In our investigation, the OAR's sensitivity was 100%. Ankle fractures suggest a specificity of 45.8%, a positive predictive value of 48.4% and a negative predictive value of 96.5%. The OAR likewise claimed the performance of unnecessary radiographic examinations by 31.1% [17]. Several factors may explain the discrepancies in sensitivity and specificity across studies. First, differences in study populations, such as age distribution, injury severity, or prevalence of fractures, can influence OAR performance.

For example, our study's fracture prevalence (69.0%) was higher than the 15% reported in the literature [14, 18], potentially inflating sensitivity but reducing specificity due to a smaller proportion of true negatives. Second, variations in clinical expertise and training in applying OAR may contribute to inconsistent specificity. In settings with less experienced clinicians, such as general practitioners versus orthopedic specialists, OAR may be applied more conservatively, leading to more false positives. Third, injury characteristics, such as the presence of edema or subtle fractures, may complicate OAR interpretation, particularly in pediatric or elderly populations. Beceren et al. (2013) reported a sensitivity of 74% (95% CI: 69-79%) and specificity of 65% (95% CI: 65-72%) in a diverse cohort, while Das et al. found 98% sensitivity (95% CI: 91-100%) but only 45% specificity (95% CI: 39-50%) [19-20]. These variations suggest that contextual factors, such as patient demographics and clinical settings, significantly impact OAR's diagnostic performance. The impact of these discrepancies on our findings is twofold. The high sensitivity (100%) reinforces OAR's reliability as a screening tool to rule out fractures, ensuring patient safety across diverse populations, including children over five years. However, the low specificity (13.6%) limits its utility for confirming fractures, leading to unnecessary radiographs in 19 of 22 non-fracture cases. This over-referral may strain ED resources and expose patients to avoidable radiation, particularly concerning younger patients, where radiation risks are higher. To address this, clinicians could integrate additional clinical factors, such as pain severity or injury mechanism, as suggested by Morais et al. [15], to improve specificity without compromising sensitivity. Furthermore, the high fracture prevalence in our study (69.0%) compared to the literature (15%) suggests a selection bias due to non-probability convenience sampling, which may have skewed our specificity downward by including more severe cases.

The study's limitations, including the small sample size ($n=71$), single-center setting, and non-probability convenience sampling, may further contribute to the observed low specificity. A larger, multicenter study with a more representative sample could provide greater generalizability. Additionally, the lack of a power analysis limits the statistical robustness of our findings. Assuming a 15% fracture prevalence and 95% sensitivity, a sample size of approximately 200 patients would be required for 80% power, suggesting our study may be underpowered for detecting subtle differences in specificity.

CONCLUSIONS

In a group of people (n=71) who have acute ankle injuries, the Ottawa Ankle Rules (OARs) demonstrated 100% sensitivity and negative predictive value for detecting fractures and no false negatives, but specificity was low at 13.6%, resulting in 19 false positives. Fractures were present in 69.0% of cases and were found mostly to be bimalleolar (25.4%) and tri-malleolar (18.3%). Medial malleolus pain ($p<0.001$) and inability to bear weight ($p=0.003$) had the strongest capability to predict fractures clinically.

Authors' Contribution

Conceptualization: AUR

Methodology: HMF

Formal analysis: SS

Writing and Drafting: AUR, FKJ, UR, AUZ, SS

Review and Editing: AUR, FKJ, HMF, UR, AUZ, SS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Association of Serum Uric Acid with Cardiovascular Diseases in Pakistani Adults: A Cross-Sectional Analysis

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ABSTRACT

Numerous researchers have identified a strong link between increased levels of serum uric acid and cardiovascular disease. **Objectives:** To find out the association of serum uric acid with cardiovascular disease, independent of major confounding variables including age, sex, hypertension, diabetes, dietary habits, and lifestyle factors. **Methods:** A descriptive cross-sectional study was carried out at Fazaia Ruth Pfau Medical College. Data collection involved demographic, anthropometric, blood pressure, biochemical measurements, and electrocardiography. SPSS-22 was used for data analysis. Statistical methods included t-tests, one-way ANOVA, Mann-Whitney U test, and Pearson correlation were applied. To find the strength of association, a multivariate regression model was applied, and the odds ratio was calculated. **Results:** The frequency of hyperuricemia was 27.5%. Previous medical history of hypertension found a strong, significant association among the groups. The Frequency of cardiovascular diseases, including acute coronary disease, myocardial infarction, and cardiac failure, was 47%, 29.1% and 6% in the normouricemia group and 54.9%, 25.5% and 6.9% in the hyperuricemia group, respectively. Multivariate regression analysis revealed that the severity of cardiovascular diseases increased linearly with increasing serum uric acid concentration. Interestingly, the serum uric acid concentration was high in the cases of myocardial infarction in comparison to other cardiovascular diseases. The cardiovascular disease odds ratio was 1.84 to 2.45 times as the serum uric acid concentration rose above 9mg/dL. **Conclusions:** The Current study identified a significant association of hyperuricemia with cardiovascular diseases. The severity of cardiovascular diseases was observed to rise with increasing serum uric acid levels, and this link remained significant.

INTRODUCTION

Uric acid is a metabolic byproduct generated from the urine metabolism, derived from both endogenous sources and dietary intake [1]. Early research highlighted a potent effect of hyperuricemia in the pathophysiology of hypertension, cardiovascular diseases, diabetes, and kidney disorders [2]. Several physiological explanations have been suggested for its adverse effects on vascular function and blood pressure regulation [3]. Hypertension and diabetes are the known leading risk factors for

cardiovascular disease-related deaths. The study on global burden of disease reported that cardiovascular diseases are responsible for nearly 31% of all deaths worldwide [4]. Among cardiovascular disease-related fatalities, around 90% result from coronary artery disease, which involves restricted blood supply to the heart muscle caused by narrowed or obstructed coronary vessels. Maintaining vascular homeostasis is crucial for cardiovascular function [5]. Hypertension and diabetes contribute to vascular



damage, and hyperuricemia leads to vascular damage through mechanisms such as increased oxidative stress, stimulation of the renin-angiotensin-aldosterone system (RAAS), depletion of mitochondrial DNA, and a decline in intracellular ATP levels [6]. Hypertension may damage vascular structures due to continuous mechanical stress, while elevated uric acid has also been implicated in vascular injury. serum uric acid (Sr.UA) enhances oxidative stress by stimulating NADPH oxidase enzymes, which are responsible for synthesizing reactive oxygen species in vascular cells. Additionally, it inhibits endothelial nitric oxide synthase, resulting in decreased nitric oxide production. This reduction impairs vasodilation, promotes vasoconstriction, and ultimately contributes to endothelial dysfunction [7, 8]. Moreover, serum uric acid can activate pro-inflammatory molecules and the RAAS pathway, which together disrupt vascular integrity and facilitate atherosclerotic plaque formation, ultimately reducing cardiac blood supply [8]. Many researchers have identified a correlation between elevated levels of Sr.UA and cardiovascular disease (CVD). However, variables such as age, sex, ethnicity, lifestyle, diet, and coexisting conditions like hypertension, diabetes, and dyslipidemia can influence this relationship [9]. These confounding factors make a connection between increased Sr.UA levels and CVD somewhat contentious [10, 11].

Serum uric acid has been increasingly implicated in vascular dysfunction and cardiovascular disease through multiple biological mechanisms affecting endothelial and inflammatory pathways. The independent contribution of elevated serum uric acid to cardiovascular disease remains unclear due to inconsistent findings and the influence of major confounding factors across studies. This study aims to investigate the contribution of Sr.UA to cardiovascular disease, independent of major confounding variables including age, sex, hypertension, diabetes, dietary habits, and lifestyle factors.

METHODS

A descriptive cross-sectional study was carried out from December 2024 to February 2025 at Fazaia Ruth Pfau Medical College. The study got ethical approval from the Fazaia Ruth Pfau Medical College (Ref. No: FRPMC-IRB-2024-69). Informed consent was taken before the study. Data confidentiality was strictly upheld, and anonymization procedures were implemented before analysis. The study included 370 participants aged 18 and above, encompassing both male and female, diagnosed with cardiovascular diseases, hypertension, or diabetes, while those patients were excluded who were either having any chronic infection or diagnosed case of cancer, or were pregnant, lactating, or taking uric acid-lowering medications. The Open Epi calculator was used to find out

the sample size. Participants in the study were categorized into 2 categories according to the Sr.UA level, including normouricemia and hyperuricemia groups. Data collection involved demographic, anthropometric, and biochemical measurements. Participants were assessed in the morning following a minimum fasting duration of 12 hours. Demographic information, medical history, and lifestyle behaviors such as diet and physical activity were collected via a structured questionnaire. Measurements of anthropometric data like height, weight, and waist circumference were recorded by a Secastadiometer and a digital weighing scale. A standardized formula (kg/m^2) was used to calculate BMI, and central obesity was labelled if the waist circumference exceeded 94cm and 80cm in male and female respectively, while obesity was classified at a BMI of 30 kg/m^2 or more. Blood pressure was measured twice using the OMRON 907 automated device after a minimum five-minute rest, and the mean was calculated. If systolic blood pressure was $\geq 140 \text{ mmHg}$ or diastolic blood pressure was $\geq 90 \text{ mmHg}$, then the patient was labelled as hypertensive. An expert cardiologist diagnosed the cardiovascular disease by physical examination and electrocardiogram (ECG). The cardiovascular diseases were classified into three sub-classes, including acute coronary syndrome (ACS), myocardial infarction (MI), and heart failure (HF). Sr.UA concentration was tested using the Mindray BS-200E analyzer from venous blood samples. Sr.UA concentration more than 7 mg/dL in men and more than 6 mg/dL in women was used to define hyperuricemia. A semi-automated clinical chemistry analyzer was used to measure random blood sugar, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides. Data were analyzed by Statistical Package for Social Sciences (SPSS), version 22.0. Numerical variables were presented as means with standard deviations, while categorical variables were summarized using frequencies and percentages. Statistical analyses included independent t-tests and one-way ANOVA for normally distributed data, while for the data that did not follow a normal distribution, the Mann-Whitney U test was used. Qualitative data were assessed by chi-square tests. Pearson's correlation was utilized to evaluate associations among variables such as age, BMI, blood pressure, Sr.UA levels, and CVD incidence. Results were significant if the p-value was ≤ 0.05 . To determine the association of cardiovascular diseases in relation to rising Sr.UA concentration, a multivariate regression analysis was conducted, and the odds ratio at a 95% confidence interval was calculated.

RESULTS

About 370 participants were included in the study; out of them, 268 participants had normal uric acid levels, while

102 participants had hyperuricemia. The frequency of hyperuricemia was 27.5% cases, among them 21.1% were male, while 6.4% were their counterparts. The mean age of the study participants was 38.95 ± 10.9 years and 42.31 ± 9.7 years among normouricemia and hyperuricemia groups, respectively, with a significant association. Previous medical history of hypertension found a strong, significant association among the groups, but no association of diabetes mellitus or smoking was reported. At the time of study, the systolic blood pressure, diastolic blood pressure, body mass index (BMI), and waist circumference measurements also reported a strong and significant association among the groups. Frequency of CVD, including ACS, MI, and HF, was 47%, 29.1% and 6% in the normouricemia group and 54.9%, 25.5% and 6.9% in the hyperuricemia group, respectively, while no cardiac disease was found in 17.9% and 12.7% cases of the normouricemia and hyperuricemia group, respectively. Characteristics of the study participants of the two groups are presented in table 1.

Table 1: Characteristics of Study Participants (n=370)

Variables	Normouricemia (n=268)	Hyperuricemia (n= 102)	p-Value
Demographic Variables			
Age (Years)	38.95 ± 10.9	42.31 ± 9.7	0.024
Gender			
Male	167 (62.3%)	66 (64.7%)	0.242
Female	101 (37.7%)	36 (35.3%)	
History			
Diabetes mellitus	139 (51.8%)	55 (53.9%)	0.451
Hypertension	158 (58.9%)	57 (55.9%)	0.002
Smoking	153 (57.1%)	50 (49%)	0.582
Clinical Findings			
Systolic BP (mmHg)	134.6 ± 14.6	139.2 ± 12.4	0.001
Diastolic BP (mmHg)	85.1 ± 11.7	89.5 ± 12.9	0.007
BMI (kg/m²)	26.9 ± 4.7	28.7 ± 5.2	<0.001
Waist Circumference (cm)	91.8 ± 11.1	94.8 ± 10.6	<0.001
Biochemical Parameters			
Glucose (mg/dL)	153 ± 2.5	162 ± 3.4	0.925
Sr.UA (mg/dL)	6.15 ± 1.05	12.4 ± 1.7	0.000
TC (mg/dL)	172.5 ± 38	168 ± 32	0.243
HDLC (mg/dL)	42 ± 11	48 ± 13	0.032
LDLC (mg/dL)	105 ± 18	82 ± 15	0.004
Triglycerides (mg/dL)	187 ± 42	209 ± 32	0.012
Diagnosed Cases of Cardiovascular Disease			
No	48 (17.9%)	13 (12.7%)	<0.001
Acute Coronary Syndrome	126 (47.0%)	56 (54.9%)	
Myocardial Infarction	78 (29.1%)	26 (25.5%)	
Cardiac failure	16 (6.0%)	7 (6.9%)	

Results showed a link between hyperuricemia and the severity of cardiovascular disease as the non-cardiac study participants were having 5.6 ± 1.9 mg/dL mean serum uric acid level with standard deviation while 6.9 ± 2.1 mg/dL, $7.7 \pm$

2.5 mg/dL and 10.4 ± 2.7 mg/dL mean serum uric acid concentration with standard deviation were noted among patients of ACS, MI and HF respectively, as mentioned in figure 1.

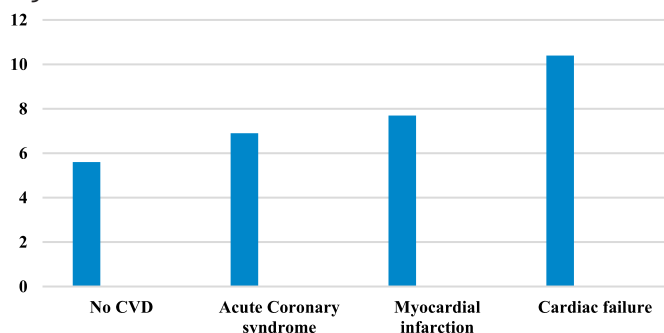


Figure 1: An Increase in Sr.UA with Severity of Cardiovascular Disease

Sr.UA concentration was divided into quartiles, including less than 5mg/dl uric acid concentration, 5-7mg/dl, 7-9mg/dl, and more than 9mg/dl uric acid concentration, and then the frequency of cardiovascular disease was assessed in each quartile. Results found that the severity of cardiovascular diseases increased linearly with increasing Sr.UA. Interestingly, higher levels of Sr.UA were found in the cases of MI when compared to other cardiovascular diseases, as shown in figure 2.

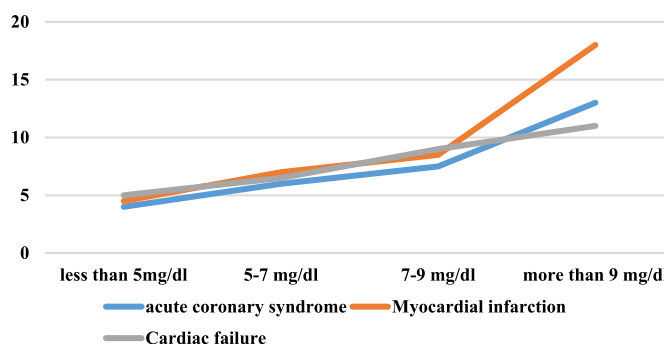


Figure 2: Sr.UA Quartile and Frequency of CVD

Multivariate regression analysis was done to find out the strength of association of CVD in each quartile of Sr.UA. Results reported that the odds ratio of cardiovascular disease was 1.42 times when the Sr.UA level was 5-7mg/dL and 1.84 times in the 3rd quartile, while it reached up to 2.45 times as the serum uric acid level rose above 9mg/dL. On the other hand, when confounding factors like age, gender, TC, HDLC, LDLC, triglycerides, hypertension and diabetes, were adjusted, the odd ratio of cardiovascular diseases remained significant in 3rd and 4th quartile of Sr.UA (7-9mg/dL and ≥ 9 mg/dL) but it decreased to 1.64 times in 3rd quartile and 2.09 times in 4th quartile as mentioned in table 2.

Table 2: Multivariate Regression Model of Sr.UA Quartile and Risk of CVD

Sr.UA Concentration	Model 1	Model 2	p-Value
Quartile	Odd Ratio (95% Confidence Interval)		
5-7 mg/dl (2 nd)	1.42 (0.96-1.88)	1.23 (0.88-1.72)	0.091
7-9 mg/dl (3 rd)	1.84 (1.35-2.52)	1.64 (1.05-2.12)	<0.001
≥9 mg/dl (4 th)	2.45 (1.84-3.39)	2.09 (1.32-2.98)	<0.001

DISCUSSIONS

Literature revealed a strong link between elevated Sr.UA and a rise in blood pressure, although the strength and nature of this association can vary depending on individual demographic characteristics such as age and gender. Studies also indicate that higher uric acid may increase the likelihood of CVD; the exact causal relationship is still being debated [12]. The current study noted a strong correlation of Sr.UA with age, BMI, systolic and diastolic blood pressure, waist circumference, and risk of developing cardiovascular disease. Similar patterns were reported in a Ghanaian study, particularly among women over 45, where Sr.UA was statistically correlated with age, BMI, and waist circumference [13]. In another large-scale Chinese study, higher BMI and waist circumference were identified as risk factors for developing hyperuricemia [14]. U.S.-based research found that individuals who were both overweight and had hyperuricemia had a significantly higher chance of hypertension and developing cardiovascular diseases. Longitudinal data from the Gusu cohort further suggested that obesity may contribute to hyperuricemia, which in turn partially explains the development of high blood pressure. Mediation analysis showed that uric acid played a partial intermediary role between excess weight and increased blood pressure, leading to coronary artery disease [15]. The present study also reported a strong association of hyperuricemia with CVD, leaving behind the commonly known confounding factors such as age, gender, total cholesterol, HDL, LDL, and triglycerides. The severity of cardiovascular diseases was observed to rise with increasing serum uric acid levels, and this link remained significant even when diabetes and hypertension, both established cardiovascular disease risk factors, were accounted for. Current results reported that the odds ratio of cardiovascular disease was 1.42 times when the Sr.UA was 5-7mg/dL and reached up to 2.45 times as the serum uric acid level rose above 9mg/dL. On the other hand, when confounding factors were adjusted, the odds ratio of cardiovascular diseases remained significant, but it decreased to 1.64 to 2.09 fold. Over the years, numerous large-scale investigations, such as the NHANES I follow-up study, the URRAH study, the Brisighella Heart Study, and the AMORIS study, examined this association. Data from the URRAH (Uric Acid Right for Heart Health) project indicated a higher chance of developing lethal cardiac

issues with hyperuricemia and suggested threshold values for reduced risk at <5.26mg/dL and 5.49mg/dL for both genders [16, 17]. Likewise, another analysis of the AMORIS data, which followed 417,734 individuals for 11.8 years, concluded that hyperuricemia increased the likelihood of acute myocardial infarction and both ischemic and hemorrhagic strokes [18]. In the Brisighella Heart Study, involving 1,557 participants, serum uric acid levels were used to predict MI, left ventricular hypertrophy, and arrhythmias detected via ECG [19]. In addition, a meta-analysis of 21 cohort studies reported a link between hyperuricemia and cardiovascular diseases in both healthy and high-risk populations, with a stronger correlation in the latter group [20]. Another large meta-analysis involving 402,997 individuals found only a modest increase in coronary heart disease risk linked to serum uric acid, casting some doubt on its function as an independent risk determinant [21]. Likewise, reviews and experimental data from the United Kingdom noted that serum uric acid's association with coronary heart disease might be influenced by other risk factors [22]. Further support comes from research on obese individuals and populations in China, Turkey, Korea, and Pakistan, where increasing Sr.UA was strongly correlated with more serious vascular disease [23, 24]. The current study also found an increased frequency of hyperuricemia in cases of cardiovascular disease, aligning with previous findings from Pakistan, which reported a correlation of hyperuricemia with heart failure risk indicators. The current study reported that ACS, MI, and HF were 54.9%, 25.5% and 6.9% in hyperuricemia patients. A large-scale study by Wheeler et al. encompassing over 9,000 cases and approximately 155,000 controls from eight nations, concluded that hyperuricemia is not a reliable predictor of CVD in asymptomatic individuals [25]. Likewise, NHANES III data involving over 11,000 participants did not identify any Sr.UA for CVD or vascular disease mortality, making the overall evidence on serum uric acid's role in cardiovascular disease somewhat inconclusive. A potential reason for these conflicting findings may be differences in population characteristics, such as lifestyle and diet, that can significantly influence the Sr.UA and CVD relationship. Despite various studies, none have comprehensively examined the association while fully accounting for lifestyle and diet. The current study's strength lies in its adjustment for these additional variables, demonstrating that hyperuricemia can enhance the risk of cardiovascular disease by approximately 2.09 times after controlling for both conventional and lifestyle-related confounders. This study's cross-sectional design limits causal interpretation between serum uric acid and cardiovascular disease. Additionally, single-time measurement of serum

uric acid may not reflect long-term exposure or variability related to diet, renal function, or medication use. Prospective cohort studies with repeated uric acid measurements and detailed dietary and metabolic profiling are needed to clarify the causal role of hyperuricemia in cardiovascular disease development.

CONCLUSIONS

The current study identified a significant association of hyperuricemia with cardiovascular diseases. The severity of cardiovascular diseases was observed to rise with increasing serum uric acid levels, and this link remained significant. Therefore, individuals who do not show clear symptoms of cardio-metabolic disorders but exhibit hyperuricemia should undergo cardiovascular evaluations.

Authors' Contribution

Conceptualization: NA

Methodology: NA, MZ, MKA, SZA

Formal analysis: MK, SZA

Writing and Drafting: AH, MZ, MKA, NL

Review and Editing: NA, AH, MZ, MKA, MK, SZA, NL

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Causes of Acute Abdomen Diagnosed Through Gray-Scale Ultrasonography in Adults at A Tertiary Care Hospital, Lahore

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ABSTRACT

Acute abdomen is a severe and sudden onset of pain over a short span of time, requiring urgent diagnosis and treatment. The prevalence of acute abdomen is found to be 5 percent in emergency department cases and a lower percentage in the OPD cases. **Objectives:** To diagnose the causes of acute abdomen via gray-scale ultrasonography in adults at a tertiary care hospital. **Methods:** The Study design was a descriptive cross-sectional. Data was collected through proforma and reports, and collected from the Diagnostic Center CMH Lahore. Data analysis was done through IBM SPSS software version 26.0, and the association between causes and the gender of the patient was calculated via chi chi-square test. **Results:** Out of 186 patients, 45.7% were male and 54.3% female, with a mean age of 47.44 years. Common symptoms/signs included nausea/vomiting (72.6%), fever (50%), abdominal tenderness (52.7%), and abdominal distension (33.9%). Moderate pain was the most prevalent severity of pain in 41.9% patients. RHC was the most prevalent region of pain (71%). Ultrasound diagnoses included cholelithiasis (20.4%), hydronephrosis (13.4%), acute cholecystitis (12.4%), renal colic (11.8%), and acute pancreatitis (8.1%), respectively. Other diagnoses were liver abscess (2.7%), splenic lesions (1.6%), and an unremarkable study (18.82%). **Conclusions:** The Current study concludes that there is a significant association between acute cholecystitis and the gender of the patient. It also highlights the significance of ultrasound in diagnosing the causes of acute abdomen, with cholelithiasis, hydronephrosis, renal colic, and acute cholecystitis as the most frequent causes of acute abdomen.

INTRODUCTION

Acute abdomen refers to a wide range of surgical, medical, and gynecological issues, fluctuating from minor to mortal conditions that necessitate hospitalization, complete examinations, and handling [1, 2]. Acute abdominal pain is most prevalent in the 20-29 age group in the technologically advanced world, with a male superiority. It is accountable for 36.4% of surgical emergencies [3]. Due to the wide variety of causes of acute abdomen, differential diagnosis is problematic [4]. Acute abdomen symptoms vary from mild, persistent dull aches to pronounced guarding and rigidity. Diagnosing life-threatening conditions at early stages is somehow difficult because

many serious and benign intra-abdominal complaints present with similar symptoms [5]. Mostly signs and symptoms of patients presenting with acute abdomen are vomiting, nausea, fever, abdominal tenderness [6]. The latest technology and a trained clinical eye are sometimes required to demonstrate it and compare it with surgical results [7]. While imaging techniques have increased diagnostic accuracy and reduced time to diagnosis, the history and physical examination are still the mainstays for evaluating acute abdominal discomfort [8]. Investigative studies play a key role in evaluating an acute abdomen. Laboratory tests alone are not enough; imaging studies are



also vital for a thorough evaluation. Patients with an acute abdomen initially visit a primary healthcare provider, who usually has access to only a few diagnostic tests. The choice of diagnostic method should be based on the likelihood of making a diagnosis and the potential risks of radiation exposure [9]. Perhaps the most notable of the many notable technological developments in all areas of medicine is ultrasonography [10]. One of the most popular imaging modalities that aids in confirming the clinician's diagnosis is ultrasound [11]. USG is a noninvasive, real-time imaging modality that has made it a popular choice for assessing patients with an acute abdomen. It is particularly helpful when a diagnosis must be made quickly [12]. It is anticipated that this method will speed up and improve the diagnosis and care of individuals with acute pathology [13]. Causes of acute pain in the abdomen, such as appendicitis, acute pancreatitis, acute cholecystitis, ovarian torsion, ruptured aortic aneurysm, lacerated spleen or liver, and a lot of others, can be easily diagnosed on ultrasonography. These conditions may require emergency treatment because they can be life-threatening if not treated on an emergency basis. An untreated acute abdomen can cause various serious complications [14]. The diagnostic accuracy of ultrasound for the diagnosis of causes of acute abdomen has been the subject of numerous investigations; nevertheless, the results of these earlier studies have varied [15]. Previous studies have limited literature about the root causes of acute abdomen in adults diagnosed through gray-scale ultrasound. They have mainly focused on the comparison of imaging modalities to diagnose the acute abdomen. They have mainly discussed a single or major cause of acute abdomen, thus have limited clinical information about the minor causes like hydronephrosis, liver abscess, splenic lesions, etc.

Most studies relied on retrospective data collection. The current study diagnoses the root causes of acute abdomen via gray-scale ultrasonography. This will help to enhance the patient outcomes for further treatments by diagnosing the root cause of acute abdomen at the acute/early stage of disease without sacrificing the patient's valuable time, and this will also support in minimizing the occurrence of pointless surgeries and lessening the likelihood of further subsequent complications. This study aimed to determine the causes of acute abdomen diagnosed through gray-scale ultrasonography in adults at a tertiary care hospital.

METHODS

This descriptive cross-sectional study was conducted at the Diagnostic Center of Combined Military Hospital Lahore between September and December 2024. This study was conducted in line with ethical standards set by the ethical committee of Combined Military Hospital, Lahore Medical College, and Institute of Dentistry, Lahore,

Pakistan. (Ref. No. 76/ERC/CMH/LMC). Written and verbal consent was taken from eligible participants. All information and data collection were kept confidential. Participants remained anonymous throughout the study. This study was conducted in accordance with the Declaration of Helsinki. Data were collected from 186 patients (both male and female), including young adults, middle-aged adults, and older adults [16]. The sample size was calculated through the WHO Geneva calculator. The prevalence of one of the causes of acute abdomen is found to be 14% [1]. The Cochran formula was used to determine the sample size $n = \frac{Z_{1-\alpha/2}^2 \cdot p(1-p)}{d^2}$ [17]. $P(\text{anticipated population proportion}) = 0.14$, $d(\text{absolute precision}) = 0.05$, $1-\alpha(\text{confidence level } \%) = 95$, $Z \text{ value (at 95\% CL)} = 1.96$, and $n(\text{sample size}) = 186$. Patients were selected through a non-probability convenience sampling technique. Patients above 15 years of age, including both male and female patients, presenting with symptoms (e.g., pain, tenderness, nausea, vomiting, etc.) of acute abdomen were included in the study. However, bedridden patients from Intensive Trauma Care (surgical/medical) who were not able to come to the diagnostic center of a tertiary care hospital, patients with a history of recent abdominal trauma or injury, pregnant females, patients with known or suspected malignancy, and patients with a history of recent surgery (post-operative) were excluded. Ultrasound machine (company name: Toshiba, Aloka, XARIO 100G, LOGIC GE) and Transducers such as curved linear (3-5MHz), linear high frequency transducer (7 MHz above) were used as equipment. All patients who fulfilled the inclusion/exclusion criteria were included in the current study. Consent was taken from all patients. The procedure was explained thoroughly to the patient. Patient preparation was done carefully. History was taken, including previous or recent surgeries of the abdomen, previous or recent trauma of abdomen, diabetes, hypertension, etc. Symptoms like fever, pain, and nausea/vomiting were asked about by the patient. Any signs like abdominal tenderness, rigidity, swelling, or distension were noted. The region of pain was noted, and pain intensity was recorded according to NPRS [18]. Patient positioning was done by the Technologist according to the examination of the region of interest. Ultrasound was performed by using a curvilinear transducer (3-5MHz) or high frequency linear transducer (7MHz above) by a radiologist. Measurements of organs in the region of interest were noted and filled in the proforma after the examination, accordingly, by the approval of the radiologist. Size, texture, and echogenicities of abnormal findings were mentioned in the proforma. Final diagnosis was given by the radiologist, and we mentioned the final diagnosis in the proforma. Images were obtained, and the

record was saved (including reports and diagnoses) according to the consent of the patient. The data collection tool was structured proforma and ultrasound reports/images. All data were analyzed through IBM SPSS (version 26). Descriptive analysis frequency and percentages were calculated for qualitative data (gender, history, sign/symptoms, region of pain, severity of pain, causes of acute abdomen, and association b/w gender and causes of acute abdomen), whereas mean and standard deviation were calculated for quantitative data (age of patients, pain duration). Inferential analysis was conducted using the Chi-square test to calculate the association between the gender of patients and causes of acute abdomen. A p-value ≤ 0.05 was considered a statistically significant value.

RESULTS

In the current study, 186 patients presenting with symptoms of acute abdomen were evaluated to determine the prevalence of its causes in adults using gray-scale ultrasonography. Among these, 85 (45.7%) were male and 101 (54.3%) were female. The mean age of the study population was 47.44 ± 16.76 years. Among all participants, 135 (72.6%) reported nausea/vomiting, 93 (50%) had fever, and 98 (52.7%) experienced abdominal tenderness, which were the most common clinical symptoms. Regarding pain severity, 51 (27.4%) had mild pain, 78 (41.9%) had moderate pain, and 57 (30.7%) experienced severe abdominal pain, with moderate pain being the most prevalent (Table 1).

Table 1: Descriptive Analysis of Patients' Symptoms

Variables	Responses	n (%)
Nausea/vomiting	No	51 (27.4%)
	Yes	135 (72.6%)
Fever	No	93 (50.0%)
	Yes	93 (50.0%)
Tenderness	No	88 (47.3%)
	Yes	98 (52.7%)
Swelling	No	161 (86.6%)
	Yes	25 (13.4%)
Abdominal distension	No	123 (66.1%)
	Yes	63 (33.9%)
Guarding and rigidity	No	119 (64.0%)
	Yes	67 (36.0%)
Severity of pain	Mild (1 to 3)	51 (27.4%)
	Moderate (4 to 6)	78 (41.9%)
	Worst (7 to 10)	57 (30.7%)
Total		186 (100.0%)

The results showed that Out of 186 patients, 7 (3.8%) patients were diagnosed with Appendicitis through gray scale ultrasound, 15 (8.1%) patients were diagnosed with Acute pancreatitis, 23 (12.4%) patients were diagnosed with acute Cholecystitis, 22 (11.8%) patients were

diagnosed with Renal colic on gray scale ultrasound, 25 (13.4%) patients were diagnosed with Hydronephrosis through ultrasonography, 2 (1.1%) patients were diagnosed with Inflammatory bowel disease, Intestinal obstruction was diagnosed in 1 (0.5%), 38 (20.4%) cases were reported for Cholelithiasis, Liver abscess was detected in 5 (2.7%) patients, 3 (1.6%) patients were diagnosed with Splenic lesions/abscess on ultrasound, 5 (2.7%) cases were reported as hemorrhagic Renal cysts (single and multiple both), 1 (0.5%) case was reported as Choledocholithiasis and 35 (18.8%) patients were reported as Normal (had unremarkable study on ultrasound).

Table 2: Frequency of Causes of Acute Abdomen

Causes	Responses	n (%)
Appendicitis	No	179 (96.2%)
	Yes	7 (3.8%)
Acute pancreatitis	No	171 (91.9%)
	Yes	15 (8.1%)
Acute Cholecystitis	No	163 (87.6%)
	Yes	23 (12.4%)
Renal colic	No	164 (88.2%)
	Yes	22 (11.8%)
Hydronephrosis	No	161 (86.8%)
	Yes	25 (13.4%)
Inflammatory Bowel Disease	No	184 (98.9%)
	Yes	2 (1.1%)
Intestinal obstruction	No	185 (99.5%)
	Yes	1 (0.5%)
Cholelithiasis	No	148 (79.6%)
	Yes	38 (20.4%)
Liver abscess	No	181 (97.3%)
	Yes	5 (2.7%)
Splenic lesions/abscess	No	183 (98.4%)
	Yes	3 (1.6%)
Renal cyst (hemorrhagic)	No	181 (97.3%)
	Yes	5 (2.7%)
Choledocholithiasis	No	185 (99.5%)
	Yes	1 (0.5%)
Unremarkable study	No	151 (81.2%)
	Yes	35 (18.8%)
Total		186 (100.0%)

A male patient presented with severe pain in the right and left lumbar regions for the past 8 hours, accompanied by fever and hyperemesis. Laboratory tests were performed 2 hours before imaging. Transabdominal ultrasonography revealed multiple renal calculi in the right kidney, the largest measuring 3.9 mm (Figure 1).



Figure 1: Transabdominal Ultrasound Showing Multiple Renal Calculi in the Right Kidney (Largest Measuring 3.9 mm)

Another case involved a female patient presenting with severe pain in the right hypochondrium region for 8 hours and marked abdominal tenderness. Transabdominal ultrasound revealed multiple tiny calculi (largest > 4 mm) with posterior acoustic shadowing, confirming cholelithiasis (Figure 2).



Figure 2: Transabdominal Ultrasound Showing Cholelithiasis with Multiple Tiny Calculi (Largest > 4 mm) Producing Posterior Acoustic Shadowing

The study results showed that out of 186 patients (including males and females), 15 males and 8 females had acute cholecystitis with chi sq. value 4.029 and P value 0.045 showing significant association with gender of patient because it has P value less than 0.05, all other causes of acute abdomen such as appendicitis, pancreatitis, renal colic, cholelithiasis, liver abscess, intestinal obstruction, splenic lesion, hydronephrosis, IBD, renal cyst (hemorrhagic), choledocholithiasis had $P \geq 0.05$, Chi-sq. The test shows a non-significant association between the gender of the patient and these causes of acute abdomen (Table 3).

Table 3: Association of Causes of Acute Abdomen with Gender

Variables		Gender of the patient		Total Count %	Chi sq. Value	p-Value
		Male Count & %	Female Count & %			
Appendicitis	No	81 (95.3%)	98 (97.0%)	179 (96.2%)	0.384	0.536
	Yes	4 (4.7%)	3 (3.0%)	7 (3.8%)		
Acute pancreatitis	No	80 (94.1%)	91 (90.1%)	171 (91.9%)	1.005	0.316
	Yes	5 (5.9%)	10 (9.9%)	15 (18.1%)		
Acute Cholecystitis	No	70 (82.4%)	93 (92.1%)	163 (87.6%)	4.029	0.045*
	Yes	15 (17.6%)	8 (7.9%)	23 (12.3%)		
Renal colic	No	77 (90.6%)	87 (86.1%)	164 (88.2%)	0.876	0.349
	Yes	8 (9.4%)	14 (13.9%)	22 (11.8%)		
Hydronephrosis	No	72 (84.7%)	89 (88.1%)	161 (86.6%)	0.462	0.497
	Yes	13 (15.3%)	12 (11.9%)	25 (13.4%)		
Inflammatory Bowel Disease	No	84 (98.8%)	100 (99%)	184 (98.9%)	0.15	0.0902
	Yes	1 (1.2%)	1 (1.0%)	2 (1.1%)		
Intestinal obstruction	No	85 (100.0%)	100 (99.0%)	185 (99.5%)	0.846	0.358
	Yes	0 (0%)	1 (1.0%)	1 (0.5%)		
Cholelithiasis	No	68 (80%)	80 (79.2%)	148 (79.6%)	0.018	0.894
	Yes	17 (20%)	21 (20.8%)	38 (20.4%)		
Liver abscess	No	81 (95.3%)	100 (99.0%)	181 (97.3%)	2.436	0.119
	Yes	4 (4.7%)	1 (1.0%)	5 (2.7%)		
Splenic lesions /abscess	No	83 (97.6%)	100 (99.0%)	183 (98.4%)	0.54	0.462
	Yes	2 (2.4%)	1 (1.0%)	3 (1.6%)		
Renal cyst (hemorrhagic)	No	83 (87.6%)	98 (97.0%)	181 (97.3%)	0.067	0.795
	Yes	2 (2.4%)	3 (3.0%)	5 (2.7%)		
Choledo- cholithiasis	No	84 (98.8%)	101 (100%)	185 (99.5%)	1.195	0.274
	Yes	1 (1.2%)	0 (0.0%)	1 (0.5%)		
Unremarkable study	No	72 (84.7%)	79 (78.2%)	151 (81.2%)	1.272	0.259
	Yes	13 (15.3%)	22 (21.8%)	35 (18.8%)		

DISCUSSION

Acute abdominal pain requires immediate attention and treatment. Surgeons and other medical professionals continue to face diagnostic challenges, as it remains one of the most frequent causes of hospital admissions worldwide. Early identification of the underlying cause is crucial for timely decision-making regarding appropriate management, whether conservative or surgical [19]. Patients who receive structured and focused diagnosis and treatment have much lower morbidity and mortality rates [20]. A 2023 study aimed to determine the causes of acute abdomen [21]. According to that study, the most frequent diagnoses were cholecystitis (7.9%), appendicitis (14.5%), and perforation (18.9%), indicating a higher prevalence of acute surgical conditions. In contrast, the current study, involving 186 patients, found that acute cholecystitis (12.4%), hydronephrosis (13.4%), and cholelithiasis (20.4%) were the most common diagnoses. Fewer cases of appendicitis (3.8%) and perforation were observed, suggesting a broader range of gastrointestinal problems in the present population. Both studies emphasized the diagnostic value of ultrasound in evaluating abdominal conditions. In 2015, another study reported that

cholelithiasis was more prevalent in females (6.8%) than in males (4.7%) and identified age and female sex as major risk factors [22]. The current study also noted a higher frequency of cholelithiasis and related symptoms among females, with abdominal discomfort (24.7%), nausea or vomiting (72.6%), fever (50%), and abdominal tenderness (52.7%) being the most common clinical findings.

The current study had several limitations. As ultrasound is operator-dependent, results may vary depending on the skill and experience of the examiner. Self-reported pain may introduce variability in symptom assessment. Furthermore, obesity and deeper lesions may limit ultrasound sensitivity. Future studies should compare the diagnostic accuracy of ultrasound with other imaging modalities like CT scans or MRIs. Follow-ups should be done by researchers in the future to determine how patients' conditions changed or how accurate the ultrasound diagnosis was. They should also concentrate on the management of causes of acute abdomen along with diagnosis.

CONCLUSIONS

The current study concludes that there is a significant association between acute cholecystitis and the gender of the patient. It also highlights the significance of ultrasound in diagnosing the causes of acute abdomen, with cholelithiasis, hydronephrosis, renal colic, and acute cholecystitis as the most frequent causes of acute abdomen.

Authors' Contribution

Conceptualization: NS,

Methodology: MS, ZS, AR

Formal analysis: AR

Writing and Drafting: MS, ZS, AR, AA, HQ, MBB, YK

Review and Editing: MS, ZS, AR, AA, HQ, MBB, YK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Evaluating Perception of Undergraduate Medical Students About Integrated Modular System

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ABSTRACT

The Integrated Modular System (IMS) is a structured program that begins with basic medical concepts and integrates all medical science components both horizontally and vertically. **Objectives:** To assess total perception scores, sub-variable scores, and the associations between research and demographic variables. **Methods:** An analytical cross-sectional study was conducted at Gomal Medical College using a quantitative approach with undergraduate students. Stratified random sampling was applied. The sampling frame comprised official enrollment lists from GMC's registrar. Strata were defined by academic year (Year 1-Final Year) to ensure proportional representation. Within each stratum, students were randomly selected using Google Sheets' RAND function to generate random numbers assigned to roll numbers. The top 40 unique random numbers per year were selected. A self-administered questionnaire, scored on a five-point Likert scale, assessed student perceptions across four sub-variables and three demographic variables. Scores were categorized as poor, fair, or good using Bloom's criteria. SPSS version 27.0 was used to compute frequencies, percentages, and perform chi-square and Fisher's exact tests. **Results:** Out of 200 participants, 72.5% had fair perception, 16.5% good, and 11.5% poor. No significant association was found between gender or residence and total perception score. However, a significant association existed between students' year of study and their perception score. **Conclusions:** Students generally had an average yet cautiously positive perception of IMS, especially regarding learning behaviour and future outcomes. Concerns remain about achieving IMS goals and resource availability. DME should enhance evaluation guidelines and time allocation, while administration must improve self-directed learning resources.

INTRODUCTION

The medical education system, supported by adequate resources and proper implementation, directly influences students' learning habits, clinical skills, critical thinking, and research capabilities [1]. With great advancement in every field of science and technology, medical sciences have also been going through a tremendous amount of upgrading and refinement by shifting toward an interdisciplinary approach [2]. The outdated conventional system failed to match expanding curricula, prompting the need for a modern, well-planned, and efficiently timed learning approach [1, 3]. Strengthening the integration of basic science education with clinical practice is

recognized as an effective approach to improving medical education and can serve as a foundational strategy for curriculum development [4]. An integrated modular system is a structured program which starts with the basic concepts of medicine and incorporates all components of medical sciences in a horizontal as well as vertical manner [5, 6]. The Integrated Modular System promotes coordinated, system-based teaching, where departments align content like physiology and pathology in a liver module requiring cross-departmental and institutional collaboration [7]. Integrated curricula blend early clinical exposure with continued science teaching, unlike



traditional models that separate science and clinical training by years [8]. This approach broadens professional knowledge and skills, while also supporting better career guidance and employability for graduates [9]. The evaluation of the effectiveness of the integrated modular system among students in every medical college is essential to find out the advantages, drawbacks and areas that need further improvement [3]. The majority of students appreciated the integrated modular system of teaching in a study conducted at a public sector medical college [10]. Another research concluded that the majority of students were satisfied with the integrated curriculum but were not satisfied with the time allocation for each module [11]. A clear institutional vision is essential for adopting an integrated curriculum, but the rapid rise of medical colleges and the lack of experienced educators in Pakistan may stall progress [12].

As a new system, the Integrated Modular System may face challenges during adaptation, which can be addressed by incorporating student feedback to reveal its effectiveness and underlying issues [13]. No prior research has explored students' perceptions of the Integrated Modular System (IMS) at Gomal Medical College, Dera Ismail Khan. This study aims to assess whether IMS meets its objectives, the adequacy of available resources, and its impact on learning and career readiness. Findings guide improvements in curriculum, resource allocation, and policy, helping enhance the system's effectiveness and aligning it with students' educational needs.

METHODS

The study used a quantitative, cross-sectional design at Gomal Medical College (GMC), Dera Ismail Khan, from October to December 2024. Ethical approval was obtained from the Ethical Review Committee of GMC, MTI, Dera Ismail Khan (144/GJMS/JC). A sample of 200 students was selected using stratified random sampling via Google Sheets, with 40 students chosen from each year. Five strata were created, each representing an academic year, and students were randomly selected from each stratum using their assigned roll numbers. The sample size was determined using the Raosoft calculator, assuming a 95% confidence level, 5.40% margin of error, and 63% response distribution, based on a population of 571 students. Inclusion criteria included all undergraduate students at GMC; those who did not consent were excluded. Data were collected using a self-administered, validated questionnaire approved by the Community Medicine Department and piloted with 20 students. The Cronbach alpha value was calculated as 0.745. A five-point Likert scale was used for responses (1 = Strongly Disagree to 5 = Strongly Agree). The primary variable was student perception, divided into four subdomains: achievement of

aims/objectives, resource availability, learning behaviour, and future outcomes each with five items. Demographic data (gender, residence, year) was also recorded. Mean scores calculated based on Likert scores for perception and subdomains were calculated and categorized using Bloom's criteria: <3 as "Poor," 3–3.9 as "Fair," and 4–5 as "Good." Statistical analysis was done using SPSS version 27.0, which included frequencies, percentages, chi-square and/or Fisher's exact test, with a significance level of $p < 0.05$ and 95% confidence interval.

RESULTS

The demographic characteristics of the participants are presented in table 1.

Table 1: Demographic Characteristics of the Participants

Years	Male	Female	On-campus	Off-campus	Total
1 st Year	26	14	31	9	40
2 nd Year	24	16	28	12	40
3 rd Year	28	12	30	10	40
4 th Year	26	14	33	7	40
Final Year	29	11	33	7	40
Total	133 (66.5%)	67 (33.5%)	155 (77.5%)	45 (22.5%)	200

After analyzing students' perceptions of the Integrated Modular System (IMS), 22 students (11%) had a poor overall perception, 145 (72.5%) had a fair perception, and 33 (16.5%) had a good perception. The first sub-variable, "achievement of aims and objectives," showed 19.5% poor, 57.5% fair, and 23% good perception. For "availability of resources," 40% had a poor perception, 46.5% fair, and only 13.5% good, indicating concerns about resource adequacy. The third sub-variable, "improvement in learning behaviour," revealed a more positive outlook, with 12% poor, 47.5% fair, and 40.5% good perception. The final sub-variable, "future outcomes," showed 14% poor, 41% fair, and 45% good perception, reflecting optimism about long-term benefits. These findings collectively highlight cautious acceptance of the IMS, with particular concerns about resources but hope for future outcomes and learning improvements, as mentioned in figure 1.

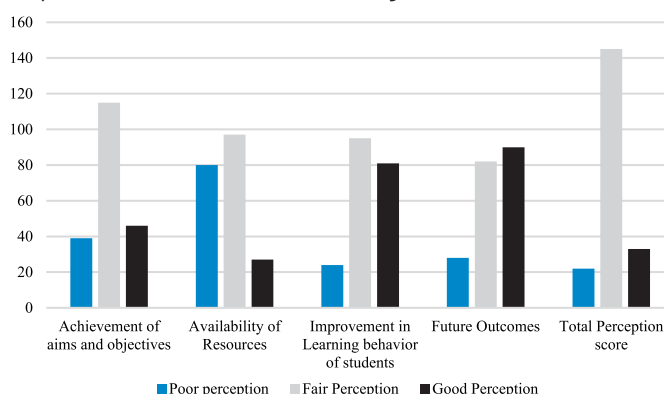


Figure 1: Students' Perceptions of the Integrated Modular System

Chi-square analysis showed no significant association between total perception score and gender ($p=0.435$) or residence ($p=0.254$). A significant association was found with year of study ($p=0.026$). Confidence intervals were calculated to generalize perception scores to the population, as mentioned in table 2.

Table 2: Chi-Square Analysis Between Total Perception Score and Gender

Perception Category	Group	Lower	Upper
Poor Perception	Overall	5%	18%
	Male	7%	21%
	Female	2%	13%

Fair Perception	On-campus	5%	18%
	Off-campus	4%	16%
	Overall	64%	81%
	Male	62%	80%
	Female	63%	81%
	On-campus	65%	83%
Good Perception	Off-campus	53%	73%
	Overall	10%	25%
	Male	8%	23%
	Female	12%	27%
	On-campus	7%	22%
	Off campus	16%	33%

The analysis shows how often each of the sub-variables

was rated on a 5-point Likert scale, from "Strongly Agree" to "Strongly Disagree," based on responses from 200 people. The frequency of students was represented as n. Explore the data to see how each item was rated and uncover the trends in the responses, as in table 3.

Table 3: Sub-Variables Rated on A 5-Point Likert Scale, Based on Responses from 200 People

Items	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Sub-variable 1: Achievement of Aims and Objectives of IMS					
The integration of basic medical sciences and their clinical correlates strengthens both your medical concept and clinical skills.	93	75	19	7	6
Learning objectives are precise, clear and delivered accurately.	14	93	50	30	13
The end-of-modular assessments are according to the learning objectives, and are graded timely manner.	37	80	41	28	14
The subjects among the modules are integrated Properly and no repetition of topics is observed.	41	75	31	42	11
The teacher's evaluation and the curriculum feedback are taken regularly at the end of the module by the DME.	22	28	35	66	49
Sub-variable 2: Availability of Resources					
The resources for self-directed learning, like the library, are always available to the students.	28	46	27	42	57
The number of faculty available for each The department is enough.	38	93	40	22	7
The faculty is well-trained according to the requirements of IMS.	24	64	50	44	18
IMS provides ample Opportunities for high-quality research.	24	58	57	44	17
The time allotted to each module is sufficient to cover all topics completely.	26	45	26	67	36
Sub-variable 3: Improvement in the Learning Behaviour of Students					
Scenario-based learning helps you apply your theoretical knowledge and in critically.	88	72	21	14	5
Small group discussions enhance collaboration, participation and communication skills among students.	78	71	24	15	12
Students prefer to prepare the whole syllabus rather than focusing on frequently asked questions.	37	66	49	32	37
IMS fosters collaboration and teamwork among students.	38	80	49	25	8
IMS promotes lifelong learning habits.	30	75	56	24	15
Sub-variable 4: Future Outcomes					
Students find the IMS very relevant to real-world practice.	45	44	43	16	12
The integrated modular system accommodates different learning styles and preferences.	32	99	39	22	8
IMS prepares the students very well for the professional exams.	56	72	44	19	9
The IMS prepares you very well for future specialization or residency programs.	41	71	58	17	13
The students of GMC would like to recommend IMS to future medical students.	73	70	27	14	16

DISCUSSIONS

The concept of an integrated curriculum in medical education with an organ system approach was introduced in the Case Western University School of Medicine in 1952 and quickly gained widespread acceptance. It has been studied in China since the 1990s [14]. Subsequently, Khyber Medical University, Peshawar, adopted this approach in its affiliated colleges in 2018, aligning with global trends to improve the quality and coherence of medical education. The purpose of our study was to evaluate the perceptions of medical students currently enrolled at Gomal Medical College regarding the modern educational system introduced at their institution. In our study, most students (72.5%) exhibited a Fair response based on their total perception scores. This finding was consistent with Masood *et al.* findings, which also reported a satisfactory or impartial level of perception among 45.4% students [15]. 72.6% students strongly affirmed that integrated teaching helps in clinically applying basic knowledge in a study by Wajid *et al.* This finding WAS consistent with the responses to the first item of our questionnaire [16]. Studies have also shown that the integrated PBL curriculum model positively influences the development of clinical thinking skills in undergraduate medical students. The PBL group showed similar pre-test high-level clinical thinking as the control group (82.81% vs. 81.43%) but significantly higher post-test results (92.13% vs. 85.71%), indicating the PBL curriculum's effectiveness [17]. 58% of our participants were positive about the proper integration of subjects in each module, while 52% participants felt that it was well to very well integrated in a study conducted in Ethiopia [18]. Additionally, 40% of our students were satisfied with assessment strategies, while 51.3% of respondents in a study conducted by Atta *et al.* were dissatisfied with assessments [19]. Students were utterly dissatisfied with the role of DME in teachers' evaluation and curriculum feedback, as observed in our study. No relevant study was found that evaluated the role of DME in the effective implementation of IMS. Aziz *et al.* highlighted in a qualitative study about the challenges in curriculum development and interdepartmental collaboration within integrated modular curricula [11]. Regarding satisfaction with faculty, 32% of our students agreed, and 25% were neutral, which contrasts with a study of Atta *et al.* where 46.3% were strongly satisfied with the teaching strategy [19]. A significant portion (33.5%) disagreed and (29.8%) strongly disagreed with the time allotment for each module, according to our study, aligning with findings by Jalil and Usmani, in which 21.9% strongly disagreed and 29.8% disagreed when asked about the appropriate time given for module completion [20]. Over half of the students were concerned about learning resource availability,

similar to Masood *et al.* findings, where 34.4% students were not satisfied with computers and internet access, but 44.4% students agreed with the availability of other resources [15]. Scenario-based learning was deemed helpful by over 70% of students, compared to only 24.2% who found it useful in the study by Jalil and Usmani [20]. Small group discussions were also greatly appreciated by the respondents of our research 97.1% participants found it useful in another study, and also 55.1% participants acknowledged the role of IMS in encouraging teamwork and collaboration among students in a study by Fatima *et al.* [3]. No statistically significant difference in perception by gender was observed in our study, which is in accordance with the analysis carried out by Wajid *et al.* [16]. There was a significant difference in students' perception by year of study as analyzed in our study, which was in conformance with the study conducted by Jalil and Usmani. [20]. Additionally, there was no significant difference observed in the perception of on-campus and off-campus students. No relevant article could be found that associated the residence status of students with their perception of IMS. A major limitation of this study is its focus on a single institution, which restricts the generalizability of results. Including multiple institutions in future research would offer a broader perspective. The exclusion of faculty and administrative views also limits the depth of analysis. Based on our findings, in future, we recommend that the DME standardize teacher evaluation and curriculum feedback, revise module time allocation, and strengthen library and internet facilities to support effective self-directed learning.

CONCLUSIONS

GMC students show a generally positive perception of IMS, consistent with earlier studies. IMS is valued for enhancing learning behaviour and professional development, with significant differences by year but not gender or residency. However, students expressed concerns about DME's evaluation role and poor support for self-directed learning. Positive feedback was noted for scenario-based learning and teamwork, highlighting the system's alignment with real-world practice and diverse learning needs.

Authors' Contribution

Conceptualization: FUR

Methodology: NF, MUB, MS, NM, UU, ZUH

Formal analysis: NF, MS, NM

Writing and Drafting: NF, MUB, MAYK, UU

Review and Editing: NF, MUB, FUR, MS, NM, UU, ZUH

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Relationship of Lower Urinary Tract Symptoms with Post Void Residual Urine and Prostatic Volume

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ABSTRACT

Benign prostatic hyperplasia (BPH) is a frequent occurrence in older male. **Objectives:** To assess the correlation between International Prostate Symptoms Score (IPSS), prostate volume, and post-void residual volume (PVR). **Methods:** This was an analytical cross-sectional study conducted in the Urology Department of Sheikh Zayed Hospital, Rahim Yar Khan. Eighty-four men aged 40-70 years with BPH and LUTS for $\geq$ two months were recruited consecutively. Participants completed the IPSS, and PVR was assessed by abdominal sonography and prostate volume through transrectal ultrasound. A urinary tract infection was labelled by the growth of $\geq$ 105 CFU/ml of pathogenic microorganisms. Pearson correlation between IPSS and prostate volume and post-void urinary volume was calculated at 5% significance level. **Results:** Mean age was 57.9 ± 6.9 years, and 63.1% were ≤ 60 years of age. Mean prostate volume was 68.9 ± 17.0 cm³, and PVR was 191.5 ± 53.3 ml. Mean IPSS was 16.3 ± 6.4 , with 67.9% having moderate LUTS. UTI prevalence was 54.8%. IPSS correlated positively and strongly with prostate volume ($r = 0.911$) and PVR ($r = 0.920$; $p < 0.001$). UTI was more common in patients > 60 years (80.6% vs. 39.6%) and in those with moderate (56.1%) and severe (100%) versus mild (13.3%) LUTS. **Conclusions:** IPSS showed a positive correlation with prostate volume and PVR, highlighting the utility of combined symptom scoring and ultrasound in managing benign prostatic enlargement.

INTRODUCTION

Urologists, in their routine practice, deal with older patients having lower urinary tract symptoms (LUTS), which affect patients' quality of life adversely [1]. Although the main reason for LUTS in older males is benign prostatic hyperplasia (BPH), LUTS is linked to a variety of conditions, including systemic metabolic diseases [2]. A simple physical examination, a review of sexual function, and a medical history are all included in the early assessment of males with LUTS [3]. When a patient first presents with such symptoms, he is evaluated by scoring the symptoms, getting his complete urine microscopy, and determining post-void residual (PVR) urine. A reliable method to assess

the subjective intensity of LUTS and their evolution over time is the International Prostate Symptoms Score (IPSS) is commonly utilized in routine practice for symptom scoring [4]. After passage of urine, the residual urine, which is retained in the urinary bladder, is called PVR (post-void residual) urine volume. This is one important test used in the initial evaluation of LUTS secondary to BPH [5]. Because PVR is easy to use, accessible, and reasonably priced, urologists commonly use it in their everyday clinical practice to evaluate LUTS secondary to BPH [6]. Another crucial factor in the treatment of BPH patients is the evaluation of prostate volume. Although digital rectal



examination (DRE) can estimate prostate volume, ultrasonography, especially transrectal ultrasound (TRUS), is now the gold standard because it is more accurate. Prostate volume and the intensity of LUTS have been correlated in many investigations, although the findings have been mixed. Significant correlations were found in some of the investigations, but not in others [7]. Two hundred and ninety patients who had LUTS, giving a clue of BPH, were the subjects of prospective correlational research. The self-administered IPSS questionnaire was utilized to gauge the severity of the symptoms. A transrectal ultrasound was used to measure the volume of the prostate. The study found that, with an average IPSS score of 16.41 ± 7.43 , most patients (55%) reported moderate symptoms. Prostate volume and IPSS were significantly positively correlated [8]. One hundred males experiencing LUTS were recruited in a research study. A carefully crafted questionnaire was used to evaluate each subject. The mean volume of the prostate was 78.4 ± 30.7 ml, and the IPSS was mild, moderate, and severe in 28%, 22%, and 50% of cases, respectively. Urine volume mean after voiding was 69.3 ± 39.8 ml. The IPSS, prostate volume, PVR, and quality of life were found to be significantly correlated [9]. Further research was required due to the ongoing debates and information gaps about the association between prostatic volume, PVR urine, and LUTS, as well as the unknown thresholds for when elevated PVR contributes to symptom severity. Since there was currently conflicting information about how PVR and prostate size interact to affect LUTS, this study attempted to investigate these interactions. By looking at these elements, the study wanted to improve treatment plans and diagnostic standards, which will eventually improve patient care and quality of life.

Lower urinary tract symptoms in older men are commonly assessed using IPSS, prostate volume, and post-void residual urine, yet these parameters are routinely used despite variable evidence of their interrelationships. Existing studies report inconsistent and conflicting associations between IPSS, prostate volume, and PVR, with unclear thresholds for clinically significant PVR contributing to symptom severity. This study aims to assess the correlation between International Prostate Symptoms Score (IPSS), prostate volume, and post-void residual volume (PVR).

METHODS

This analytical cross-sectional study was performed at the Urology Department of Sheikh Zayed Hospital, Rahim Yar Khan, over a study period of 6 months from 25th January 2025 to 24th July 2025 after approval from the institutional ethics review committee (Ref no. 43/IRB/SZMC/SZH). From all subjects, written informed consent was taken before the

start of the study. Approval was also taken from the institutional ethical committee, and the principles highlighted in the Declaration of Helsinki. A total of 84 patients with benign prostatic enlargement (based on digital rectal examination and prostate volume > 30 ml on ultrasound), aged 40–70 years and LUTS for a minimum of 2 months, and with an IPSS ≥ 8 were consecutively recruited in the present study. Patients with urethral stricture, prostatic carcinoma, neurogenic or overactive bladder, and prior surgery for benign prostatic enlargement were excluded from the study. All subjects filled the self-administered IPSS, consisting of seven items on a score ranging from 0–5, with total score of 35. IPSS is used for grading LUTS. IPSS was developed in 1992 [10] and found to have a good internal consistency (Cronbach's $\alpha = 0.60$ to 0.98) and good test-retest reliability (Intra-class correlation = ICC = 0.59 to 0.99) [11]. All patients were provided with help to fill in the IPSS questionnaire. Patients were classified as having mild (0–7), moderate (8–19), and severe (20–35) LUTS. A transabdominal ultrasound was performed immediately by a consultant radiologist with ≥ 5 years' post-fellowship experience to determine the PVR (ml) and prostate volume. Under full aseptic measures, transrectal ultrasound was performed in the left lateral position by use of a 6.6 MHz probe, which was well lubricated. The prolate ellipsoid formula ($\text{length} \times \text{height} \times \text{width} \times \pi/6$) was used to calculate the prostate volume. A urinary tract infection was labelled if 10^5 CFU/ml of a single pathogen was cultured from a clean catch urine specimen. A minimum sample size of 84 patients was calculated through an online sample size calculator <https://sample-size.net/correlation-sample-size/> using the correlation formula: $N = [(Z\alpha + Z\beta)/C]^2 + 3$. Where $C = 0.5 * \ln[(1+r)/(1-r)]$, assuming a 5% significance level, 20% type II error (β), and 0.304 correlation (r) between prostate volume and IPSS [12]. Data analysis was done through SPSS version 27.0. Numerical data were normally distributed as determined through the Shapiro-Wilk test. Descriptive statistics are run as mean $\pm$ SD for numerical data and frequency and percentages for categorical data. Correlation between IPSS and prostate volume and PVR was assessed through the Pearson correlation coefficient (r) at 5% significance level. Confounding and effect modification were controlled through stratification on patient characteristics using the chi-square test for categorical and correlation was measured again.

RESULTS

The mean age of the participants was 57.9 ± 6.9 years, and 53 (63.1%) were 60 years or below. The mean prostate volume was 68.9 ± 17.0 cm³, and the PVR volume was 191.5 ± 53.3 ml. The mean of IPSS was 16.3 ± 6.4 , and 57 (67.9%) of the patients had moderate LUTS. Urinary tract infection

was prevalent in 46(54.8%) of the patients (Table 1).

Table 1: Characteristics of Patients Presenting with LUTS (n=84)

Characteristics	Mean $\pm$ SD, n (%)
Age	
Years	57.9 $\pm$ 6.9
≤ 60 Years	53 (63.1%)
> 60 Years	31 (36.9%)
Volume	
Prostate Volume (cm ³)	68.9 $\pm$ 17.0
PVR (ml)	191.5 $\pm$ 53.3
IPSS Score	16.3 $\pm$ 6.4
Grades of LUTS	
Mild (1-7)	15 (17.9%)
Moderate (8-19)	57 (67.9%)
Severe (20-35)	12 (14.3%)
Urinary Tract Infection	
Yes	46 (54.8%)
No	38 (45.2%)

IPSS: International Prostate Symptom Score, LUTS: Lower urinary tract symptoms, and PVR: Post-void residual urine.

Out of 46 patients with urinary tract infection, the most common pathogen identified was *E. coli* (n=15, 32.6%) followed by *K. pneumoniae* (n=8, 17.4%) and *P. aeruginosa* (n=7, 15.2%) (Figure 1).

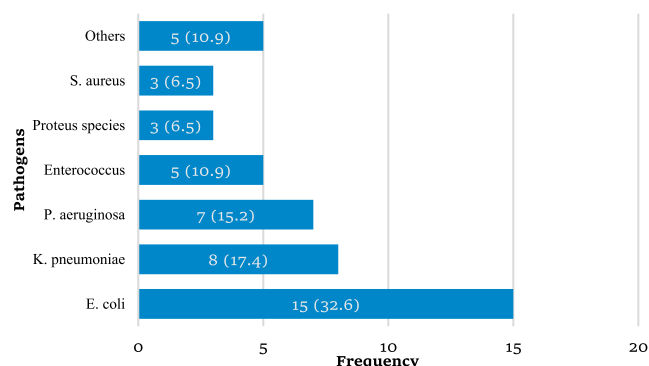


Figure 1: Uropathogens Isolated from Patients Presenting with Lower Urinary Tract Symptoms (n=84)

*Others: Enterobacter (2), Citrobacter (1), Acinetobacter species (1), and Serratia species (1)

IPSS had a strong, positive, and significant correlation with prostate volume ($r = 0.911$) and PVR volume ($r = 0.920$) (Table 2).

Table 2: Correlation of IPSS with Prostate Volume and PVR in Patients Presenting with LUTS (n=84)

Factors	Pearson Correlation	p-Value
Prostate Volume (cm ³)	0.911	<0.001*
PVR (ml)	0.920	<0.001*

*statistically significant

After stratification on patient characteristics correlation of IPSS with prostate volume and PVR remained strongly positive and significant (Table 3).

Table 3: Effect of Patient Characteristics on Correlation of IPSS with Prostate Volume and PVR in Patients Presenting with LUTS (n=84)

Factors	Pearson Correlation	p-Value
Prostate Volume (cm³)		
≤ 60 Years	0.859	<0.001*
> 60 Years	0.912	<0.001*
UTI - Yes	0.851	<0.001*
UTI - No	0.949	<0.001*
PVR Volume (ml)		
≤ 60 Years	0.890	<0.001*
> 60 Years	0.900	<0.001*
UTI - Yes	0.890	<0.001*
UTI - No	0.894	<0.001*

UTI: Urinary tract infection

After stratification on patient characteristics, the prevalence of UTI was significantly more common in patients above 60 years (80.6% vs. 39.6%) compared to ≤ 60 years' patients and in patients with severe and moderate LUTS compared to mild symptoms (100% and 56.1% vs. 13.3%) (Table 4).

Table 4: Effect of Patient Characteristics on Prevalence of UTI in Patients Presenting with LUTS (n=84)

Patient Characteristics		Urinary Tract Infection		p-Value
		Yes	No	
Age Groups	≤ 60 Years	21 (39.6%)	32 (60.4%)	<0.001*
	> 60 Years	25 (80.6%)	6 (19.4%)	
IPSS	Mild (1-7)	2 (13.3%)	13 (86.7%)	<0.001*
	Moderate (8-19)	32 (56.1%)	25 (43.9%)	
	Severe (20-35)	12 (100%)	0 (00%)	

*chi-square test

DISCUSSION

Compared to our study, Udo et al. reported that most of the patients (41.7%) were between the ages of 60 and 69, with a mean age of 65.1 ± 9.6 years [12]. Awaisu et al. found that the mean age was 64.2 ± 9.0 years [8], while Badmus et al. found that the mean age was 64.4 ± 8.9 years [13]. Patients' earlier healthcare-seeking behavior may be the main cause of our study's lower mean age when compared to other research studies. Our research population may have sought medical care for LUTS earlier because they were more aware of the condition or had easier access to healthcare services. The age distribution may be skewed downward by regional variations in comorbidities, diet, and lifestyle, which may contribute to the earlier onset of LUTS and prostate-related problems. In our study, half of the participants had a urinary tract infection. According to a study, patients presenting with BPH and LUTS had a 46.5% prevalence of UTIs. Long-term catheterization, poor bladder emptying, and age above 60 were all substantially linked to an elevated risk of UTI [14]. Another research reported that 5.9% of

patients with prostate carcinoma and hyperplasia had recurring infections, and 35.6% of patients had de novo UTIs. The study highlighted how bladder outlet obstruction raises these individuals' chance of developing UTIs [15]. Frequent or prolonged indwelling catheters, comorbid conditions such as diabetes mellitus, variations in bacterial resistance profile, different practices of personal hygiene, hydration status, or access to proper toilets could all be contributing factors to our patients' high rate of UTIs, especially in settings with limited resources. The correlation between UTI and LUTS, and BPH highlights the importance of careful UTI screening and treatment in these patients to avoid complications and enhance patient prognosis. Udo *et al.* and Mbouché *et al.* reported mean IPSS values of 14.58 ± 6.17 and 13.2 ± 4.6 , respectively, which are nearly comparable to our results [12, 16]. In contrast, a comparable study conducted in Nepal by Agrawal *et al.* [17] found a higher mean IPSS of 23.5 ± 2.8 . The variation may be caused by late presentation and various health-seeking patterns. In our study two two-thirds of patients had moderate LUTS. These findings align with those of Udo *et al.* and Ofoha *et al.* who found that most study groups reported moderate symptoms [12, 18]. The mean prostate volume (measured through abdominal scan), as determined by Barry *et al.* was $69.84 \text{ cm}^3 \pm 63.5 \text{ cm}^3$ [10]. Robinson *et al.* documented a mean volume of $66.13 \pm 30.43 \text{ cm}^3$ in another investigation on the link between prostate volume determined through transrectal scan and prostate-specific antigen (PSA) level in similar study environment [19]. These relate to what we have seen. However, Badmus *et al.* found a larger mean of $83.8 \pm 37.7 \text{ cm}^3$ [13]. The latter's use of a transrectal technique and the former's higher sample size may be the cause of the discrepancies. The numbers, however, exceed the mean prostate volumes of 40.1 cm^3 and 48.0 cm^3 measured in Sweden [20] and the US [21]. This may be explained by racial and regional variations, as well as the fact that patients in developed parts of the world tend to present earlier. This study observed that IPSS had a strong, positive, and significant correlation with prostate volume and PVR volume. IPSS and prostate volume were found to be significantly positively correlated in a cross-sectional study of 103 BPH patients in Karachi, Pakistan. The study concluded that symptoms of irritative voiding were more closely linked to an increase in prostatic volume [22]. A retrospective investigation including 45 patients with histologically verified BPH was carried out by Ngwa-Ebogo *et al.* Prostate volume and IPSS were shown to be somewhat positively related ($r=0.410$, $p=0.006$) [23]. Prostate volume and IPSS were shown to be significantly correlated ($p=0.002$) in another study that assessed the relationship between the two variables and the maximum urine flow rate in BPH patients. This suggests that higher

prostate volumes are linked to more severe symptoms [8]. Prostate volume and IPSS demonstrated a weak positive connection ($r = +0.109$; $P = 0.28$) in a study of 100 men with BPH [24]. The association points to a pattern consistent with our findings, even though it was not statistically significant. Together, these research articles favor the association between higher IPSS scores and increasing PVR volumes and increased prostate volume, underscoring the significance of thorough evaluation in the treatment of BPH. By assessing the correlation between IPSS, prostate volume, and PVR, as well as the occurrence of UTIs in BPH patients, our work presents a significant clinical problem. This data will help to improve management and diagnostic approaches. The proven, non-invasive, and generally recognized techniques of IPSS, transabdominal ultrasound for PVR, and transrectal ultrasound for prostate volume improve the accuracy of collected data. By connecting symptomatology and infectious consequences, evaluating UTI prevalence in conjunction with LUTS characteristics gives the results more depth and clinical value. This study adds valuable regional evidence by demonstrating a strong relationship between IPSS, prostate volume, and PVR in men with BPH, an area with limited local data. It underscores the role of combining symptom scoring with ultrasound as a reliable, non-invasive, and cost-effective tool for assessing disease severity. Additionally, it highlights the significant burden of UTI among older patients and those with severe LUTS, a finding often underexplored. These insights help bridge existing gaps in the literature and support improved diagnostic and management strategies for BPH in resource-constrained settings. To improve generalizability, future research should involve a larger and more varied population from several centers. Prostate growth, UTI recurrence or chronicity, and symptom progression can all be evaluated using a prospective cohort design in the future. Actionable insights into managing UTIs in patients with BPH can be obtained by incorporating culture-sensitivity data.

Our study's statistical power was limited due to its small sample size of 84 people, and its conclusions might not apply to more diverse or sizable groups. The study was only conducted at one hospital, which limits the data's generalizability to other healthcare environments or geographic locations. Because the study design is cross-sectional, it is impossible to evaluate the causal links or the evolution of infections and symptoms. Although the presence of UTI was observed, the study omits details on the organisms causing the infection or patterns of antibiotic resistance, which are crucial for treatment planning. There could be a possibility of measuring errors, and self-report bias. To improve generalizability, future research should involve a larger and more varied population

from several centers. Prostate growth, UTI recurrence or chronicity, and symptom progression can all be evaluated using a prospective cohort design in future. Actionable insights into managing UTIs in patients with BPH can be obtained by incorporating culture-sensitivity data.

CONCLUSIONS

The study concluded that there was a positive and significant correlation between IPSS, prostate volume, and PVR in men with BPH. Furthermore, urinary tract infections were more prevalent in older patients and those with more severe symptoms, underscoring the significance of combining ultrasonography examination with symptom score for efficient clinical evaluation and treatment.

Authors' Contribution

Conceptualization: MZF

Methodology: MZF, SAH, SG, SH, MS, MIA

Formal analysis: MZF, SG, SH

Writing and Drafting: MIA

Review and Editing: MZF, SAH, SG, SH, MS, MIA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Local Recurrence Rate after Clear Margins in Wide Local Excision in Soft Tissue Sarcoma 2 Years after Index Surgery

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ABSTRACT

Soft tissue sarcomas include a diverse collection of uncommon, malignant neoplasms originating in mesenchymal tissues. Recent cancer studies indicate that they comprise around 1% of all malignancies globally. **Objectives:** To evaluate the incidence of local recurrence among patients who achieved clear surgical margins following wide local excision for soft tissue sarcoma. **Methods:** This cross-sectional retrospective study was conducted at the Orthopedic Department of Shifa International Hospital, Islamabad. Sixty patients participated in this investigation. In this investigation, patients who underwent wide local excision and attained clear surgical margins were enrolled after being diagnosed with histologically confirmed soft tissue sarcoma. **Results:** The study included 60 sarcoma patients (63.3% males, mean age 46.15 ± 22.74 years). Two-year recurrence occurred in 8 (13.3%) cases, mostly synovial sarcoma. Recurrence showed no significant association with histologic subtype, therapy type, surgical margin, or tumor grade ($p > 0.05$). **Conclusions:** This study corroborates existing literature on the recurrence patterns of STS, emphasizing the significance of histological subtypes, comorbidities, and surgical margins in influencing patient outcomes. Continued research into the molecular underpinnings of STS and the development of targeted therapies are crucial for improving prognosis and reducing recurrence rates.

INTRODUCTION

Soft tissue sarcomas (STSs) are uncommon and infrequent neoplasms. STSs are a diverse category of infrequent and malignant neoplasms originating from mesenchymal tissue [1]. According to recent cancer statistics they account for approximately 1% of all cancers worldwide [2]. STSs arise most commonly in the deep soft part of the extremities. Still, they can also form in subcutaneous tissue, head and neck, trunk wall, intraabdominal, retroperitoneal, and pelvic areas [3]. Soft tissue sarcomas can arise at any site but they commonly tend to affect the extremities (60%). More than 150 subtypes of STS with different development, progression, and recurrence patterns have been identified by the researchers [4]. The

tumor is difficult to diagnose and treat because of its rarity and the variety of histological subtypes [5]. Surgical excision along with adjuvant or neoadjuvant chemotherapy and radiation therapy is the cornerstone of the curative treatment for localized STSs [6]. The main goal of treatment is to achieve clear surgical margins for minimizing the recurrence and improving patient outcomes. The literature does not clearly define the length of surgical margin resection; for low-grade STSs, a marginal excision of less than 2 cm is adequate, but for high-grade STSs, a broad excision of more than 2 cm is necessary to reduce local and systemic recurrence [7]. Some researchers advise safety margins of up to 4 cm in



various histological subtypes of STSs because a considerable percentage of these tumors, including angiosarcoma, dermatofibrosarcoma, and myxofibrosarcoma, can form microscopic finger-like extensions that can infiltrate the surrounding local soft tissue and fascial plane and change the rate of local recurrence even after the primary excision [8]. STSs mostly affect the extremities, most commonly the lower extremity. STSs in the extremity are prone to recurrence despite having the complete resection primarily [9]. Most STSs possess pseudo capsules throughout their peripheries, functioning as a reactive zone that delineates the tumor cells from adjacent healthy tissues. The most viable surgical method involves resection along the pseudo capsule borders; nevertheless, this leads to a comparatively elevated recurrence rate [10]. Widening the surgical plane to noncancerous tissue and beyond the pseudo capsule decreases the chances of local recurrence and improves clinical outcomes. In extremities and trunk wall sarcomas, widening of margins includes the surrounding subcutaneous fat, muscles, and skin [11]. Wound complications after the surgical resection of STSs depend on the location of the tumor, larger tumor volume, and perioperative treatment with radiation [12]. In extremities, the local recurrence incidence varies from 5% to 10%; however, it is not the primary cause of mortality, since it may be addressed with extensive reoperation or amputation when necessary. The primary focus of surgery should be limb-sparing and achieving the highest functional outcomes while respecting the appropriate margins [8]. Despite the advancements in surgical techniques and preoperative care, local recurrence is a major clinical concern, and it impacts not only the patient's survival but also the subsequent management and often requires secondary surgery [13]. The primary goal of the study is to analyze cases of local recurrence occurring within 2 years post-index surgery and help provide clinicians with valuable information to optimize treatment strategies and improve patient outcomes.

Wide local excision with clear margins is the standard curative approach for soft tissue sarcomas, yet local recurrence remains a clinically significant problem despite apparently adequate surgery. There is limited and inconsistent evidence on the incidence and predictors of early local recurrence in patients with soft tissue sarcoma who achieve clear surgical margins, particularly within the first two postoperative years. To evaluate the incidence of local recurrence among patients who achieved clear surgical margins following wide local excision for soft tissue sarcoma. Specifically, the study focuses on cases occurring within the first 2 years after the index surgery, aiming to provide insights into the early recurrence

patterns and potential predictors of disease control. This study aimed to assess the local recurrence rate and identify risk factors associated with recurrence in patients who underwent wide local excision for soft tissue sarcoma and achieved clear surgical margins.

METHODS

This cross-sectional retrospective study was conducted at the Orthopedic Department of Shifa International Hospital Islamabad, from September 2024 to August 2025 after approval from the Institute Review Board (Ref. No. 414-24). Meanwhile, the retrospective data was collected for the same duration, September 2023 to August 2024, after permission from the Medical Superintendent under the principles of the Helsinki Declaration. The sampling technique used was non-random, convenient sampling technique. Every patient's preoperative data was collected, including any comorbidities that they have. Pre-operative data were obtained by two means. The first method was obtaining patient Confidential Medical Record (CMR) files from our hospital's Medical Records Department and extracting pre-operative and perioperative data and documentation from it. The second method was assessing patient's Electronic Medical Records (EMR) and obtaining the investigations, biopsy reports, and radiological investigation reports from it. Informed consent was obtained from all the patients. This study included 60 patients. The sample size was calculated using 4% prevalence of the local recurrence of soft tissue sarcoma, 95% level of significance and an 80% power of the study [14]. Patients were eligible if they met the criteria like, 1) Patients diagnosed with histologically confirmed soft tissue sarcoma and who underwent wide local excision and achieved clear surgical margins. 2) Patients with histologically confirmed clear surgical margins (defined as the absence of tumor cells at the inked resection margins). 3) Patients with a minimum follow-up period of 2 years post-index surgery. Patients were excluded if they did not followed certain criteria e.g., Risk factors in these patients were carefully sought from an extensive literature review. After a thorough evaluation, patients with evidence of metastatic soft tissue sarcoma at time of diagnosis, those who were missing data or had incomplete medical records, and those with a concurrent or prior history of other malignancies unless disease free and with no recurrence in the past 5 years were excluded. There was a thorough evaluation of the participants of this study and those that did not meet the rigorous criteria were excluded from the research. Defined as the reappearance of soft tissue sarcoma at or near the site of the original excision, confirmed by histological examination or imaging studies (e.g., MRI, CT scan). The make and model of Shifa International Hospital's CT scan machine is Toshiba

Aquilion One 640-slice CT scanner. The MRI machine is a super-conducting 3-Tesla MRI system. Defined as the absence of tumor cells at the inscribed resection margins, as determined by medical records. All the data was collected from medical records of the patients. The surgical approach involves excising the soft tissue sarcoma along with a sufficient margin of healthy tissue to reduce the likelihood of local recurrence. The degree of excision may vary depending on the tumor's size, location, and the surrounding anatomical structures. Data analysis was conducted using SPSS version 23.0. Mean $\pm$ S.D was calculated for quantitative variables i.e., age, height, weight and BMI. Frequency and percentages were calculated for qualitative variables i.e., comorbidities, histologic subtype of sarcoma and recurrence within 2 years. Stratification was done for age, gender, histologic subtype of sarcoma, adjuvant therapy, surgical margin width and tumor grade. Post-stratification chi-square test was applied. A p-value of <0.05 was taken as significant.

RESULTS

The mean age of the cases was 46.15 ± 22.74 years. There were 38 (63.3%) male and 22 (36.7%) female patients in this study. There were 15 (25%) hypertensive and 15 (25%) diabetic patients found in this study. The most prevalent type of sarcoma seen in this study was synovial sarcoma, found in 40 (66.7%) cases (Table 1).

Table 1: Descriptive Statistics of Demographic and Clinical Variables

Variables	Category	Mean $\pm$ SD / N (%)
Age (years)	—	46.15 $\pm$ 22.74
Gender	Male	38 (63.3%)
	Female	22 (36.7%)
Height (cm)	—	165.12 $\pm$ 16.18
Weight (kg)	—	70.93 $\pm$ 20.75
BMI (kg/m ²)	—	21.37 $\pm$ 3.92
Comorbidities	Hypertension	15 (25%)
Histologic Subtype of Sarcoma	Diabetes	15 (25%)
	IHD	1 (1.7%)
	Synovial sarcoma	40 (66.7%)
	Pleomorphic sarcoma	3 (5%)
	Liposarcoma (left thigh)	8 (13.3%)
	Myxoid spindle cell sarcoma	2 (3.3%)
	Glioblastoma	2 (3.3%)
	Mucoid spindle cell squamous cell carcinoma	2 (3.3%)
	Myxosarcoma	1 (1.7%)
	Angioleiomyoma	1 (1.7%)
	Leiomyosarcoma	1 (1.7%)

In this study, recurrence within two years was observed in 8 (13.3%) patients. Histologic subtypes of Sarcomas were identified by microscopic examination based on their tissue of origin (Table 2).

Table 2: Frequency Distribution of Two-Year Recurrence

Recurrence within Two Years	Frequency (%)
Yes	8 (13.3%)
No	52 (86.7%)

The stratification of recurrence according to gender and age group showed insignificant results with p-values of 0.866 and 0.462, respectively (Table 3).

Table 3: Stratification of Recurrence Within Two Years with Respect to Age and Gender

Variables	Category	Recurrence within Two Years		p-Value
		Yes	No	
Gender	Male	6 (75%)	32 (61.5%)	0.866
	Female	2 (25%)	20 (38.5%)	
Age (years)	12-22	1 (12.5%)	11 (21.2%)	0.462
	23-33	2 (25%)	4 (7.7%)	
	34-44	1 (12.5%)	12 (23.1%)	
	45-55	1 (12.5%)	10 (19.2%)	
	56-66	1 (12.5%)	6 (11.5%)	
	67-77	1 (12.5%)	6 (11.5%)	
	78-88	1 (12.5%)	3 (5.8%)	

The stratification of 2-year recurrence with respect to histologic subtype of sarcoma showed insignificant results. Two-year recurrence was found in 7 cases of synovial sarcoma and in 1 case of pleomorphic sarcoma however, the p-value was >0.05 (Table 4).

Table 4: Stratification of Recurrence Within Two Years with Respect to Histologic Subtype of Sarcoma

Variables	Recurrence within Two Years		p-Value
	Yes	No	
Synovial Sarcoma	7 (87.5%)	33 (63.5%)	0.833
Pleomorphic Sarcoma	1 (12.5%)	2 (3.8%)	
Liposarcoma (Left Thigh)	0 (0.0%)	8 (15.4%)	
Myxoid Spindle Cell Sarcoma	0 (0.0%)	2 (3.8%)	
Glioblastoma	0 (0.0%)	2 (3.8%)	
Mucoid Spindle Cell Squamous Cell Carcinoma	0 (0.0%)	2 (3.8%)	
Myxosarcoma	0 (0.0%)	1 (1.9%)	
Angioleiomyoma	0 (0.0%)	1 (1.9%)	
Leiomyosarcoma	0 (0.0%)	1 (1.9%)	

Recurrence occurred in 2 (25%) neoadjuvant and 6 (75%) adjuvant therapy cases ($p=0.254$). It was observed in 7 wide local excisions and 1 wide en bloc resection (R0) cases ($p=0.973$). Based on tumor grade, recurrence was found in 2 (25%) grade 1, 4 (50%) grade 2, and 1 (12.5%) each of grade 3 and 4 tumors ($p=0.607$) (Table 5).

Table 5: Stratification of Recurrence Within Two Years with Respect to Adjuvant Therapy, Surgical Depth, and Tumor Grade

Variables	Category	Recurrence within Two Years		P-Value
		Yes	No	
Adjuvant Therapy	Neoadjuvant	2 (25%)	28 (53.8%)	0.254
	Adjuvant	6 (75%)	24 (46.2%)	
	Total	8 (100%)	52 (100%)	
Surgical Margin Width	Wide Local Excision	7 (87.5%)	42 (80.8%)	0.973
	Wide En Bloc Resection (R0)	1 (12.5%)	7 (13.5%)	
	Limb-Sparing Surgery	0 (0.0%)	1 (1.9%)	
	Mohs Surgery Technique	0 (0.0%)	1 (1.9%)	
	Synovectomy	0 (0.0%)	1 (1.9%)	
	Total	8 (100%)	52 (100%)	
Tumor Grade	Grade 1	2 (25%)	13 (25%)	0.607
	Grade 2	4 (50%)	15 (28.8%)	
	Grade 3	1 (12.5%)	16 (30.8%)	
	Grade 4	1 (12.5%)	8 (15.4%)	
	Total	8 (100%)	52 (100%)	

DISCUSSIONS

A wide variety of rare malignant tumors that originate in mesenchymal tissues are collectively known as soft tissue sarcomas (STS). They represent about 1% of all malignancies worldwide, according to recent cancer studies. The recurrence rate after STS therapy ranges from 20% to 25% and typically appears within 2 to 3 years following primary surgery. The mean age of cases in our study was 46.15 ± 22.74 years, including 38 males (63.3%) and 22 females (36.7%). Among these, 15 (25%) patients had hypertension and 15 (25%) had diabetes. In a previous study, the average age was reported as 32.52 ± 18.17 years, with 49.3% male and 50.7% female participants [14]. In our study, synovial sarcoma was the most prevalent histologic subtype, observed in 40 (66.7%) cases. Similarly, fibrosarcoma (36%), rhabdomyosarcoma (26%), liposarcoma, and leiomyosarcoma were also reported as common histological types in earlier research. Rare malignancies (categorized as "Others") included neurofibrosarcoma, alveolar soft tissue sarcoma, myxofibrosarcoma, haemangiosarcoma, haemangiopericytoma, pleomorphic sarcoma, primitive neuroectodermal tumor (PNET), and malignant peripheral nerve sheath tumor [15]. In another investigation involving 951 patients with extremity sarcoma, liposarcoma, fibrosarcoma, and malignant fibrous histiocytoma (MFH) were the most frequent types [16]. Similarly, MFH and fibrosarcoma were the predominant forms reported in Nigeria [17]. Data from the Florida Cancer Registry (1981-2004) recorded malignant fibrous histiocytoma (31.5%), liposarcoma (19.0%), fibrosarcoma (6.0%), and leiomyosarcoma/gastrointestinal stromal tumor (43.5%) [18]. These variations highlight the importance of defining

regional disease trends to identify epidemiological differences. In the present study, stratification of two-year recurrence according to histologic subtype showed no significant association. Recurrence was noted in 7 cases of synovial sarcoma and 1 case of pleomorphic sarcoma, with a $p > 0.05$. Overall, recurrence within two years was observed in 8 (13.3%) patients, aligning with previously reported recurrence rates of 12-15% [19-20]. Another study reported that following initial resection, 36.7% of patients had positive margins, and 18.9% experienced local recurrence [21]. In our study, recurrence occurred in 2 (25%) cases receiving neoadjuvant therapy and 6 (75%) receiving adjuvant therapy; however, the difference was not statistically significant ($p = 0.254$). Local recurrence rates after excision with positive margins have been reported between 80% and 90%, but recent advances in imaging, adjuvant and neoadjuvant radiotherapy, and improved surgical techniques have reduced these rates to 7-15% [22].

While this study provides valuable insights, it is limited by its single-center design and relatively small sample size. The inclusion of multiple histological types and anatomical sites may also introduce bias. Future multicenter studies with larger cohorts are needed to validate these findings. Additionally, integrating molecular and immunohistochemical analyses could help identify factors influencing recurrence and support personalized therapeutic approaches.

CONCLUSIONS

This study corroborates existing literature on the recurrence patterns of STS, emphasizing the significance of histological subtypes, comorbidities, and surgical margins in influencing patient outcomes. Continued research into the molecular underpinnings of STS and the development of targeted therapies are crucial for improving prognosis and reducing recurrence rates.

Authors' Contribution

Conceptualization: AI

Methodology: AI, LM, HA, SMA

Formal analysis: AI

Writing and Drafting: AI, ZN, SH

Review and Editing: AI, ZN, LM, SH, HA, SMA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Comparison of Letrozole and Clomiphene in Infertile Male Patients with Oligoasthenozoospermia

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ABSTRACT

Infertility often causes significant emotional distress, and in about 50% of cases, male factors such as oligoasthenozoospermia play a key role in the challenges you're facing. **Objectives:** To compare two medications, clomiphene citrate and letrozole, to see which one works better for improving sperm count and motility in men with oligoasthenozoospermia. **Methods:** This non-randomized controlled study was conducted at District Headquarter Teaching Hospital in D.I. Khan with 140 men diagnosed with oligoasthenozoospermia. Participants were divided into two groups of 70, receiving either letrozole or clomiphene citrate. Sperm concentration and motility were measured at three months, with improvements compared between the two groups. Statistical analysis was performed using SPSS version 21, with p-values <0.05 considered significant. **Results:** Both letrozole and clomiphene significantly improved sperm concentration and motility, with letrozole showing greater improvement in both parameters compared to clomiphene citrate. An increase of 48.23% in sperm concentration was observed in the letrozole group, while the clomiphene citrate group showed a 26.26% increase at 12 weeks post-treatment. Sperm motility improved by 42.08% with letrozole and by 18.55% with clomiphene citrate at the 12-week mark. **Conclusions:** Both letrozole and clomiphene citrate have been shown to improve sperm parameters in men diagnosed with oligoasthenozoospermia. The letrozole group showed a more significant effect than the clomiphene group.

INTRODUCTION

Worldwide, infertility causes substantial socio-emotional and psychological strain, and in Nigeria, it continues to be a sensitive issue, leading to social stigma, marital conflicts, neglect, and economic disadvantage for women. African men frequently link sexual potency with fertility, which can result in a reluctance to seek medical evaluation [1]. About 15% of sexually active couples are affected by infertility, with male infertility factors responsible for 50% of these cases [2]. Despite the development of advanced assisted reproductive technologies (ART) for male factor infertility,

many couples still face barriers to effective treatment. ART remains largely inaccessible in many regions, and where available, its high cost—especially for ICSI—makes it difficult for men with severely impaired semen quality to have biological children [3-6]. In addition, the preference for genetically related children leads many couples to reject sperm donation as an option for assisted reproduction [7]. Male infertility is sometimes attributed to unknown causes, where men present with reduced semen quality without a clear explanation; this condition, known as idiopathic



oligoasthenoteratozoospermia, represents about 25% of cases [8]. Idiopathic male infertility is diagnosed when a thorough clinical and laboratory assessment fails to reveal a specific cause for the impaired fertility. Furthermore, studies indicate that several therapeutic strategies have been applied to idiopathic male infertility, such as antioxidants, selective estrogen receptor modulators, and aromatase inhibitors; however, their effectiveness remains limited [9, 10]. The effectiveness of anti-estrogens and aromatase inhibitors is attributed to their ability to reduce estrogen feedback on the hypothalamus and pituitary, thereby enhancing endogenous testosterone synthesis. Clomiphene, an anti-estrogen, binds to estrogen receptors in the hypothalamus and pituitary, inhibiting the action of endogenous estrogen. This disinhibition enhances the hypothalamic-pituitary-gonadal axis, increasing gonadotropin secretion and promoting spermatogenesis [11, 12]. According to meta-analyses, clomiphene citrate, an estrogen antagonist, demonstrates a favorable safety profile and is associated with significant improvements in sperm concentration and motility relative to placebo. Clomiphene citrate enhances semen quality, reducing the reliance on IVF and ICSI while making intrauterine insemination a more viable treatment option [13]. Letrozole is a non-steroidal aromatase inhibitor that works by competitively binding to the heme subunit of cytochrome P450, preventing the conversion of androgens to estrogens and leading to elevated levels of circulating androgens. Evidence showed that Letrozole is also being used for men with idiopathic infertility and has been shown to improve the testosterone/estrogen ratio, sperm concentration as well as sperm motility [9, 10]. This is also beneficial in obese hypogonadal men to elevate the intra-testicular testosterone level [10, 14].

Although there are several studies on the medical management of male factor infertility with varied reported efficacy. Nevertheless, there is no standard recommended therapy for the management of those with idiopathic male factor infertility, and no study has been conducted to compare the effectiveness of letrozole and clomiphene citrate in the treatment of male factor infertility. This study aims to evaluate the difference in semen parameter improvements between letrozole and clomiphene citrate in men diagnosed with oligoasthenozoospermia.

METHODS

This non-randomized controlled trial was carried out in the Department of Urology of District Headquarter Teaching Hospital, Dera Ismail Khan. The study was conducted from March to June 2025 after receiving ethical clearance from the Gomal Medical College, Dera Ismail Khan (Ref. No. 229/GJMS/JC). Men presenting with abnormal semen concentration and motility, assessed for infertility at the

Urology Department of District Headquarter Teaching Hospital, Dera Ismail Khan, and who consented to participate, comprised the study population. Men with ongoing abnormal semen concentration and motility, as evidenced by at least two abnormal test results during infertility assessment. Abnormal sperm count in this study was considered as a sperm count below 15 million/mL on two separate occasions, at least two weeks apart, and a motility rate of active sperm lower than 34% on two separate assessments, spaced two weeks apart [15]. Men diagnosed with obstructive azoospermia, chronic kidney or hepatic failure, poorly controlled diabetes, normal semen profiles, or a lack of interest in participating were excluded from the study. The sample size for patient recruitment was determined based on the formula used for randomized controlled trials with continuous outcome measures [16]. Based on 80% statistical power and a 5% margin of error, the minimum required sample size was calculated to be 64. After adjusting for a projected 10% dropout rate, the final minimum sample size was increased to 70 per group by the convenience sampling technique. Eligible patients who presented at the clinic and agreed to participate were recruited at the respective study centers. Patients received comprehensive information regarding the study and the method of sample collection. SPSS version 21.0 was used for statistical processing. Data cleaning was conducted before performing a comparative analysis. Descriptive statistical methods were applied to compare baseline characteristics between the two treatment groups, with results displayed in tables. Inferential statistical methods included the Chi-square test to assess associations involving categorical data, while a two-sample t-test was used to determine differences in average values of specific quantitative measures between two classifications. Statistical decisions were based on a 5% significance level.

RESULTS

The study involved 140 patients, with 70 participants allocated to each of the two study arms. Out of the total participants, 9 were not included in the statistical evaluation. This included 3 in the letrozole arm and 4 patients in the clomiphene citrate arm who lost to follow-up and 2 patients who were unable to continue due to severe side effects (one in each study group). Most participants from both study arms fell within the 20 to 40-year age range, comprising 35 (43%) in the letrozole arm and 38 (56.7%) in the clomiphene citrate group. A majority of participants reported an infertility duration of under five years, including 56.06% (n=37) in the letrozole arm and 55.38% (n=36) in the clomiphene citrate arm. A value of 3.192 was obtained from the chi-square test, with a p-value of 0.445. Additionally, the baseline sperm concentration

for the letrozole and Clomiphene Citrate groups was $10.23 \pm 1.13 \times 10^6$ and $9.66 \pm 0.95 \times 10^6$, respectively, with a t-test value of 0.95 and a p-value of 0.39. Similarly, the initial sperm motility was recorded as 21.35 ± 1.47 for letrozole and 22.78 ± 1.28 for Clomiphene Citrate, with a corresponding t-test of 1.92 and a p-value of 0.05 (Table 1).

Table 1: Comparative Socio-Demographic Characteristics Between the Study Groups

Variables		Letrozole	Clomiphene	Test Statistics	p-Value
Age Group (Years)	20-40	36 (54.54%)	37 (57.81%)	—	—
	41-60	30 (45.45%)	28 (43.75%)		
Duration of Infertility (Years)	<5	37 (56.06%)	36 (55.38%)	—	—
	5-10	29 (43.93%)	29 (44.61%)		
Pre-Treatment Sperm Concentration	—	$10.23 \pm 1.13 \times 10^6$	$9.66 \pm 0.95 \times 10^6$	0.95	0.39
Pre-Treatment Sperm Motility	—	21.35 ± 1.47	22.78 ± 1.28	1.92	0.05

The study presents the outcome measure for the letrozole group, showing a mean pre-treatment sperm concentration of $10.23 \pm 1.13 \times 10^6$ among the 66 participants included in the analysis. At 12 weeks, this value rose to $15.16 \pm 1.12 \times 10^6$, with a 48.23% increase observed in 53 participants. Before treatment, sperm motility was 21.35 ± 1.47 . After 12 weeks, it reached 30.33 ± 1.40 (a 40.08% increase), based on results from 47 participants (Table 2).

Table 2: Outcome Measure in the Letrozole Group

Variables	Letrozole (Mean $\pm$ SD)	% of Increment	Participants Showing Improvement, n (%)
Pre-Treatment Sperm Concentration	$10.23 \pm 1.13 \times 10^6$	—	—
Post-Treatment (12 Weeks) Sperm Concentration	$15.16 \pm 1.12 \times 10^6$	48.23%	53 (80.30%)
Pre-Treatment Sperm Motility	21.35 ± 1.47	—	—
Post-Treatment (12 Weeks) Sperm Motility	30.33 ± 1.40	42.08%	47 (71.21%)

The study showed that, before treatment, the average sperm concentration in the Clomiphene Citrate group was $9.66 \pm 0.95 \times 10^6$, based on the data from 65 participants. At 12 weeks post-treatment, the mean sperm concentration increased to $12.19 \pm 1.26 \times 10^6$, reflecting a 26.26% improvement, as observed in 48 participants. Sperm motility before treatment was measured at 22.78 ± 1.28 . At the 12-week mark following treatment, this value rose to 27.00 ± 1.22 18.55% increase based on observations from 41 participants (Table 3).

Table 3: Outcome Measure in the Clomiphene Citrate Group

Variables	Clomiphene (Mean $\pm$ SD)	% of Increment	Participants Showing Improvement, n (%)
Pre-Treatment Sperm Concentration	$9.66 \pm 0.95 \times 10^6$	—	—
Post-Treatment (12 Weeks) Sperm Concentration	$12.19 \pm 1.26 \times 10^6$	26.26%	48 (73.8%)
Pre-Treatment Sperm Motility	22.78 ± 1.28	—	—
Post-Treatment (12 Weeks) Sperm Motility	27.00 ± 1.22	18.55%	41 (63.07%)

The average sperm concentration before treatment was $10.23 \pm 1.13 \times 10^6$ in the letrozole group and $9.66 \pm 0.95 \times 10^6$ in the group treated with clomiphene citrate. The t-statistic was calculated as 0.95, with a corresponding p-value of 0.39. After 12 weeks post-treatment, the sperm concentration was $15.16 \pm 1.12 \times 10^6$ in the letrozole group and $12.19 \pm 1.26 \times 10^6$ in the clomiphene group. The t-test value was 2.61 with a p-value of 0.02, indicating a significant difference compared to the pre-treatment values. The pre-treatment sperm motility in the letrozole group was 21.35 ± 1.47 , and in the clomiphene group was 22.78 ± 1.28 , having a t-value of 1.92 and a p-value of 0.05. Following the treatment, sperm motility averaged 30.33 ± 1.40 in the letrozole group, compared to 27.00 ± 1.22 in the clomiphene citrate group. The difference was statistically significant, with a t-value of 2.41 and a p-value of 0.03 (Table 4).

Table 4: Compares The Outcome Measure in Both the Letrozole and The Clomiphene Groups

Variables	Letrozole (Mean $\pm$ SD)	Clomiphene (Mean $\pm$ SD)	t-Test	p-Value
Pre-Treatment Sperm Concentration	$10.23 \pm 1.13 \times 10^6$	$9.66 \pm 0.95 \times 10^6$	0.95	0.39
Post-Treatment (12 Weeks) Sperm Concentration	$15.16 \pm 1.12 \times 10^6$	$12.19 \pm 1.26 \times 10^6$	2.61	0.02*
Pre-Treatment Sperm Motility	21.35 ± 1.47	22.78 ± 1.28	1.92	0.05
Post-Treatment (12 Weeks) Sperm Motility	30.33 ± 1.40	27.00 ± 1.22	2.41	0.03*

DISCUSSION

Improvements in semen quality were observed with both clomiphene citrate and letrozole; however, letrozole was associated with a statistically greater increase in terms of increased sperm density and motility compared to clomiphene citrate. No statistically significant differences were observed in the sociodemographic profiles of participants between the clomiphene citrate and letrozole groups. The majority of individuals reported infertility duration of less than five years. While both drugs contributed to improved sperm parameters, letrozole produced a significantly greater enhancement in both quantitative and motility parameters, outperforming

clomiphene citrate [17, 18]. The findings of this study were consistent with previous researchers, who observed a significant rise in sperm levels and their ability to move effectively after six months of daily 2.5 mg letrozole treatment [19]. These discrepancies between the use of clomiphene citrate and letrozole are connected with their pharmacological effects: clomiphene citrate acts on the estrogen receptors through enclomiphene and zuclophene, and letrozole decreases the level of estrogen, negative feedback on the hypothalamus and pituitary [20]. The results of the clomiphene group are also congruent with the previous studies that indicated that a three-month program resulted in an increase in sperm concentration and motility, but the extent of the improvement was smaller than the one reported in a meta-analysis of randomized controlled trials [21]. These differences could be related to the changes in dosage (2550 mg/day) and to the time of treatment (312 months) [22]. Both of the drugs were tolerated. In the group with letrozole, 1.5% stopped the treatment because of the decrease in libido; and the reported side effects such as headache (3%), nausea (13.6%), dry mouth (10%), and fatigue (6 per cent), were lower than the previous research where they were daily taking doses of 2.5mg of letrozole [23, 24]. The total increase in sperm concentration was less than a meta-analysis that had clomiphene citrate and vitamin E and hence combination therapy could produce a better result [25]. In their other reports, they saw an improvement in semen parameters in the majority of the patients in three to six months of treatment with clomiphene [26]. There was however, no significant difference in pregnancy rates or in semen quality between a six-month double-blind, placebo-controlled WHO trial of 25 mg/day clomiphene citrate. All the side effects of clomiphene citrate like nausea, fatigue, headache, and slight nervousness, were short-lived and tolerated [27, 28]. Regardless of the shortcomings such as a non-randomized design, a short 12-week follow-up and no pregnancy outcome data, the use of letrozole has potential in the management of oligoasthenozoospermia. Subsequent research must embrace randomized, parallel designs of follow-up of greater duration to determine hormonal and fertility outcomes.

The study's limitations include its non-randomized design, which may introduce bias, and the short follow-up period of 12 weeks, which doesn't assess long-term effects or pregnancy outcomes. It also lacked blinding, which could have influenced the results, and did not control for confounding factors like age and lifestyle. Additionally, the study focused only on sperm parameters and didn't explore long-term side effects or fertility outcomes, limiting the overall understanding of treatment efficacy. There is a growing need for further studies on male factor infertility.

This includes researching various combinations of medical therapies for male infertility to address and reduce this overlooked health issue.

CONCLUSIONS

This study shows that letrozole and clomiphene citrate can help improve sperm quality in men with Letrozole showed better results than clomiphene citrate in treating oligoasthenozoospermia. Hence, letrozole and clomiphene citrate may play an important supportive role alongside other artificial reproductive methods. In cases where increasing semen concentration and motility is essential for better outcomes with these techniques.

Authors' Contribution

Conceptualization: MI

Methodology: MS

Formal analysis: MI

Writing and Drafting: MS, MA, MM, S, ASD

Review and Editing: MS, MI, MA MM, S, ASD

All authors approved the final manuscript and take responsibility for the integrity of the work

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Original Article

Comparison of Incision Given with Electrocautery Versus Stainless Steel Scalpel for Neck Dissection in Oral Cancer Patients

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ABSTRACT

Both scalpels and electrocautery are frequently used for incisions during surgery, and each has an impact on postoperative scarring, bleeding, and operating efficiency. Objective examination of neck scars is clinically significant since visible scars may affect quality of life. **Objectives:** To evaluate the differences between scalpel and electrocautery incisions in neck dissection about of scar quality, surgical time, and blood loss as determined by the Manchester Scar Scale (MSS). **Methods:** In a prospective comparative cross-sectional study, a total of 76 patients who were having neck dissections at Sharif Medical and Dental College were included and divided into two equal groups (n=38 for scalpels and another 38 for electrocautery). The Mann-Whitney U test was used to examine intraoperative blood loss and surgical duration. Thirty days after surgery, the MSS was used to evaluate the scar's colour, gloss, contour, and distortion. The results were compared using the Chi-square test. **Results:** Both surgical time (33 vs. 42 minutes, $p<0.001$) and blood loss (123 mL vs. 240 mL, $p<0.001$) were dramatically decreased by electrocautery. There were no significant differences in scar colour ($p=0.341$), contour ($p=0.359$), or distortion ($p=0.364$) between the groups; however, glossy scars were more common with electrocautery (34.2% vs. 15.8%, $p=0.022$). **Conclusions:** Except for a higher frequency of shiny scars, electrocautery gives comparable scar results to knife incisions, but with a shorter operating time and less blood loss. When choosing a technique, aesthetic considerations are still crucial.

INTRODUCTION

In head and neck oncology, surgeons have historically dissected the neck using a stainless steel blade and electrocautery. For addressing head and neck carcinoma, neck dissection is crucial. Numerous methods have been developed to protect important structures while doing surgery. [1] The second most frequent carcinoma in Pakistan for both genders was lip and mouth cancer. The cervical lymphatic system of the neck may be affected by cancer of the oral cavity that originates in the tongue, cheek mucosa, floor of the oral cavity, or alveoli. The lymphatic drainage network of the mouth cavity is first divided into local before splitting into deeper cervical

lymph nodes. The main known risk factors consist of consuming the betel nut, drinking alcohol, and cigarette smoking. Although diagnosis and treatment options for people with oral cancer have greatly improved in recent years, the death rate (about 50%) continues to be significant [2]. In order to accurately analyze surgical scar outcomes, a number of scar assessment techniques have been developed and laid out in research. The Vancouver Scar Scale (VSS), that emphasizes vascularity, pigmentation, pliability, and height, and the Patient and Observer Scar Assessment Scale (POSAS) are two of those that are most popular. These types of scales have been



utilized for neck and head and skin procedures in the past to guarantee uniform evaluation of scar excellence [3]. The scarring, as well as cervicofacial impairments, have been found to significantly impact the overall standard of life for patients with cancers of the head and neck. The surgical techniques employed or the direct progression of cancer may result in facial deformity. It has been acknowledged as a persistent danger to self-esteem in addition to being the most stressed part of the neck and head region. In reality, individuals with cancer of the head and neck may have a significant incidence of anxiety and sadness due to facial disfigurement [4, 5]. Steel scalpels and electrocautery were regularly used in head and neck surgeries. The steel scalpel's primary benefits are precision, simplicity of usage, and low impact on nearby tissue [6, 7]. Nevertheless, it can cause serious bleeding from the incision and cause collateral harm to surgical helpers when it gets passed to the scrubbed nurses. By blocking blood arteries before being cut, electro-surgical tools reduce hemorrhage. They break down proteins using heat energy, causing vascular blockage and ultimately blood clotting. Despite its benefits in terms of blood loss, the use of thermal electricity in wound healing may have a certain disadvantage. Thermal dispersion into the tissue around it might result in higher postoperative pain from sensory injury to nerves and additional harm to important tissues [8]. Numerous studies contrast the harmonic blade with either electrocautery or ultrasonic, or conventional scalpel and scissors. There are right now only a few investigations evaluating the two types of scalpels used for neck surgical incisions: electrocautery as well as stainless steel [1].

There is limited comparative evidence directly evaluating electrocautery versus stainless steel scalpel for neck dissection incisions, particularly regarding scar outcomes, blood loss, and incision time. This study aims to compare electrocautery and stainless-steel blade neck dissection in terms of scar formation, intraoperative bleeding, and incision duration.

METHODS

This prospective comparative cross-sectional study analysis involved 76 individuals; the sample size was determined using the WHO sample size calculation program, using a transoral technique yielding a 95% confidence level, taking the proportion of the population with neck dissection done as 73.3% at 0.10 absolute precision [1]. Patients who visited the Oral and Maxillofacial OPD between October 2023 to September 2024 were the subjects of the research project. The Sharif Medical Research Center (SMRC) granted ethical approval for the study's implementation (Ref. number SMDC/SMRC/315-23). Following informed consent, participants were divided into two groups of 38 each, designated group A and group B,

employing a non-probability convenience sampling method. Patients were allocated alternately into Group A (scalpel) and Group B (electrocautery) as they presented, until each group reached the required sample size. Patients aged 25 years and above, requiring unilateral neck dissection as part of the management of oral cancer, were included in this study. On the other hand, patients who required bilateral neck dissection, terminally ill patients with co-morbidities, patients who previously underwent neck dissection or radiotherapy, and patients with any bleeding or coagulation disorders were excluded from this study. Each patient received a thorough pre-operative examination that involved laboratory testing, radiographic assessment, and clinical examination. Every case underwent a comprehensive clinical evaluation that included a general physical examination, a maxillofacial examination, and a CT scan for radiological assessment. Gentian violet was used to outline the incision site after general anesthesia was induced and aseptic measures were completed. A modified Schobinger incision was made, with two limbs: a vertical part placed at a minimum of 2cm posterior to the area of palpable carotid pulse, creating a lazy "S," and a horizontal part placed 2 cm beneath the jaw. A stainless-steel scalpel was used to make the incision in patients in Group A, while monopolar cauterization was used in patients in Group B. From the first skin incision to its conclusion, the incision duration was measured using a timer and entered in the data collection profoma. Gauze weight was used to determine blood loss during surgery. The initial weight of each piece of dry gauze was determined before surgery, and the weight of the gauze soaked with blood was calculated again following use in the incision. Considering that 1 gram of blood lost was equal to 1 mm of blood, the weight differences were measured [9]. A portable precision scale calibrated with a precision of ± 0.1 g was used to weigh each piece of gauze. To reduce evaporation error, each gauze was weighed both before and after it was taken out of the surgery field. This guarantees accurate blood loss calculation [10]. The Manchester Scar Scale (MSS) [11] was used to evaluate scars 30 days after surgery. The continuous variables included intraoperative blood loss (milliliters) as well as surgical time (minutes). These variables were examined employing the Mann-Whitney U test after the Shapiro-Wilk test, which evaluated the normality of the data, revealed a distribution that was not normal. The Chi-square test was used to assess postoperative scar characteristics (colour, gloss, shape, and distortion) between groups. Fisher's exact test was used to verify validity for categories with anticipated frequencies less than five.

RESULTS

The scalpel group had significantly higher blood loss (239.5 mL, IQR 44) compared to the electrocautery group (123.0 mL, IQR 18; Mann-Whitney U = 37.000, $p < 0.001$). Similarly, surgical time was significantly longer with a scalpel (42.0 min, IQR 5) than with electrocautery (33.0 min, IQR 3; Mann-Whitney U = 73.500, $p < 0.001$) (Table 1).

Table 1: Comparison of Blood Loss and Surgical Time between Scalpel and Electrocautery Groups

Variables	Group A (Scalpel) Median (IQR)	Group B (Electrocautery) Median (IQR)	Mann-Whitney U	P-Value
Blood Loss (mL)	239.5 (44)	123.0 (18)	37.000	<0.001
Surgical Time (min)	42.0 (5)	33.0 (3)	73.500	<0.001

There was no statistically significant difference in the scar colour distribution between the electrocautery and scalpel groups ($\chi^2 = 3.346$, $p = 0.341$). Likewise, there were no discernible variations in the distortion ($\chi^2 = 2.021$, $p = 0.364$) or scar contour ($\chi^2 = 3.220$, $p = 0.359$). Scar shine, however, showed a significant difference, with glossy scars more common in the electrocautery group than in the scalpels group ($\chi^2 = 5.216$, $p = 0.022$) (Table 2).

Table 2: Comparison of Manchester Scar Scale (MSS) in Both Groups

Variables		Group A (Scalpel) (n=38)	Group B (Electrocautery) (n=38)	χ^2 (df)	P-Value
Colour	Perfect	21 (55.3%)	17 (44.7%)	3.346 (3)	0.341
	Slightly Mismatch	15 (39.5%)	17 (44.7%)		
	Others	2 (5.2%)	4 (10.6%)		
Shine	Matte	32 (84.2%)	25 (65.8%)	5.216 (1)	0.022*
	Shin	6 (15.8%)	13 (34.2%)		
Contour	Flush	22 (57.9%)	19 (50.0%)	3.220 (3)	0.359
	Slightly Proud	13 (34.2%)	13 (34.2%)		
	Others	3 (7.9%)	6 (15.8%)		
Distortion	None	24 (63.2%)	19 (50.0%)	2.021 (2)	0.364
	Mild/Moderate	14 (36.8%)	19 (50.0%)		

*Note: $p < 0.05$ is considered statistically significant. Only Shine showed a significant difference between groups

DISCUSSION

To avoid the built-in drawbacks of the steel scalpel, such as (1) indistinguishable tissues planes, (2) insufficient hemostasis which results in undesirable bleeding, (3) raised working time, (4) use of foreign substance (ligature) in the wounds, which increases the risk of spread of infection, (5) the likelihood of unintentional damage in the operating room, and (6) chances for tumor dissemination through lymph nodes, surgical electrocautery was developed in the early years of the twentieth century [12]. Instant hemostasis, quicker dissection, and less cumulative surgical bleeding have made this procedure quite popular since the development of contemporary

electrosurgical machines that can produce pure sinusoidal voltage [13]. Current results, which show a distinct benefit of monopolar electrocautery over conventional instruments, are comparable to those of research on tonsillectomy [14], neck dissection [15], as well as thyroid surgery [16] in terms of intraoperative bleeding and shortened surgical times. The electrocautery probably coagulates minor bleedings instantly additionally is likely the reason for the shortened duration of surgery. Reduced surgery duration may impact the hospital stay and the patient's standard of living after surgery, as well as reduce the chance of postoperative delirium [17]. According to Hasegawa et al. postoperatively, delirium, an extended stay in the hospital, and longer postoperative care in the ICU may result from older age, complicated surgical treatments, protracted operations, significant hemorrhage and blood transfusions [18]. This suggests that individuals with electrocautery might experience a higher quality of life and a decreased chance of postoperative delirium after the operation. For scar assessment, we used the Manchester Scar Scale (MSS) and concluded that there was no statistically significant difference in the two groups in terms of colour, distortion, or contour on the healed incisions. Although the shine was superior in the scalpel group, this could be due to the possibility that the electrocautery causes an increase in temperature, leading to the generation of extra electrical trauma and carbonization of the surrounding tissue, which may result in more postoperative discomfort and healing of tissue issues [19]. Current results are in consistent with the results of another study, in which the scar was assessment was done using MSS and they concluded that despite the intraoperative benefits of cautery incisions, such as decreased bleeding and quicker cutting, systematic reviews and randomized trials employing confirmed scar scales, such as the Manchester Scar Scale, have had shown no discernible difference among electrocautery along with scalpel incision approaches in regards of long-term scar quality [20]. Since the temperature of the tissue while on electrocautery application was not objectively quantified in our investigation, it was not possible to establish an association with healing results or scar shine. But according to earlier research, electrocautery produces greater local tissue temperature than scalpel incisions. This could lead to delayed wound healing and protein denaturation, which could alter the look of scars. Objective associations among electrocautery-induced temperature effects as well as scar outcomes may be established with the aid of future research that uses thermal scanning or histological analyses.

The study did not objectively measure tissue temperature during electrocautery, limiting correlation between thermal injury and wound healing outcomes. In addition,

histological evaluation of incision margins was not performed, restricting insight into microscopic tissue damage and collagen remodeling. Future studies should incorporate objective thermal assessment and histopathological analysis to better elucidate the impact of electrocautery on wound healing and scar quality.

CONCLUSIONS

Compared to using a knife for neck dissection, electrocautery shortened the operating time and decreased blood loss. Although bright scars were more common with electrocautery, scar results were generally comparable. Consequently, scalpel incisions may yield superior cosmetic results, while electrocautery gives more surgical efficiency. Efficiency and aesthetics should be balanced when choosing an approach.

Authors' Contribution

Conceptualization: IT

Methodology: IT, KA, MK, MR

Formal analysis: KA

Writing and Drafting: IT, UBA, MK, ST

Review and Editing: IT, UBA, KA, MK, MR, ST

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Original Article



Comparison of Fetomaternal Outcome between Early Planned Labor Induction and Expectant Management in Late Preterm Pre-Labor Rupture of Membrane (PPROM)

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ABSTRACT

Late preterm pre-labor rupture of membranes (PPROM) remains a clinical dilemma, with conflicting evidence regarding early induction versus expectant management. **Objectives:** To compare maternal and neonatal outcomes between early planned labor induction and expectant management in women with late preterm PPRM. **Methods:** This prospective comparative observational cohort study was conducted at the Department of Obstetrics and Gynecology, Kharadar General Hospital. A total of 134 women with late preterm PPRM (34+0 to 36+6 weeks) were enrolled and managed with either early planned induction (Group A, n=67) or expectant management (Group B, n=67). Outcomes were analyzed using Chi-square and Mann-Whitney U tests, and multivariate logistic regression was applied to adjust for maternal risk factors, including BMI, diabetes, and hypertension. **Results:** Maternal infection [40.3% vs. 23.9%, p=0.042], cesarean delivery [55.2% vs. 37.3%, p=0.038], neonatal infection [53.7% vs. 35.8%, p=0.037], and neonatal intervention [41.8% vs. 23.9%, p=0.027] were significantly higher in the induction group. Multivariate analysis showed hypertension as a strong predictor of maternal infection (aOR 11.45, 95% CI: 1.5–85.6, p=0.018) and neonatal intervention (aOR 3.22, 95% CI: 2.1–17.1, p=0.017), while obesity and diabetes significantly predicted cesarean delivery and neonatal infection. **Conclusions:** Early induction in late preterm PPRM was associated with increased maternal and neonatal complications, particularly among women with comorbidities. Expectant management with close surveillance may be safer in stable patients, especially in populations with high rates of hypertension, diabetes, and obesity.

INTRODUCTION

Preterm pre-labor rupture of membranes (PPROM) is defined as rupture of the fetal membranes before the onset of labor in pregnancies less than 37 weeks of gestation [1]. It complicates approximately 2–3% of all pregnancies and accounts for nearly one-third (approximately 25 to 30%) of preterm births worldwide [2, 3]. PPRM is associated with significant maternal and neonatal morbidity due to risks of infection, preterm delivery, and neonatal respiratory distress [2]. The management of PPRM, particularly in the late preterm period (34+0 to 36+6 weeks), remains

controversial [4]. Early planned labor induction may reduce the risk of ascending infection but can increase neonatal respiratory morbidity due to earlier delivery [4]. Conversely, expectant management allows for greater fetal maturity but carries an increased risk of chorioamnionitis, i.e. up to 50% have histological evidence despite clinical signs and symptoms, maternal sepsis, i.e. 3.47 times odd of morbidity, and adverse perinatal outcomes. i.e., more often diagnosed with respiratory distress syndrome (RDS) [5–8]. Previous international studies have reported conflicting



results, and no universal consensus exists regarding the optimal strategy [1]. In low- and middle-income countries such as Pakistan, the challenge is further compounded by variable availability of neonatal intensive care facilities, inconsistent application of antibiotic and steroid protocols, and a higher baseline burden of maternal comorbidities[9].

Evidence from local populations is limited, and guidance for clinical practice is often extrapolated from studies conducted in high-income settings, which may not be directly applicable. We hypothesized that early planned labor induction in late preterm PPRM would result in lower rates of maternal and neonatal infection without significantly increasing neonatal morbidity compared with expectant management. So, the objective of this study was to compare fetomaternal outcomes between early planned labor induction and expectant management in women with late preterm PPRM.

METHODS

This prospective comparative observational cohort study was conducted in the Department of Obstetrics and Gynecology, Kharadar General Hospital, from June 2024 to December 2024, after approval from the College of Physicians and Surgeons and the Institutional Review Board of Kharadar General Hospital, Karachi (Ref. No. CPSP/REU/OBG-2023-207-12962). Women presenting with late preterm pre-labor rupture of membranes (PPROM) between 34 and 37 weeks of gestation were consecutively enrolled. Inclusion criteria were singleton pregnancies with confirmed PPRM, while exclusions were multiple gestations, major fetal anomalies, previous classical cesarean section, placenta previa, and contraindications to vaginal delivery. Diagnosis of PPRM was established on sterile speculum examination with visualization of liquor pooling, supplemented by pH testing when required. The informed consent was taken on admission; Grouping was not randomized. Patients were assigned based on clinical evaluation at presentation and departmental protocol. Those with maternal fever $\geq 38^{\circ}\text{C}$, elevated CRP, foul-smelling discharge, or non-reassuring fetal status was managed with early planned induction, whereas clinically stable women with no signs of infection and normal fetal surveillance were managed expectantly. Induction was undertaken using Prostaglandin E2 per vaginally, repeated after 6 hours in case of no uterine contraction under continuous maternal and fetal monitoring, while expectant management consisted of inpatient observation, serial maternal vital signs, fetal surveillance with cardiotocography or biophysical profile, prophylactic antibiotics, and corticosteroids as per departmental policy. The delivery was indicated at 37 weeks or earlier if complications arose, like chorioamnionitis, non-

reassuring fetal heart rate, or completion of 37 weeks of gestation. In such situations, labor was either induced or a cesarean section was performed, depending on the clinical scenario. The primary outcomes of interest included mode of delivery, maternal infection, and neonatal infection. Secondary outcomes included cesarean section rate, hospital stay, NICU admission, respiratory support requirement, and composite neonatal intervention. Maternal infection was defined as clinical suspicion of chorioamnionitis with fever $\geq 38^{\circ}\text{C}$ and elevated C-reactive protein, which was assessed by sending venous blood samples to the institutional diagnostic laboratory. Maternal C-reactive protein levels were determined via quantitative immunoturbidimetric assay on the Roche Cobas c311 automated analyzer (Roche Diagnostics, Germany). A venous sample (3 mL) was obtained under aseptic technique at admission, and results were expressed in mg/L; values >10 mg/L were considered elevated. Neonatal infection, referred to as early-onset sepsis, is confirmed by clinical signs, laboratory markers, or culture positivity. Data were analyzed using SPSS version 22.0; categorical variables were compared with Chi-square or Fisher's exact test, continuous variables were summarized as mean $\pm$ SD or median (IQR) depending on normality tested by Shapiro-Wilk, and between-group differences were assessed with t-test or Mann-Whitney U test. Multivariable logistic regression adjusting for maternal age, body mass index, and comorbidities (hypertension, diabetes) was performed, with results expressed as adjusted odds ratios and 95% confidence intervals; $p < 0.05$ was considered statistically significant.

RESULTS

An overall of 134 pregnant women between 34 to 37 weeks of gestation with confirmed cases of pre-labor rupture of membranes were involved in the study. The baseline characteristics of 134 women with late preterm PPRM, divided into early planned labor induction (Group A, $n=67$) and expectant management (Group B, $n=67$). Most participants in both groups were 20–30 years old [Group A: 38 (56.7%), Group B: 33 (49.3%), $p=0.190$], with comparable median ages (30 vs. 31 years, $p=0.314$). Body mass index showed significant differences: obesity was more common in Group A [39 (58.2%) vs. 25 (37.3%)], with higher median BMI (30.8 vs. 28.9 kg/m², $p=0.020$). Residential status, socioeconomic class, and employment did not differ significantly between groups ($p>0.05$). Gestational age at presentation was also similar, with roughly half of the women in each group presenting at 34–35 weeks and the remainder at 36–37 weeks ($p=0.300$). Diabetes prevalence was higher in Group A (50.7% vs. 38.8%), though not statistically significant ($p=0.165$). Hypertension, however, was significantly more frequent in Group A [40

(59.7%) vs. 28 (41.8%), $p=0.038$] (Table 1).

Table 1: Initial Clinical Profile of Females with Final-Phase Preterm Pre-Labor Rupture of Membranes ($n=134$)

Characteristics	Categories	Group A (Induced) N=67	Group B (Expected) N=67	p-value*
Age (years)	20 – 30	38 (56.7%)	33 (49.3%)	0.190
	31 – 40	24 (35.8%)	22 (32.8%)	
	>40	5 (7.5%)	12 (17.9%)	
	Median (IQR)	30 (25–36)	31 (25–39)	0.314**
BMI (Kg/m ²)	Normal weight	3 (4.5%)	12 (17.9%)	0.012
	Overweight	25 (37.3%)	30 (44.8%)	
	Obese	39 (58.2%)	25 (37.3%)	
	Median (IQR)	30.8 (28.7–31.2)	28.9 (26.2–31.2)	0.020**
Residency	Rural	18 (26.9%)	25 (37.3%)	0.195
	Urban	49 (73.1%)	42 (62.7%)	
Monthly Family Income (Rs)	<50,000	18 (26.9%)	25 (37.3%)	0.380
	50,000–100,000	34 (50.7%)	27 (40.3%)	
	>100,000	15 (22.4%)	15 (22.4%)	
Employment	Employed	19 (28.4%)	16 (23.9%)	0.550
	Unemployed	48 (71.6%)	51 (76.1%)	
Gestational Age (weeks)	34–35	37 (55.2%)	31 (46.3%)	0.300
	36–37	30 (44.8%)	36 (53.7%)	
Comorbidities	Diabetes Mellitus	34 (50.7%)	26 (38.8%)	0.165
	Hypertension	40 (59.7%)	28 (41.8%)	0.038

Normal Weight = BMI 18.5 – 24.9, Over Weight = 25 – 29.9, Obese = BMI ≥ 30 , *Chi-Square test, **Mann-Whitney U test

The perinatal outcomes in women with late preterm PPRM show maternal infection occurred more frequently in the induction group [Group A: 27 (40.3%) vs. Group B: 16 (23.9%), $p=0.042$]. Cesarean delivery was also higher in Group A [37 (55.2%) vs. 25 (37.3%), $p=0.038$]. Neonatal infection rates were significantly greater in Group A [36 (53.7%) vs. 24 (35.8%), $p=0.037$], and neonatal interventions were more common [28 (41.8%) vs. 16 (23.9%), $p=0.027$] (Table 2).

Table 2: Maternal and Neonatal Outcomes between Two Groups ($n=134$)

Outcomes	Categories	Group A (Induced) n=67	Group B (Expected) n=67	p-value*
Maternal Outcomes	Maternal Infection	27 (40.3%)	16 (23.9%)	0.042
	Cesarean Section	37 (55.2%)	25 (37.3%)	0.038
Neonatal Outcomes	Neonatal Infection	36 (53.7%)	24 (35.8%)	0.037
	Neonatal Intervention	28 (41.8%)	16 (23.9%)	0.027

*Chi-Square test

The multivariate analysis of predictors for maternal outcomes in late preterm PPRM shows that for maternal infection, age, gestational age, and diabetes mellitus were not significant predictors [aOR 0.95 (95% CI: 0.9–1.1, $p=0.380$); aOR 0.95 (95% CI: 0.5–2.0, $p=0.897$); aOR 0.14 (95% CI: 0.0–2.1, $p=0.151$), respectively]. Higher BMI also

showed no significant association [aOR 1.36, 95% CI: 0.9–2.0, $p=0.104$]. In contrast, hypertension was a strong and significant predictor of maternal infection [aOR 11.45, 95% CI: 1.5–85.6, $p=0.018$]. For cesarean delivery, age and gestational age were not significant predictors [aOR 0.96, 95% CI: 0.9–1.0, $p=0.300$; aOR 0.83, 95% CI: 0.5–1.3, $p=0.441$]. However, higher BMI [aOR 1.2, 95% CI: 1.1–1.5, $p=0.046$], diabetes mellitus [aOR 2.77, 95% CI: 1.2–7.9, $p=0.047$], and hypertension [aOR 1.46, 95% CI: 1.1–4.5, $p=0.048$] were all significant predictors of cesarean section (Table 3).

Table 3: Predictors of maternal outcomes between two groups (Multivariate Analysis) $n=134$

Predictors	Maternal Infection RR (95% CI)	p-value	Cesarean Section RR (95% CI)	p-value
Age	0.95 (0.9 – 1.1)	0.380	0.96 (0.9 – 1.0)	0.300
BMI	1.36 (0.9 – 2.0)	0.104	1.20 (1.1 – 1.5)	0.046
Gestational Age	0.95 (0.5 – 2.0)	0.897	0.83 (0.5 – 1.3)	0.441
Diabetes Mellitus	0.14 (0 – 2.1)	0.151	2.77 (1.2 – 7.9)	0.047
Hypertension	11.45 (1.5 – 85.6)	0.018	1.46 (1.1 – 4.5)	0.048

RR=relative Risk, CI Confidence Interval

The multivariate analysis of predictors for neonatal outcomes in late preterm PPRM shows that for neonatal infection, higher BMI [aOR 1.3, 95% CI: 1.0–1.6, $p=0.028$], diabetes mellitus [aOR 1.53, 95% CI: 1.1–5.3, $p=0.050$], and hypertension [aOR 1.24, 95% CI: 1.1–3.9, $p=0.042$] were significant predictors, while maternal age and gestational age were not associated. For neonatal intervention, hypertension emerged as the only significant predictor [aOR 3.22, 95% CI: 2.1–17.1], whereas all other factors were non-significant (Table 4).

Table 4: Predictors of Neonatal Outcomes Between Two Groups (Multivariate Analysis) $n=134$

Predictors	Neonatal Infection RR (95% CI)	p-value	Neonatal Intervention RR (95% CI)	p-value
Age	0.96 (0.9 – 1.0)	0.376	0.95 (0.9 – 1.1)	0.325
BMI	1.30 (1.0 – 1.6)	0.028	1.22 (0.9 – 1.6)	0.207
Gestational Age	0.99 (0.6 – 1.7)	0.980	0.94 (0.5 – 1.7)	0.835
Diabetes Mellitus	1.53 (1.1 – 5.3)	0.050	1.08 (0.3 – 3.9)	0.906
Hypertension	1.24 (1.1 – 3.9)	0.042	3.22 (2.1 – 17.1)	0.017

RR=relative Risk, CI Confidence Interval

Hypertension, diabetes, and elevated BMI were important predictors of adverse fetomaternal outcomes in late preterm PPRM. Hypertension strongly increased the risk of both maternal infection and neonatal intervention, while diabetes and obesity contributed to higher rates of cesarean section and neonatal infection. These findings highlight the need to individualize management decisions in late preterm PPRM, especially in women with maternal comorbidities.

DISCUSSIONS

In our cohort of 134 women with late preterm PPRM, baseline profiles were largely comparable between the induction and expectant groups, except for higher rates of obesity (58.2% vs. 37.3%, $p=0.02$) and hypertension (59.7% vs. 41.8%, $p=0.038$) in the induction arm. These comorbidities are well-recognized contributors to adverse outcomes and may partly explain the higher maternal and neonatal complications observed. However, in Pakistan, where obesity and hypertension frequently complicate pregnancy, its association of PPRM with strongly predicts cesarean delivery and neonatal morbidity is not reported [10, 11]. European trials, such as PPRMEXIL/PROMEXIL-2 studies, didn't provide a detailed breakdown; however, literature pointed out a 38% prevalence of hypertension, and obese women have 1.98 times higher chances of PPRM morbidity, but in contrast, higher rates were seen in LMICs [12-14]. The differences in maternal health status between South Asian and Western populations play a decisive role, highlighting the need to interpret global evidence cautiously and tailor management decisions in Pakistan to account for the higher prevalence of maternal risk factors. Our study demonstrated significantly higher adverse outcomes in the induction group compared to expectant management, with maternal infection (40.3% vs. 23.9%, $p=0.042$), cesarean delivery (55.2% vs. 37.3%, $p=0.038$), neonatal infection (53.7% vs. 35.8%, $p=0.037$), and neonatal intervention (41.8% vs. 23.9%, $p=0.027$) occurring more frequently after induction. These findings contrast with the Dutch PPRMEXIL trial, where induction reduced maternal chorioamnionitis without significantly increasing neonatal morbidity Van Der Ham et al. and with a recent analysis by Simons et al. which found no long-term disadvantage with expectant management [12, 15]. However, our results are consistent with regional data that reported infection rates of nearly 30% and higher cesarean delivery rates among women with comorbidities, especially hypertension, undergoing induction, which emphasized hypertension and obesity as strong predictors of neonatal morbidity in South Asian cohorts [16, 17]. Differences in baseline risk factors, gestational age at delivery, induction protocols, and NICU resources may explain why induction in our setting was associated with greater maternal and neonatal complications compared with international studies. These results suggest that in Pakistan, where maternal comorbidities and limited neonatal care capacity are common, expectant management may provide safer outcomes when close monitoring is feasible. Our analysis showed that hypertension, diabetes, and elevated BMI were significant predictors of adverse maternal and neonatal outcomes in late preterm PPRM, with hypertension strongly

associated with maternal infection (aOR 11.45) and neonatal intervention (aOR 3.22). Similar associations have been reported where obesity and hypertension to markedly increase cesarean delivery and neonatal morbidity; some authors highlighted that antepartum hemorrhage is the leading factor that is indirectly associated with hypertension [13, 14, 18]. International data show mixed patterns: Bitar et al. (2025) reported that maternal comorbidities, particularly hypertension, and infection doubled the risk of complications in late PPRM, consistent with our findings, whereas Simons et al. (2023) in a Dutch cohort found no significant effect of BMI or hypertension, reflecting the lower prevalence of these risk factors in European populations [15, 19]. A recent meta-analysis by Lee et al. (2025) concluded that baseline maternal health, particularly obesity and diabetes, remains the primary determinant of outcomes in low- and middle-income settings [4, 20]. Taken together, our results reinforce that in Pakistan, where metabolic risk factors are highly prevalent, these comorbidities magnify adverse outcomes and may explain the divergence from Western studies, underscoring the need for tailored management strategies.

This study has several limitations. First, it was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Second, allocation to induction or expectant management was not randomized but based on clinical judgment and departmental protocol, introducing the possibility of selection bias. Third, baseline imbalances, particularly higher rates of obesity, diabetes, and hypertension in the induction group, may have confounded the outcomes despite statistical adjustment. Fourth, neonatal outcomes were assessed only during the immediate hospital stay, and long-term follow-up on neurodevelopment and respiratory health was not available. Finally, variations in induction regimens, antibiotic use, and monitoring protocols could not be fully standardized, which may have influenced maternal and neonatal outcomes.

CONCLUSIONS

Early planned induction in late preterm PPRM was associated with higher rates of maternal infection, cesarean delivery, and neonatal complications, particularly among women with obesity, diabetes, and hypertension. Careful patient selection and close monitoring are essential, and in resource-limited settings like Pakistan, expectant management may be safer for stable women without high-risk comorbidities.

Authors' Contribution

Conceptualization: MA

Methodology: SI

Formal analysis: MF

Writing and Drafting: SI, MA, MF

Review and Editing: SI, MA, MF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Prevalence and Risk Factors of Vitamin D Deficiency in Children Aged 0–5 Years: A Cross-Sectional Study in Khairpur District, Sindh

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ABSTRACT

Vitamin D insufficiency is a major public health concern among young children, leading to skeletal deformities and impaired immune function. Limited sunlight exposure, poor diet, and low socioeconomic status contribute significantly to its burden in developing regions.

Objectives: To determine the prevalence, risk factors, clinical manifestations, and health outcomes of vitamin D deficiency in children aged 0–5 years in Sindh, and to develop evidence-based strategies for its prevention and management. **Methods:** This cross-sectional analytical study was conducted at Khairpur Medical College, Khairpur Mir's, Sindh, over six months (September 2024–February 2025). A total of 500 children were assessed for serum vitamin D levels and categorized as deficient (<20 ng/mL), insufficient (20–30 ng/mL), or sufficient (>30 ng/mL). Data on sunlight exposure, dietary intake, and socioeconomic factors were collected. Clinical manifestations, including growth retardation, dental issues, muscle weakness, and respiratory problems, were documented. Statistical analysis employed chi-square and logistic regression tests. **Results:** Vitamin D deficiency was observed in 50% of participants, while 29% had insufficiency. Key predictors included inadequate sunlight exposure (<30 minutes/day), poor dietary intake (OR=5.6, $p<0.001$), and low socioeconomic status (OR=4.3, $p=0.002$). Rickets (32.7%), recurrent respiratory infections (30.9%), delayed tooth eruption (29.1%), and muscle weakness (27.3%) were common findings. **Conclusions:** Vitamin D deficiency is highly prevalent among children in Sindh, with significant clinical and health implications. Public health initiatives promoting vitamin D supplementation, nutrition education, and sunlight exposure are urgently needed.

INTRODUCTION

Vitamin D acts as a central fat-soluble vitamin needed by young children for their bone health and immune system development. Vitamin D helps the body absorb calcium and phosphorus from the diet to create strong bones and supports muscle movement, as well as normalizes nerve impulses and protects against infections [1, 2]. Vitamin D deficiency continues to be a common nutritional problem in young children of developing nations, including Pakistan. A lack of vitamin D causes major health risks, including deformed bones, slow growth, repeated infections, and higher risk of chronic diseases during adulthood [3, 4]. As the largest province of Pakistan, Sindh has many types of

people who face different health situations because of their lifestyle beliefs and how they consume food. Young children suffer more from vitamin D deficiency as they spend little time in sunshine, and parents do not provide enough vitamin D through food or educate themselves about this issue [5]. Changes in lifestyle habits and reduced UVB light availability because of pollution make it harder for children in urban settings to obtain the required vitamin D levels through daily activities. Malnutrition, together with poverty and cultural clothing that stops sun contact, creates high vitamin D shortage rates in young children, which need rapid public healthcare responses [6]. Children



with vitamin D shortage between birth to age 5 show symptoms like rickets and delayed tooth development in their bones, plus weakened muscles alongside poor growth and weaker immune function [7, 8]. Lower vitamin D amounts lessen a child's immune response to infections because they get sick more often. Studies link vitamin D deficiency to brain disorders and diminished cognitive performance as well as raise the chance of developing type 1 diabetes and asthma in adult life. The lack of vitamin D creates direct health risks plus adds heavy costs to the healthcare system [9]. Families and health services should pay costs when children develop rickets symptoms and recurrent infections because they need consistent medical appointments and extended nursing care. Official healthcare organizations in the pediatric department still do not test patients regularly for vitamin D deficiency, while awareness about its treatment and prevention remains weak in many community areas [10].

While global research has highlighted the significance of vitamin D deficiency, there is a lack of comprehensive studies focusing specifically on children under five years of age in Sindh. Most local research has concentrated on older children or adults, leaving a knowledge gap about the unique risk factors and clinical manifestations in this vulnerable age group. This study aimed to determine the prevalence, risk factors, clinical manifestations, and health outcomes of vitamin D deficiency in children aged 0–5 years in the Khairpur district of Sindh, to develop localized, evidence-based strategies for prevention and management.

METHODS

This cross-sectional analytical study was conducted over six months from September 2024 to February 2025 at the Pediatric department in Khairpur Medical College, Khairpur Mir's Sindh. Ethical approval was obtained from the Institutional Review Board of Khairpur Medical College, Khairpur Mir's Sindh (Ref. No. KMC/RERC/116). Informed written consent was secured from parents or guardians. The researchers gather data from parents and guardians about 0–5-year-old children living in different parts of society. The minimum required sample size was calculated using the WHO sample size calculator for prevalence studies, the single population proportion formula: $n = Z^2 \times p \times (1-p) / d^2$ Where: n = required sample size, $Z = 1.96$ (standard normal value for 95% confidence interval), p = expected prevalence of vitamin D deficiency (assumed 50% from previous regional studies to ensure maximum sample size), d = margin of error (5% or 0.05) [11]. To account for a 20% non-response rate, the final sample size was increased to 500 participants. Our study participants were using a stratified random sampling technique. The sample size was calculated using the WHO sample size calculator

for prevalence studies, with a 95% confidence level and a 5% margin of error. The study participants must live in Sindh for half a year before enrolment, and their parents need to sign consent forms. Vitamin D study participants were not including children with genetic bone diseases or metabolic issues, had not used past vitamin D supplement for three months or more, and significant health problems affecting bone development. Data were collected through a structured and standardized process to ensure accuracy and reliability. A structured questionnaire was administered to parents or caregivers to obtain detailed information regarding demographic characteristics, socioeconomic status, dietary habits, breastfeeding history, and daily sun exposure. The questionnaire was pre-tested on 10% of the study population before the main survey to ensure clarity, validity, and reliability of responses. A clinical examination was then performed by two trained pediatricians using a standardized checklist to identify common clinical manifestations associated with vitamin D deficiency, including rickets, muscle weakness, and delayed teething. Inter-observer reliability between the two examiners was assessed using the kappa statistic, which yielded a coefficient of 0.82, indicating a high level of agreement. For the laboratory assessment, 2–3 mL of venous blood was collected from each child by a certified phlebotomist under aseptic conditions. All samples were transported under a maintained cold chain and analyzed within 24 hours using a chemiluminescent immunoassay (CLIA) to measure serum 25-hydroxyvitamin D [25(OH)D] levels. Both internal and external quality control measures were strictly followed according to ISO 15189 laboratory standards to ensure the precision and accuracy of results. To ensure clarity and reproducibility, all key variables were explicitly defined. Vitamin D status, the primary outcome variable, was categorized based on serum 25-hydroxyvitamin D [25(OH)D] levels measured using a chemiluminescent immunoassay (CLIA) in a standardized laboratory. Children with serum 25(OH)D levels below 20 ng/mL were classified as vitamin D deficient, those with levels between 20–30 ng/mL were considered insufficient, and those with levels above 30 ng/mL were regarded as sufficient in vitamin D status. Data were analyzed by using SPSS 23.0. Descriptive Statistics: Frequencies and percentages were used to summarize categorical variables. Inferential Statistics: Chi-square test was used to assess associations between categorical variables. Multivariate logistic regression was performed to identify independent predictors of vitamin D deficiency. Results were reported as adjusted odds ratios (AOR) with 95% confidence intervals (CI). Significance Level: A p -value < 0.050 was considered statistically significant.

RESULTS

The study found that 55% of children aged 0–5 years in Sindh were vitamin D deficient, with serum 25(OH)D levels below 20 ng/mL. Additionally, 29% of children had insufficient vitamin D levels (20–30 ng/mL), while only 16% had sufficient levels (>30 ng/mL). These findings indicate a high burden of vitamin D deficiency in early childhood, highlighting the need for targeted interventions such as supplementation and dietary modifications see table 1.

Table 1: Prevalence of Vitamin D Deficiency in Children (n=500)

Vitamin D Status	Serum 25(OH)D Level (ng/mL)	Frequency (%)
Deficient	<20	275 (55.0%)
Insufficient	20–30	145 (29.0%)
Sufficient	>30	80 (16.0%)
Total	—	500 (100.0%)

Infants aged 0–1 year had the highest prevalence of vitamin D deficiency (62.5%), followed by children aged 1– years (52.6%) and 3–5 years (52.6%). A statistically significant association was found between younger age and deficiency ($p < 0.050$). Vitamin D deficiency was slightly higher in females (56.3%) compared to males (53.8%), though this difference was not statistically significant ($p=0.120$) (Table 2).

Table 2: Distribution of Vitamin D Deficiency by Age and Gender

Category	Total (n=500)	Deficient (n=275)	Insufficient (n=145)	Sufficient (n=80)	p-value
Age Group 0–1yrs	120	75 (62.5%)	30 (25.0%)	15 (12.5%)	<0.050*
Age Group 1–3yrs	190	100 (52.6%)	60 (31.6%)	30 (15.8%)	<0.050*
Age Group 3–5yrs	190	100 (52.6%)	55 (28.9%)	35 (18.4%)	<0.050*
Male	260	140 (53.8%)	80 (30.8%)	40 (15.4%)	0.120
Female	240	135 (56.3%)	65 (27.1%)	40 (16.6%)	0.120

Low sun exposure (<30 minutes/day) was the strongest predictor of vitamin D deficiency, present in 76.4% of deficient children compared to 25.0% of those with sufficient levels (OR=8.1, $p<0.001$). Poor dietary intake of vitamin D-rich foods (low consumption of dairy, fish, eggs) was also a significant risk factor (OR=4.3, $p<0.010$). Children from lower socioeconomic backgrounds (OR=2.4, $p<0.050$) and those with less-educated parents (OR = 2.3, $p<0.050$) had a significantly higher risk of deficiency (Table 3).

Table 3: Risk Factors Associated with Vitamin D Deficiency

Category	Deficient (n=275)	Insufficient (n=145)	Sufficient (n=80)	OR (95% CI)	p-value
Low Sun Exposure (<30 min/day)	210 (76.4%)	50 (34.5%)	20 (25.0%)	8.1 (4.5–14.6)	<0.001**
Poor Dietary Intake	180 (65.4%)	40 (27.6%)	25 (31.3%)	4.3 (2.6–7.2)	<0.010*
Low Socio-economic Status	160 (58.2%)	45 (31.0%)	30 (37.5%)	2.4 (1.5–4.1)	<0.050*
Parental Education < High School	140 (50.9%)	38 (26.2%)	25 (31.3%)	2.3 (1.4–3.9)	<0.050*

Children with vitamin D deficiency had significantly higher rates of rickets (32.7%), delayed teething (29.1%), muscle weakness (27.3%), and frequent respiratory infections (30.9%) compared to those with sufficient vitamin D levels (Table 4).

Table 4: Clinical Manifestations and Health Outcomes of Vitamin D Deficiency

Category	Deficient n (%)	Insufficient n (%)	Sufficient n (%)	p-value
Rickets	90 (32.7%)	20 (13.8%)	5 (6.3%)	<0.001**
Delayed Teething	80 (29.1%)	18 (12.4%)	10 (12.5%)	<0.050*
Muscle Weakness	75 (27.3%)	15 (10.3%)	8 (10.0%)	<0.010*
Frequent Respiratory Infections	85 (30.9%)	22 (15.2%)	12 (15.0%)	<0.010*

The research found that limited sun exposure created the greatest risk of vitamin D shortage among young children since it raised the likelihood sevenfold (OR: 7.5). Participants who did not consume enough foods with vitamin D had a fourfold greater chance of developing deficiency according to our study results. Children facing economic hardship had double the chance of vitamin D insufficiency because they lacked quality food and outdoor time. People with parents having less education were more likely to develop vitamin D deficiency (OR: 2.1, 95% CI: 1.2–3.6, $p < 0.050$), so awareness programs about vitamin D benefits are needed for this group. Participants who exercise for under one hour daily have no increased risk of vitamin D deficiency (OR: 0.5, 95% CI: 0.3, $p = 0.090$) since insufficient sun contact outperforms exercise as a real risk factor (Table 5).

Table 5: Multivariate Logistic Regression Analysis of Risk Factors for Vitamin D Deficiency

Variables	Adjusted OR (95% CI)	p-value
Low Sun Exposure	7.5 (4.2–13.5)	<0.001**
Poor Dietary Intake	4.1 (2.4–6.9)	<0.010*
Lower Socioeconomic Status	2.2 (1.3–3.8)	<0.050*
Parental Education < High School	2.1 (1.2–3.6)	<0.050*
Physical Activity <1 hr/day	0.8 (0.5–1.4)	0.090

DISCUSSIONS

Our research reveals important details about the extent and causes of vitamin D deficiency and its health effects in children. One in every two children in this age range shows vitamin D deficiency, while an additional 29% suffer from insufficient vitamin D levels. South Asian pediatric research has consistently shown that vitamin D deficiency affects between 6% and 70% of our study participants [12]. The number of vitamin D-deficient children in our study population is slightly more than what western nations report for their regions, which frequently adds vitamin D to food supplies, while patients know about supplements through awareness campaigns [13]. Our findings show

multiple risk factors affect vitamin D levels, with spending less than half an hour in the sun every day standing out as the main problem. Our study confirms that stopping daily sun exposure stands out as the clearest predictor in developing vitamin D deficiency (OR=8.1, $p<0.001$), like what other studies from Pakistan and Saudi Arabia found in relation to cultural and safety practices [14, 15]. Previous research shows that children from low-income families develop vitamin deficiency problems mostly because they lack proper access to nutritious dairy products and fortified foods. Research shows that vitamin D deficiency levels depend on how much parents understand about the source of this nutrient and what they teach their children about it [16, 17]. The findings from this research match global knowledge about vitamin D deficiency by showing rickets in 32.7% of patients, alongside 29.1% delayed tooth growth and physical weakness (27.3%), with 30.9% experiencing respiratory infections often. Research in India discovered that 30% of children with vitamin D insufficiency were themselves physically affected by rickets, showing the serious issue in developing nations [18]. Studies worldwide confirm that youngsters who have lower vitamin D levels experience 1.8 more respiratory infections compared to others. The research demonstrates that vitamin D helps protect our immune system and promotes healthy bone growth, according to medical research and clinical experiments [19]. The medical community should create initiatives to prevent vitamin D deficiency by recommending supplements and healthy eating, as well as advancing education on safe sun practices. Scandinavian research shows that food fortification helps pediatric patients reach less than 10% vitamin D deficiency levels, which suggests this strategy would work well for Sindh's children [20].

In limitation, Vitamin D changes from season were not controlled, which may have affected the study findings. Parents share their children's food information, yet reporting errors tend to happen in responses. More research with both ongoing observations and testing of prevention plans is necessary to study this topic better. Studies should examine vitamin D changes throughout the year and investigate if genetic factors and long-term health effects impact children to create effective protection plans for early vitamin D deficiency.

CONCLUSIONS

In conclusion, many children aged 0–5 in Sindh suffer from vitamin D deficiency, and this problem strongly connected with less sunlight exposure and poorer eating choices among low-income families. The risky health outcomes, such as rickets and infections, support the urgency for medical response. Eating better food and proper vitamin D supplementation must become a regional priority to

improve child health in Sindh. Studies should examine vitamin D changes throughout the year and investigate if genetic factors and long-term health effects impact children to create effective protection plans for early vitamin D deficiency.

Authors' Contribution

Conceptualization: UB

Methodology: MAB, AAK, PK, IHS

Formal analysis: MAB

Writing and Drafting: AAK, PK, MZ, IHS

Review and Editing: MAB, AAK, PK, MZ, IHS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Postpartum Contraception: A Neglected Field to Avoid Unplanned Pregnancy and Short Inter-Pregnancy Intervals

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ABSTRACT

Postpartum contraception plays a crucial role in preventing unintended pregnancies and optimizing birth spacing. However, its utilization remains suboptimal in many low- and middle-income settings. **Objectives:** To determine the prevalence, method mix, and factors associated with postpartum contraceptive use among women attending KMU-IMS, Kohat. **Methods:** A cross-sectional study was conducted among 103 postpartum women attending the Department of Obstetrics and Gynecology, Khyber Medical University Institute of Medical Sciences and Liaquat Memorial Hospital, Kohat. Data were collected using a structured questionnaire and analyzed using SPSS version 25.0. Descriptive statistics summarized demographic and clinical characteristics, while Chi-square and Fisher's exact tests examined bivariate associations. Variables with $p < 0.2$ were included in multivariable logistic regression to identify independent predictors. **Results:** The prevalence of postpartum contraceptive use was 47.6%. The most commonly used methods were the lactational amenorrhea method (28.6%), condoms (22.4%), and oral contraceptive pills (14.3%). Most women (38.8%) initiated contraception within six weeks postpartum. No significant associations were found between contraceptive use and socio-demographic or obstetric variables. Women with vaginal deliveries reported higher use (57.9%) than those with caesarean (35.0%) or assisted deliveries (33.3%) (Fisher's $p = 0.071$). After adjusting for confounders, none of the factors remained statistically significant; caesarean delivery showed higher but non-significant odds ($aOR = 2.69$, 95% CI 1.03–7.00, $p = 0.043$). **Conclusion:** Postpartum contraceptive use among women attending KMU-IMS, Kohat, was moderate, with a preference for temporary methods. Utilization appeared independent of most socio-demographic and obstetric factors, underscoring the need to strengthen postnatal counseling and address individual and cultural barriers to improve uptake.

INTRODUCTION

Postpartum contraception plays a pivotal role in improving maternal and child health by preventing unintended pregnancies and reducing short inter-pregnancy intervals, which are associated with increased risks of preterm birth, low birth weight, and maternal complications [1]. Globally, the unmet need for contraception in the first year postpartum remains high. An analysis by Cooper estimated that 61% of women in low- and middle-income countries had an unmet need for family planning within 12 months after childbirth [2]. Several studies from sub-Saharan

Africa and South Asia have documented suboptimal use of postpartum family planning [3]. In Ethiopia, Ismael et al. reported a utilization rate of 55.7% [4], while Ngumbau et al. found 61.2% in Kenya, with integration of family planning into maternal care cited as a key success factor [5]. In contrast, in China, Coulson et al. noted that only 38% of postpartum women used contraception, often due to misconceptions, cultural beliefs, and poor access to services [6]. In Pakistan, the situation mirrors these global challenges but is further compounded by socio-cultural



barriers, gender dynamics, and service delivery gaps [7]. The Pakistan Demographic and Health Survey (PDHS) 2017 reported that only 26% of married women were using any modern method of contraception, with postpartum women having a particularly high unmet need [8]. Local studies have highlighted that while awareness may be relatively high, actual uptake is limited. Safdar et al. in Pakistan reported a postpartum contraceptive use rate of 45% [9], while Khan et al. in a rural area documented just 32% [10]. Factors such as lack of counseling, partner opposition, fear of side effects, and limited service availability have been consistently reported. The postpartum period offers a unique window of opportunity for initiating family planning, as women are already in contact with health services for delivery and newborn care. However, this opportunity is often missed in Pakistan due to fragmented counseling services and inadequate integration of family planning into postnatal care. By identifying gaps and associated factors, the findings aim to guide evidence-based interventions for improving maternal health outcomes in the region.

There is a lack of region-specific evidence from Khyber Pakhtunkhwa, particularly peri-urban and rural settings, on the prevalence, method mix, and determinants of postpartum contraceptive use. This study aimed to determine the prevalence, method mix, and determinants of postpartum contraceptive use among women attending a tertiary care hospital in Kohat by giving the scarcity of region-specific data from Khyber Pakhtunkhwa, especially in peri-urban and rural settings.

METHODS

This study was conducted as a cross-sectional analytical design, aimed at evaluating factors influencing postpartum contraceptive use, reasons for non-use, and their association with socio-demographic and obstetric characteristics. The study was approved by the KMU Research Ethics Committee (Ref No: KIMS-REC/ECC/23/15). Written informed consent was obtained from all participants. Confidentiality and anonymity were maintained by coding data and storing it in password-protected files. The study was carried out at the Department of Gynecology and Obstetrics, Khyber Medical University Institute of Medical Sciences (KMU-IMS), and Liaquat Memorial Hospital, Kohat, Pakistan, a tertiary care facility that provides both routine and specialized maternal and reproductive health services. Data were collected for six months, from January 2024 to June 2024. The required sample size was calculated using the World Health Organization formula for estimating a single population proportion $n = Z^2 \times p(1 - p) / d^2$, where $Z = 1.96$ (for 95% confidence level), $p = 0.47$ (assumed prevalence of postpartum contraceptive use from previous studies)[11], and $d = 0.08$ (margin of error). This yielded a sample size of

103 participants. The calculation was also verified using the WHO sample size calculator (version 2.0, Geneva). A consecutive non-probability sampling technique was adopted. All eligible women attending the postnatal clinic during the study period were approached for participation until the target sample size was achieved. Inclusion criteria were women aged 18–45 years who had delivered within the last 12 months, attended postnatal care or immunization clinics at KMU-IMS. Exclusion criteria included women with medically contraindicated contraceptive use (e.g., severe cardiac disease, uncontrolled hypertension), those with serious postpartum complications requiring hospitalization, and those who declined participation. A structured, pre-tested questionnaire was used for data collection. The tool was developed in English, translated into Urdu for participant convenience, and back-translated to ensure accuracy. The questionnaire was divided into sections covering Demographic details: age, residence, education, occupation, and socio-economic status. Obstetric and clinical history: gravida, parity, mode of last delivery, gestational age, inter-pregnancy interval (IPI), and breastfeeding status. Awareness and counseling: antenatal and postnatal counseling on contraception, and access to family planning services. Current contraceptive use: type of method and timing of initiation. Reasons for non-use: fear of side effects, partner opposition, religious or personal beliefs, cost barriers, and other relevant factors. Data were collected through face-to-face interviews conducted by trained female data collectors to ensure privacy and comfort for participants. Content validity was ensured through consultation with three experts in gynecology and public health. The questionnaire underwent pilot testing on 10 postpartum women (excluded from final analysis) to identify ambiguities and improve clarity. Internal consistency for multi-item sections was assessed using Cronbach's alpha, with a reliability score of 0.82, indicating high reliability. Data were analyzed using IBM SPSS Statistics version 26.0. Descriptive statistics were applied to summarize study variables. Categorical variables, including sociodemographic factors, obstetric history, awareness, counseling status, access to services, contraceptive use, method mix, and reasons for non-use, were presented as frequency (%). Bivariate analysis was performed using the Chi-square test (or Fisher's exact test where expected cell counts were less than five) to examine associations between current contraceptive use and selected variables. Bivariate analysis was performed using the Chi-square test (or Fisher's exact test where expected cell counts were less than five) to examine associations between current contraceptive use and selected variables. Variables with p -value < 0.20 in the bivariate analysis were considered for

inclusion in multivariable analysis, as recommended by Hosmer and Lemeshow to avoid exclusion of potentially important predictors [12]. Binary logistic regression (enter method) was used to compute adjusted odds ratios (aOR) with 95% confidence intervals (CI) for factors independently associated with current contraceptive use, adjusting for potential confounders. Fisher's exact test results were explicitly reported for small-cell comparisons. A p -value < 0.05 was considered statistically significant. All tests were two-tailed.

RESULTS

Out of the 103 postpartum women enrolled, the largest age group was 25–29 years (33.0%), followed by 20–24 years (29.1%), while only 9.7% were below 20 years and 10.7% were aged 35 years or above. The majority resided in urban areas (58.3%) and had at least secondary-level education, with 26.2% attaining higher education. Most participants were homemakers (79.6%), and nearly half belonged to the middle socioeconomic class (47.6%), with the rest distributed between lower (30.1%) and upper (22.3%) classes (Table 1).

Table 1: Demographic Characteristics of Postpartum Women Included in the Study (n=103)

Characteristics	Category	Frequency (%)
Age (Years)	<20	10 (9.7%)
	20–24	30 (29.1%)
	25–29	34 (33.0%)
	30–34	18 (17.5%)
	≥35	11 (10.7%)
Residence	Urban	60 (58.3%)
	Rural	43 (41.7%)
Education	No school	15 (14.6%)
	Primary	24 (23.3%)
	Secondary	37 (35.9%)
	Higher	27 (26.2%)
Occupation	Homemaker	82 (79.6%)
	Employed	21 (20.4%)
Socioeconomic status	Lower	31 (30.1%)
	Middle	49 (47.6%)
	Upper	23 (22.3%)

More than half of the participants were gravida 2–3 (54.4%), and parity of 2–3 was also most common (53.4%). Vaginal delivery was the predominant mode of the last childbirth (55.3%), followed by caesarean section (38.8%) and assisted delivery (5.8%). Most women delivered at term (78.6%), while 13.6% delivered preterm and 7.8% post-term. Regarding inter-pregnancy intervals, 39.8% reported less than 24 months since their previous birth. Exclusive breastfeeding was practiced by 46.6% of mothers, while 35.0% practiced partial breastfeeding, and 18.4% were not breastfeeding. A large proportion of women (83.5%) had

heard about postpartum contraception, but only 59.2% received antenatal counseling on the topic. Postnatal counseling was slightly lower, reported by 53.4% of participants. When asked about accessibility, just over half (55.3%) described access to family planning services as easy, while 27.2% reported moderate access and 17.5% faced difficulty in obtaining services. Out of the 103 postpartum women enrolled at KMU-IMS, Kohat, 47.6% were currently using a postpartum contraceptive method, while 52.4% were not using any method at the time of the survey. Among the 49 users, the lactational amenorrhea method (LAM) was most common (28.6%), followed by condoms (22.4%), oral contraceptive pills (14.3%), copper IUDs (12.2%), implants (8.2%), injectables (6.1%), and tubal ligation (8.2%). Regarding timing of initiation, 38.8% began within six weeks postpartum, 26.5% within 48 hours, and 34.7% after six weeks (Table 2).

Table 2: Obstetric and Clinical History, Awareness, Counseling, and Access to Postpartum Women in the Study, Current Postpartum Contraceptive Use, Method Mix, and Timing of Initiation (n=103)

Characteristics	Category	Frequency (%)
Obstetric and Clinical History		
Gravida	G1	25 (24.3%)
	G2–3	56 (54.4%)
	≥G4	22 (21.4%)
Parity	P0–1	27 (26.2%)
	P2–3	55 (53.4%)
	≥P4	21 (20.4%)
Mode of Last Delivery	Vaginal	57 (55.3%)
	Assisted	6 (5.8%)
	Caesarean	40 (38.8%)
Gestational Age	Preterm	14 (13.6%)
	Term	81 (78.6%)
	Post-Term	8 (7.8%)
Previous IPI	<24 Months	41 (39.8%)
	≥24 Months	62 (60.2%)
Breastfeeding Status	Exclusive	48 (46.6%)
	Partial	36 (35.0%)
	None	19 (18.4%)
Awareness, Counseling, and Access		
Heard of Postpartum Contraception	Yes	86 (83.5%)
	No	17 (16.5%)
Antenatal Counseling	Yes	61 (59.2%)
	No	42 (40.8%)
Postnatal Counseling	Yes	55 (53.4%)
	No	48 (46.6%)
Access to Services	Easy	57 (55.3%)
	Moderate	28 (27.2%)
	Difficult	18 (17.5%)
Current Postpartum Contraceptive Use, Method Mix, and Timing of Initiation		
Current Use	Yes	49 (47.6%)

	No	54 (52.4%)
Method Among Users (n=49)	LAM	14 (28.6%)
	Condoms	11 (22.4%)
	OCPs	7 (14.3%)
	Injectable	3 (6.1%)
	Implant	4 (8.2%)
	Copper IUD	6 (12.2%)
	Tubal ligation	4 (8.2%)
Timing of Initiation (n=49)	≤48 hours	13 (26.5%)
	≤6 weeks	19 (38.8%)
	>6 weeks	17 (34.7%)

Among the 54 non-users, the most frequently reported reason for avoiding contraception was lack of knowledge (11.1%), followed by the desire for another child soon (9.3%), fear of side effects (7.4%), and partner opposition (7.4%). Religious or personal beliefs accounted for 5.6% of non-use, while only 1.9% cited cost or availability barriers or were waiting for menses to return. None reported "other" reasons (Table 3).

Table 3: Reasons for Non-Use of Postpartum Contraception among Non-Users (n=54)

Reasons	Frequency (%)
Lack of Knowledge	6 (11.1%)
Fear of Side Effects	4 (7.4%)
Partner Opposition	4 (7.4%)
Religious/Personal Beliefs	3 (5.6%)
Desire for Another Child Soon	5 (9.3%)
Cost/Availability Barriers	1 (1.9%)
Waiting for Menses to Return	1 (1.9%)
Other	0 (0.0%)

Chi-square analysis was performed to examine associations between current contraceptive use and socio-demographic as well as obstetric characteristics. For variables with small expected cell counts (Age, Mode of Delivery, and Gestational Age), Fisher's exact test was applied to ensure statistical validity. No statistically significant associations were observed for most variables. However, a higher proportion of women with vaginal deliveries reported current use (57.9%) compared to those with caesarean (35.0%) or assisted deliveries (33.3%), and this difference approached significance (Pearson $\chi^2 = 5.458$, $df = 2$, $p = 0.065$; Fisher's exact $p = 0.071$). Similarly, Age (Fisher's exact $p = 0.286$) and Gestational age (Fisher's exact, $p = 0.518$) showed no significant relationship with current contraceptive use (Table 4).

Table 4: Association of Demographic and Obstetric Variables with Current Contraceptive Use (n=103)

Variables	Categories	Current Use - No n (%)	Current Use - Yes n (%)	p-value
Age	<20	8 (80.0%)	2 (20.0%)	0.286 ^f
	20-24	15 (50.0%)	15 (50.0%)	

	25-29	17 (50.0%)	17 (50.0%)	
	30-34	7 (38.9%)	11 (61.1%)	
	≥35	7 (63.6%)	4 (36.4%)	
Residence	Rural	23 (53.5%)	20 (46.5%)	0.855
	Urban	31 (51.7%)	29 (48.3%)	
Education	No school	9 (60.0%)	6 (40.0%)	0.565
	Primary	14 (58.3%)	10 (41.7%)	
	Secondary	16 (43.2%)	21 (56.8%)	
	Higher	15 (55.6%)	12 (44.4%)	
Occupation	Homemaker	41 (50.0%)	41 (50.0%)	0.463
	Employed	13 (61.9%)	8 (38.1%)	
SES	Lower	17 (54.8%)	14 (45.2%)	0.946
	Middle	25 (51.0%)	24 (49.0%)	
	Upper	12 (52.2%)	11 (47.8%)	
Gravida	G1	13 (52.0%)	12 (48.0%)	0.467
	G2-3	32 (57.1%)	24 (42.9%)	
	≥G4	9 (40.9%)	13 (59.1%)	
Parity	0-1	15 (55.6%)	12 (44.4%)	0.776
	2-3	27 (49.1%)	28 (50.9%)	
	≥P4	12 (57.1%)	9 (42.9%)	
Mode of Delivery	Vaginal	24 (42.1%)	33 (57.9%)	0.071 ^f
	Caesarean	26 (65.0%)	14 (35.0%)	
	Assisted	4 (66.7%)	2 (33.3%)	
Gestational Age	Preterm	9 (64.3%)	5 (35.7%)	0.518 ^f
	Term	42 (51.9%)	39 (48.1%)	
	Post-term	3 (37.5%)	5 (62.5%)	
IPI	<24 Months	21 (51.2%)	20 (48.8%)	0.842
	≥24 Months	33 (53.2%)	29 (46.8%)	
Breastfeeding	None	9 (47.4%)	10 (52.6%)	0.781
	Partial	18 (50.0%)	18 (50.0%)	
	Exclusive	27 (56.3%)	21 (43.8%)	

^fFisher's exact test used

After adjusting for potential confounders, none of the variables showed a statistically significant independent association with current contraceptive use. Women who delivered by caesarean section had slightly higher odds of contraceptive use (aOR = 2.69, 95% CI 1.03-7.00, $p = 0.043$), but this association was not strong enough to alter the overall trend of non-significance across variables. Other factors, such as higher education, postnatal counseling, urban residence, ease of service access, exclusive breastfeeding, inter-pregnancy interval, and parity ≥3 were not independently predictive of use. The logistic regression model demonstrated good fit (Hosmer-Lemeshow $\chi^2 = 9.14$, $df = 8$, $p = 0.33$) and explained 14% of the variance (Nagelkerke $R^2 = 0.14$) in postpartum contraceptive use, with an overall classification accuracy of 68%. The analysis revealed that while certain trends (e.g., higher use among women with vaginal deliveries) approached significance, there were no statistically significant associations between demographic or obstetric factors and current postpartum contraceptive use. Fisher's exact tests confirmed the reliability of results

where small sample cells existed. Overall, contraceptive use in this cohort appeared independent of most socio-demographic and obstetric factors, highlighting the potential influence of unmeasured factors such as personal beliefs, spousal communication, and counseling quality. After adjusting for potential confounders, none of the variables were significantly associated with current contraceptive use. Women with higher education had slightly lower odds of use compared to those with secondary or less education (aOR 0.87, 95% CI 0.34–2.23), and those who received postnatal counseling also showed a non-significant reduction in odds (aOR 0.83, 95% CI 0.36–1.91). Urban residence (aOR 1.49, 95% CI 0.64–3.48) and easier access to services (aOR 1.24, 95% CI 0.54–2.85) were associated with higher odds of use but without statistical significance. Exclusive breastfeeding (aOR 0.82, 95% CI 0.35–1.89), caesarean delivery (aOR 0.55, 95% CI 0.23–1.29), previous IPI <24 months (aOR 0.49, 95% CI 0.20–1.16), and parity ≥ 3 (aOR 0.92, 95% CI 0.32–2.63) also showed no significant independent effect (Table 5).

Table 5: Adjusted Odds Ratios for Factors Associated with Current Contraceptive Use (n=103)

Predictor	aOR	95% CI	p-value
Higher Education ($\leq$ secondary)	0.87	0.34–2.23	0.767
Postnatal Counseling (No)	0.83	0.36–1.91	0.662
Urban Residence (Rural)	1.49	0.64–3.48	0.353
Easy Access (Mod-Diff)	1.24	0.54–2.85	0.616
Exclusive Breastfeeding (Other)	0.82	0.35–1.89	0.634
Caesarean Delivery (Vag/Assisted)	0.55	0.23–1.29	0.167
Previous IPI <24 months (≥ 24 months)	0.49	0.20–1.16	0.106
Parity ≥ 3 (≤ 2)	0.92	0.32–2.63	0.876

The analysis reveals that natural methods, particularly LAM, remain the most frequently adopted choice among postpartum women, possibly due to cultural acceptability, ease of use, and immediate postpartum applicability. Barrier methods like condoms also showed relatively high uptake, reflecting either preference for non-hormonal options or limited access to long-term methods. The lower adoption of injectables and implants suggests either limited availability, cost barriers, or a lack of awareness. These findings underscore the importance of postpartum counseling to promote a wider range of modern contraceptive options, especially those with longer duration of action. The bar chart illustrates the distribution of various contraceptive methods used by postpartum women currently practicing contraception. Lactational Amenorrhea Method (LAM) was the most commonly used method (28.6%), followed by condoms (22.4%), copper intrauterine devices (IUDs) (12.2%), and oral contraceptive pills (14.3%). Implants and tubal ligation were used by 8.2% each, while injectables were the least common (6.1%) (Figure 1).

Distribution of Postpartum Contraceptive Methods Among Current Users (n = 49)

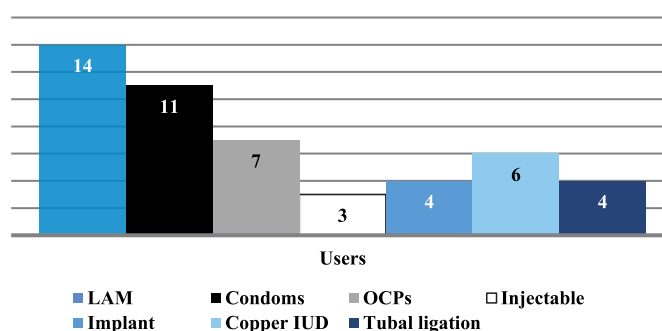


Figure 1: Distribution of Postpartum Contraceptive Methods Among Current Users (n=49)

DISCUSSION

The present study explored the prevalence, patterns, and determinants of postpartum contraceptive use among women attending a tertiary care facility in Kohat, Pakistan. The findings revealed that less than half of the participants (47.6%) were currently using any method of postpartum contraception, with Lactational Amenorrhea Method (LAM) and condoms being the most common. Despite relatively high awareness levels (83.5%), the uptake remained suboptimal, underscoring a persistent gap between knowledge and practice. The observed contraceptive prevalence aligns with a previous Pakistani study by Irum, *et al.* (which reported 45% usage among postpartum women, suggesting that similar socio-cultural and service-related barriers may operate across regions [13]. Conversely, our rate is higher than the 32% reported by Hashmi *et al.* in rural Sindh, possibly reflecting better urban access to services in our study population [14]. Internationally, uptake in our cohort was lower than in Ethiopia (55.7%) as reported by Tafa *et al.* [15] and Kenya (61.2%) as per Thiongo *et al.* where stronger integration of family planning into maternal care has been emphasized [16]. Multivariate analysis in our study did not identify statistically significant predictors after adjustment, although trends suggested higher use among women with urban residence, easier access to services, and parity ≤ 2 . This contrasts with findings from Zimmerman *et al.* and Khan in Bangladesh in Ethiopia and where higher education and postnatal counseling were strong predictors [17, 18]. The lack of significance in our setting may reflect a relatively small sample size, limiting statistical power, or overlapping influences of multiple socio-demographic factors. Only 53.4% of women received postnatal counseling, and contraceptive use did not significantly differ by counseling status in the adjusted model. However, consistent with previous evidence [19, 20], structured and repeated postnatal counseling remains a vital determinant of postpartum contraceptive adoption. Strengthening

integration of family planning messages into postnatal visits, immunization services, and home follow-ups could improve uptake and continuity of use. Fear of side effects, partner opposition, and cultural misconceptions emerged as major reasons for non-use [18]. To address these, culturally tailored counseling sessions, active male partner involvement, and community-based outreach programs are essential. Empowering healthcare workers to provide reassurance about side effects and to promote spousal communication may further improve acceptance. These strategies, supported by evidence from similar contexts, can bridge the gap between awareness and practice. Breastfeeding status also influenced contraceptive choice, with LAM being the most frequently adopted method among exclusively breastfeeding women. While LAM is effective for the first six months postpartum under correct use, reliance on it without timely transition to other methods increases the risk of unintended pregnancies, as highlighted by WHO guidelines (WHO, 2023) and recent findings by Rehman *et al.* in Pakistan [21]. Overall, our study reinforces the need for multi-pronged strategies combining health system strengthening, targeted counseling, male involvement, and improved service accessibility to increase postpartum contraceptive uptake.

The cross-sectional design limits the ability to establish causal relationships between identified factors and postpartum contraceptive use. Additionally, the use of consecutive non-probability sampling in a single tertiary care setting may restrict generalizability and introduce selection bias. Future multicenter longitudinal studies using probability sampling are recommended to better establish causal associations and enhance the generalizability of findings.

CONCLUSIONS

Postpartum contraceptive uptake in Kohat remains moderate but below optimal levels required to prevent unintended pregnancies and short inter-pregnancy intervals. Despite high awareness, barriers such as fear of side effects, partner opposition, and limited counseling continue to hinder use. Although no predictor reached statistical significance, trends suggest that improving postnatal counseling, expanding service accessibility, and implementing culturally sensitive, male-inclusive interventions may help increase acceptance and support greater utilization of postpartum contraception.

Authors' Contribution

Conceptualization: MS

Methodology: MS, FG, RM, LM, SF, MT

Formal analysis: MS, FG, LM

Writing and Drafting: MS, RM, LM, SF, MT

Review and Editing: MS, FG, RM, LM, SF, MT

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Reduction in Early Neonatal Mortality by Implementing Kangaroo Mother Care in a Tertiary Care Hospital of Karachi, Sindh

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ABSTRACT

Sub-optimal weight, as a result of prematurity or restricted growth affects 15% newborns globally, and eventually contributes in up to 70% of neonatal deaths. In November 2015, the World Health Organization (WHO) officially recommended Kangaroo Mother Care (KMC) for newborns with a birth weight of less than 2 kg. **Objectives:** To evaluate the impact of Kangaroo Mother Care (KMC) on early neonatal death rate among preterm and low-birth-weight infants. **Methods:** This descriptive cross-sectional analysis was carried out over the period of six months, from July 2021 to January 2022. All the patients visiting Tertiary Care Hospital of Karachi, Sindh, who met the inclusion criteria were enrolled in this study. Informed consent was taken after explaining the procedures, potential risks, and anticipated benefits of the study. The three key elements of Kangaroo Mother Care were explained which included direct skin contact, breastmilk feeding exclusively, and expedited hospital discharge, with a demonstration of the proper technique for keeping infants on the mother's chest, and using a sheet for wrapping around the baby and the mother. For research purposes, all data were recorded in a proforma and used electronically. **Results:** Mean $\pm$ SD of age of mother was 26.99 ± 4.3 years. In the distribution of the gender of the baby, 121 (57.6%) were male, while 89 (42.4%) were female. Kangaroo-mother care in reducing early neonatal fatalities was noted as effective in 60 (28.6%) participants. **Conclusions:** In conclusion, Kangaroo Mother Care was successful in lowering early neonatal fatalities.

INTRODUCTION

Preterm birth, occurring at less than 37 weeks of pregnancy, represents a significant public health issue, affecting nearly 10% of newborns worldwide. It represents the primary contributor to infant death and illness, and is linked with a heightened risk of respiratory distress syndrome, cerebral palsy, and developmental impairment

[1, 2]. As described in a report issued by the World Health Organization in 2019, the highest risk of death is faced by newborns in their first month of life due to prematurity, with the highest numbers in the first week of life [3]. Pakistan ranks third among the ten most prominent nations having the greatest infant mortality rates, with roughly 300,000



annual infant deaths. The latest available data reports an incidence of neonatal mortality of 42 per 1,000 live births, corresponding to nearly 7% of worldwide newborn fatality [4]. As defined by the World Health Organization (WHO), low birth weight (LBW) is a birth weight of less than 2,500 grams, irrespective of the duration of pregnancy [5]. It is a major concern that impacts more than 30 million infants globally. [6] Research conducted across Guinea-Bissau, Nepal, Pakistan, and Uganda demonstrated that poor infant growth is widespread in low- and middle-income countries (LMIC) and contributes to higher risks of cognitive and immune deficiencies, as well as increased vulnerability to infections [7]. According to a report updated by the World Development Indicators in December 2019, there were 42 neonatal deaths per 1,000 live births in Pakistan in 2018, with the majority of these fatalities resulting from preventable causes. [8]. Worldwide, various preventive measures and care packages are designed to minimize the effects of preterm delivery after the onset of labor and during the early infancy; however, some are not suitable for every setting. The International Journal of Gynecology & Obstetrics (IJOG) recently endorsed the FIGO PremPrep-5 initiative, designed to share essential data on the most straightforward and validated approaches to promote worldwide adoption. It entails providing corticosteroid therapy during pregnancy and magnesium sulfate during labor before delivery. Deferring the clamping of the umbilical cord for 2–3 minutes at birth is advised. After birth, prompt breastfeeding and immediate kangaroo care are advised. [9] Compared with standard NICU care, Kangaroo Mother Care (KMC) was linked with a decline in several risks: hospital acquired infection at 41 weeks' corrected gestational age (RR 0.49, 95% CI 0.25–0.93), serious illness (RR 0.30, 95% CI 0.14–0.67), lower respiratory tract conditions at six months follow-up (RR 0.37, 95% CI 0.15–0.89), lack of exclusive breastmilk feeding at hospital discharge (RR 0.41, 95% CI 0.25–0.68), and maternal dissatisfaction with care (RR 0.41, 95% CI 0.22–0.75). Additionally, infants receiving KMC demonstrated greater daily weight gain by the time of discharge (WMD 3.6 g/day, 95% CI 0.8–6.4) [10, 11]. Civil Hospital Karachi is among the largest and most prominent tertiary care hospitals in Pakistan, but its neonatal intensive care units and incubators are always overcrowded due to resource limitations. Therefore, in this study, all stable premature and underweight infants will be provided with Kangaroo Mother Care as a substitute for traditional care. This approach is expected to be cost-effective and reduce neonatal mortality resulting from preterm birth complications.

Preterm and low-birth-weight infants contribute substantially to neonatal mortality in Pakistan, highlighting

the need for effective and feasible interventions in resource-limited settings; therefore, the present study evaluates the impact of Kangaroo Mother Care (KMC) on early neonatal mortality among preterm and low-birth-weight infants in a tertiary care hospital in Karachi, Sindh. Limited local evidence exists on the impact of Kangaroo Mother Care on early neonatal mortality among stable preterm and low-birth-weight infants in tertiary care hospitals in Karachi. This study aimed to contribute valuable insights to enhance neonatal outcomes in this at-risk population by assessing the efficacy of the Kangaroo Mother Care approach.

METHODS

This cross-sectional descriptive study was carried out in the Gynecology and Obstetrics Unit at Dr. Ruth K.M. Pfau Civil Hospital, Karachi, over six months from July 2021 to January 2022. Ethical approval was obtained from the research evaluation unit CPSP (Ref. No. CPSP/REU/OBG-2018-183-8765). Data collection involved enrolling eligible patients who were willing to participate in the study and were kept as inpatients. No additional intervention was introduced for research purposes, and all enrolled neonates received standard care as per hospital protocols. The number of participants was estimated using OpenEpi version 3.01 software. The calculation was based on the formula for estimating a single population proportion: $n = Z^2 \times p \times (1-p) / d^2$ Where n is the required sample size, Z is the standard normal deviate corresponding to the desired confidence interval (1.96 for 95% confidence interval), p is the estimated proportion of the population with the characteristics of interest (36% reduction in early neonatal mortality), and d is the margin of error (6.5%). Substituting these values yielded a sample size of 210 participants [12, 13]. Participants were selected using a non-probability consecutive sampling approach. Every eligible infant born within the study period was included in the sample. This study included premature and low birth weight infants delivered before 37 completed weeks of pregnancy or with a birthweight ranging between 1.5 to 2.5 kg, respectively, who demonstrated functional sucking ability or could breastfeed using a small cup. Parents consenting to participation were included in the study. Babies requiring transfer to the neonatal intensive care unit, those whose parents did not consent, and those who were lost to follow-up in the initial seven days after birth were excluded from the research. Kangaroo Mother Care (KMC) was defined as a care approach that aims to prevent complications such as hypothermia, infections, and prolonged hospitalizations in premature and underweight neonates. It involves three main components which include continuous or intermittent direct skin bonding linking the newborn with the caregiver, support for exclusive breastmilk feeding for

the newborn, and early discharge from the hospital to home once the baby is clinically stable. KMC can be commenced immediately after birth, and once the neonate is stable and no longer requires conventional care, and is advised to be continued until the newborn reaches 40 weeks of adjusted gestational age or attains a weight of 2.5 kilograms. Based on pre-defined criteria, the effects of KMC were classified as positive or negative. Improved breastfeeding, enhanced parent-infant bonding, physiological stability (stable temperature, heart rate, and respiration), and reduction in early neonatal mortality were counted as a positive effect whereas, excessive crying, skin irritation, difficulty in handling the neonate, or any deterioration in physiological parameters was counted as a negative effect. A self-constructed structured questionnaire was designed and used for data collection and included demographic information, clinical characteristics, KMC implementation, and neonatal outcomes. Infant and maternal details such as age, gender, birth weight, gestational age, and maternal parity, and KMC-related information such as duration of direct skin contact, compliance to the KMC protocol, breastfeeding practices, and any complications observed, and outcome measures including early neonatal mortality (within 7 days), weight gain at discharge, feeding ability, and any positive or negative effects observed during KMC were included in the questionnaire. The questionnaire was tested on a small sample to ensure it was clear and reliable and the data were subsequently collected by trained staff in order to maintain consistency and accuracy. This structured questionnaire was constructed specifically for this study following a review of relevant research on Kangaroo Mother Care and its impact on newborn outcomes in order to include all the relevant information that was required. Although formal assessment of reliability and validity, was not done, but the pre-testing and supervision of data collection by trained staff ensured that the questionnaire provided reliable and accurate data collection. 11 items were included in the questionnaire, covering demographic information, KMC implementation, and neonatal outcomes. Binary scale was used to score each item (Yes=1, No=0). Zero was taken as the lowest possible result was, and 11 was the highest possible result, with higher scores indicating more positive neonatal outcomes and better adherence to the KMC protocols. Pertinent literature on KMC and neonatal outcomes was reviewed and used as a guide in designing the questionnaire. A standardized 2-day training session was conducted by UNICEF to ensure that healthcare providers, parents and family members fully understand and followed the Kangaroo Mother Care (KMC) technique correctly. The principal investigator underwent a 2-day training session conducted by UNICEF to become a certified master trainer

and then subsequently this training was trickled down to the rest of the healthcare staff involved in patient care and in this study. A practical demonstration of the KMC technique was given to the parents and carers by trained staff. Detailed explanations, hands-on demonstrations, and practical guidelines for the correct technique were included in these trainings. During the inpatient period, the parents were supervised by the staff, to ensure the proper technique was followed, and to ensure consistency across all participants. Moreover, in order to ensure ongoing adherence to the KMC protocols and to maintain consistency across all participants, regular follow-up sessions were scheduled. Neonatal mortality is defined as the death of a live born infant, within the first 28 days of life. It can be further divided into early or late, which occurs within the first seven days of life, or between days 7 and 28 respectively. Prematurity is defined as birth before 37 completed weeks of gestation, whereas those who weigh under 2.5 kilograms (2500 grams) at birth are considered to have low birth weight. Early neonatal mortality (death within the first 7 days of life) was the primary outcome variable used to assess the effectiveness of the intervention. Secondary outcome variables included ability to feed, hospital stay period, and discharge weight gain. Parents and family members were educated on the three key elements of KMC which included skin-to-skin bonding, breastmilk feeding exclusively, and shortened hospital stay. Proper KMC techniques were demonstrated to all participants, and data was recorded through the self-constructed structured questionnaire. Patient confidentiality was maintained and contact details were kept confidential, and follow-up was scheduled either virtually via telephone or face-to face through an outpatient visit within the first week of life. Data were analyzed using SPSS version 21.0, with standard deviation and mean calculated for quantitative variables such as length of pregnancy, duration of hospital stay, and newborn birthweight, and frequencies and percentages for categorical variables such as gender and effects of KMC. Stratification was used to account for effect modifiers including gestational age, time spent in hospital, birth weight, and gender, and the Chi-square or Fisher exact test was applied post-stratification. A p-value of 0.05 or lower was interpreted as suggestive of statistical significance, and results with $p \leq 0.05$, denoting statistical significance, are marked with an asterisk (*) in tables and figures.

RESULTS

In this study, 210 participants were included to establish the impacts of Kangaroo Mother Care in the reduction of early neonatal death rate among premature and underweight babies. The demographics of the neonates and mothers were the maternal age, gestational age,

length of stay and birth weight where the means of the variables, standard deviations, confidence limits and ranges have been documented (Table 1).

Table 1: Descriptive Statistics (N=210)

Variables	Mean	SD	95% CI	Min	Max	Range
Age of mother (years)	26.99	4.3	26.40 – 27.57	18	40	22
Gestational Age (weeks)	34.8	3.6	34.31 – 35.28	30	36	6
Duration of Hospital Stay (weeks)	7.3	1.9	7.04 – 7.55	1	15	14
Birth Weight (kg)	2.21	0.37	2.18 – 2.29	1.55	2.40	0.85

The results were analyzed as follows: the age (mean $\pm$ standard deviation) of the mothers was 26.99 ± 4.3 years, with a confidence interval (C.I.) of 26.40 to 27.57 years. The gestational age (mean $\pm$ standard deviation) was 34.8 ± 3.6 weeks, with a C.I. of 34.31 to 35.28 weeks. The mean $\pm$ SD duration of hospital stays was 7.3 ± 1.9 days, with a C.I. of 7.04 to 7.55 days. The mean $\pm$ SD birth weight was 2.24 ± 0.37 kg, with a C.I. of 2.18 to 2.29 kg. Among the newborns, 57.6% (n = 121) were male and 42.4% (n = 89) were female (Figure 1).

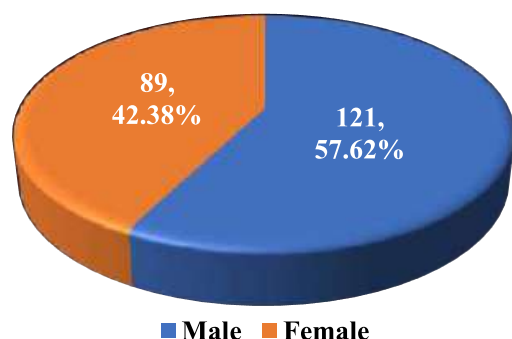


Figure 1: Distribution of Newborns by (N=210)

Regarding outcomes, 71.4% of infants showed a positive effect of Kangaroo Mother Care, while 28.6% exhibited no improvement (Figure 2).

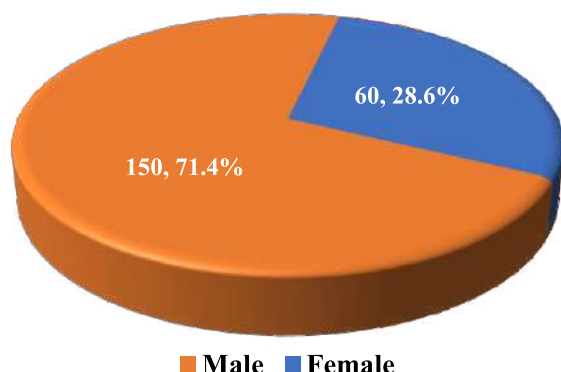


Figure 2: Distribution of Outcomes Following Kangaroo Mother Care (KMC) (N=210)

Kangaroo-mother care was determined to be successful in lowering early neonatal deaths in 60 (28.6%) participants, based on the structured 11-item questionnaire, where positive outcomes were recorded for infants showing

improved breastfeeding, stable temperature, weight gain, and survival at 7 days. Each item was scored as Yes = 1 or No = 0, and infants with positive scores on the relevant outcome measures were considered to have benefited from KMC. Stratification of factors such as the mother's age, gestational age, baby's gender, duration of hospital stays, and birth weight was performed to assess the statistical differences in relation to kangaroo-mother care. Chi-square or Fisher's exact tests were applied to assess the linkage between categorical variables and the effect of Kangaroo Mother Care, with statistically significant results indicated (Table 2).

Table 2: Stratification for Variables with Effects (N=210)

Variables	Category	Positive n (%)	Negative n (%)	p-value
Age of Mother (years)	18-30	47 (22.4%)	121 (57.6%)	0.703
	>30	13 (6.2%)	29 (13.8%)	
Gestational Age (weeks)	30-33	19 (9.0%)	33 (15.7%)	0.143
	>33	41 (19.5%)	117 (55.7%)	
Gender of Baby	Male	28 (13.3%)	93 (44.3%)	0.042*
	Female	32 (15.2%)	57 (27.1%)	
Duration of Hospital Stay	1-6	22 (10.5%)	109 (51.9%)	0.001*
	>6	38 (18.1%)	41 (19.5%)	
Birth Weight (kg)	1.5-2.0	24 (11.4%)	83 (39.5%)	0.045*
	>2.0	36 (17.1%)	67 (31.9%)	

*p $\leq$ 0.05, statistically significant

DISCUSSION

Our study had a mean maternal age of (26.99 $\pm$ 4.3) years comparable to the previous studies with mean ages ranging between 25-28 years, whereas our results indicated a 60 percent decrease in neonatal mortality with the use of Kangaroo Mother Care (KMC) as compared to a 40 percent decrease in the past studies, which could have been because of differences in the implementation strategies, the patient characteristics or the healthcare infrastructure [16]. In the same manner, a study that was carried out in COVID-19-positive mothers indicated that there was a considerable decrease in neonatal deaths, hypothermia, and severe infections, which further validated the effectiveness of KMC [17]. Maternal age (P=0.703) and gestational age (P=0.143) in our analysis had no significant relationship with the outcomes of the neonatal. The statistically significant relations were however found in birth weight (P=0.045), gender (P=0.042) and hospital stay duration (P=0.001). The difference in the resources available in healthcare, the availability of equipment, and quality of prenatal and postnatal care can be the reason behind the observed variation in the studies. The results of this tertiary care facility in Karachi also indicate the issues that can be typical of resource-constrained institutions. KMC has a wide range of physiological and psychological advantages, such as better

thermoregulation, increased cardiorespiratory stability, increased weight gain, reduced risk of infections, and increased maternal-infant bonding [18-20]. These results support KMC as an inexpensive, effective, and family-based intervention to premature and low birth weight babies. Multiple studies have also demonstrated that the constant contact with the skin will decrease levels of cortisol, normalize heart rates, and lead to better neurodevelopmental patterns in preterm infants [21]. The limitations of the current study are that pre-intervention values of neonatal parameters are not available and that confounding factors like maternal comorbid conditions, socioeconomic, and pregnancy related complications were not controlled and could have affected the outcomes. These areas should be covered in future studies in order to eliminate the independent effects of KMC.

CONCLUSIONS

The findings suggest that Kangaroo Mother Care was successful in lowering early neonatal fatalities. The impact of Kangaroo Mother Care in reducing early newborn mortality needs to be further evaluated and confirmed through comprehensive prospective cohort studies and randomized trials.

Authors' Contribution

Conceptualization: FNB

Methodology: ZK

Formal analysis: DESW, ZAP

Writing and Drafting: HMI, FNB, SS, AW

Review and Editing: HMI, FNB, ZK, DS, ZAP, SS, AW

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



The Functional Outcomes of Flexible Intramedullary Nails in the Management of Femoral Diaphyseal Fracture in Children

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ABSTRACT

About 20-25 children per 100,000 experience femoral shaft fractures annually. Intervention varied by age, type of fracture, and resources. Flexible intramedullary nailing (FIN) is a popular minimally invasive treatment of choice, allowing early mobility with the least complications.

Objectives: To evaluate the clinical effectiveness of using FIN for pediatric diaphyseal femur bone fracture treatment. **Methods:** This cross-sectional study was conducted at Ghurki Trust Teaching Hospital, Lahore, from February 2021 to August 2021, including 145 pediatric patients aged 5-12 years with closed femoral diaphyseal fractures treated with flexible intramedullary nailing (FIN). Patients with multiple fractures or metabolic bone diseases were excluded. Clinical assessments were carried out at the 3rd, 6th, 9th, and 12th postoperative weeks. Functional outcomes were examined using Flynn's criteria, and data were analyzed via SPSS version 22. **Results:** Out of the total 145 patients, 101 (69.4%) were male, while 44 (30.6%) were female. The mean age of the children was 8.32 ± 2.23 years. The time between injury and surgery was 4.27 ± 3.80 days in this study. According to Flynn's criteria, 133 (91.9%) of the patients had excellent outcomes (95% CI: 86.8% to 95.7%), while 12 (8.1%) had satisfactory outcomes at 12 weeks. No statistically significant associations were found between functional outcomes and demographic variables such as gender ($p=1.000$), age group ($p=0.360$), weight group ($p=0.323$), or fracture duration ($p=0.280$). **Conclusions:** FIN is a safe and effective treatment for pediatric femoral shaft fractures, which can help patients gain early functional recovery and reduce the risk of complications. It should be applied where necessary in clinical practice.

INTRODUCTION

Femoral shaft fractures represent one of the most frequent long-bone injuries in children since they affect 20-25 out of 100,000 children every year [1]. These bone fractures most commonly emerge from high-energy incidents, yet young children show evidence of fractures through lower-energy causes, too [2]. Physicians consider diverse factors like patient age, together with fracture configuration as well as any present injuries and societal circumstances, and operational surgical capabilities to determine the treatment strategy [3]. Traditional approaches to treating pediatric femoral fractures consist of four methods: spica casting, traction, external fixation,

and internal fixation techniques. Conservative care through hip spica casting benefits young children younger than five because their bones possess strong healing properties and remodelling capacity [4]. Spica casting entails various complications, including malunion together with joint stiffness and angulation, and limb length disparities that affect children's functional outcomes and reduce their quality of life during healing [5]. Open or severely comminuted fractures require external fixation as an alternative treatment, but users experience significant risks of pin tract infections as well as infection re-fractures along with patient discomfort [6]. Elastic Stable



Intramedullary Nailing (ESIN) now serves as the leading treatment option for femoral shaft fractures among children between 5 to 12 years of age. ESIN delivers minimally invasive stabilization that enables early mobility and smaller hospitalization times, and better outcomes than traditional non-operative treatment approaches [7]. The surgical method requires flexible intramedullary nails to be inserted from the metaphysis of the distal femur into the distal end thus providing three-point fixation and controlled bone movement, which enhances fracture healing [8]. Research demonstrates that ESIN stands as the recommended treatment option for transverse and short oblique fractures in growing patients because it upholds proper bone alignment without causing substantial effects on the developing joint area [9]. Research evidence indicates that ESIN shows outstanding results when treating pediatric femoral fractures. Tamrakar *et al.* documented that 80% of treated patients achieved excellent functional outcomes, yet 20% received satisfactory results as per Flynn's criteria [10]. ESIN provided superior treatment outcomes to spica casting since children experienced swifter recovery of function and reduced stay duration alongside accelerated return to regular activities, according to studies in reference [11]. ESIN provides various benefits, though it entails a range of complications in application. Problems within ESIN treatment frequently involve misalignment of leg positions either in a varus or valgus direction, as well as differences in limb lengths and implant wearer discomfort and hardware issues [12]. Current research in pediatric orthopedic surgery focuses on developing ESIN techniques to reduce surgery-related issues. The success of ESIN relies upon three key factors, which include selecting the right nail size and determining a precise entry point assisted by intraoperative fluoroscopy [13]. The use of ESIN produces better lasting functional results than plating when combined with less tissue damage and intact periosteal layers that naturally repair the structure [14].

The evidence behind ESIN continues to expand, but local researchers have yet to establish thorough assessments of its functional performance in treating pediatric femoral diaphyseal fractures. This research investigates the functional outcomes of ESIN for femoral shaft fractures in children by applying Flynn's criteria. The outcomes of treated patients will be evaluated for fracture healing duration and functional mobility, and complication incidence to provide valuable knowledge about ESIN suitability in pediatric care. This study aims to evaluate the clinical effectiveness of using FIN for pediatric diaphyseal femur bone fracture treatment.

METHODS

This cross-sectional study was conducted at Ghurki Trust Teaching Hospital, Lahore, from February 2021 to August 2021. Ethical approval was obtained (Ref. No. 1038/ERC/GTTH) from the institutional review board of Ghurki Trust Teaching Hospital, Lahore. Participants were included in the research after they provided their informed consent. A total of 145 patients (aged between 5 and to 12 years) with closed diaphyseal femoral fractures according to AO pediatric comprehensive classification of long bone fracture (AO-PCCF) as 32-D/4.1 (simple transverse) and 32-D/5.1 (simple short oblique) were included. Patients were excluded from the research if they had open fractures or underwent complex injuries with multiple closed lower limb fractures, or possessed metabolic bone disorders or pathological fractures. Two flexible intramedullary nails were surgically inserted in a retrograde direction following general anesthesia while performing the procedure in a supine position. No fracture table was used. Each patient received their prophylactic antibiotic medication based on their individual body weight. A priori sample size calculation was performed using G*Power software (version 3.1). For a Chi-square test, with an effect size (w) of 0.3 (medium), an alpha error probability of 0.05, and power ($1-\beta$) of 80%, the minimum total sample size required was 120. To account for potential dropouts, we aimed to enroll 150 patients. A total of 145 patients who met the inclusion criteria were finally enrolled during the study period. All patients received immobilization in an above-knee posterior slab after the surgeons used fluoroscopic guidance to perform the reduction. Physiotherapy professionals supervised our patient with strengthening exercises for the quadriceps, along with knee/hip motion exercises. The first-day postoperative evaluations included X-ray examinations to check the alignment and placement of nails. The rehabilitation program started with non-weight-bearing crutch walking either on the first or second day, based on the patient's pain level. The subjects received follow-up examinations at weeks 3, 6, 9, and 12 after their operations. Flynn's criteria for titanium elastic nail (TEN) outcome served as the assessment tool for functional results. The preoperative assessment of each participant included planning their medical background alongside pain symptom monitoring, in addition to X-ray imaging of the fracture. The assessment of patient muscle strength, together with neurological tests and lower limb function, helped determine eligibility for this surgical procedure before surgery. Clinical evaluations of patients occurred at pre-determined times of 3 weeks, followed by 6 weeks and 9 weeks, and finishing with 12 weeks. Follow-up evaluations evaluated both outcomes, including the pain levels through examination and recorded changes in

movement and function, together with detected surgical complications. The researchers used descriptive statistics to present patient demographic information along with their age group and gender identities, as well as their weight measurements and time since the fracture occurred. IBM-SPSS version 22 served to evaluate the functional outcomes. The report used frequencies with percentages for categorical data, which included gender and functional outcome categories, while it analyzed numerical data such as age and weight through means and standard deviations. To determine the association between different variables and functional outcomes, chi-square test was utilized, with p-value of $p \leq 0.05$ considered statistically significant.

RESULTS

The results were collected for a total of 145 patients. The research participants had an average age of 8.32 ± 2.23 years within an age range between 5 to 12 years. One hundred one of the subjects were male participants (69.4%) while 44 participants were female (30.6%). These patients underwent treatment after their fractures healed for an average of 4.27 ± 3.80 days within a 1-to-18-day period. The average weight in kg was 23.69 ± 5.09 (Table 1).

Table 1: Baseline Characteristics of the Study Population

Variables	Frequency/Mean $\pm$ SD
Number of Patients	145
Age (years)	8.32 ± 2.23
Gender (Male/Female)	101 (69.4%) / 44 (30.6%)
Weight (kg)	23.69 ± 5.09
Duration of Fracture (days)	4.27 ± 3.80

Postoperative functional outcomes were assessed at 12 weeks using Flynn's criteria. The results indicated that 91.9% (133 patients) achieved an excellent outcome (95% CI: 86.8% to 95.7%), while 8.1% (12 patients) had a satisfactory outcome. No patient experienced poor outcomes (Table 2).

Table 2: Functional Outcome According to Flynn's Criteria

Variables	Frequency/Mean $\pm$ SD
Excellent	133 (91.9%)
Satisfactory	12 (8.1%)

Flynn's criteria outcomes were further analyzed based on gender, age, weight, and fracture duration. As shown in Table 3, no statistically significant associations were found with gender ($p=1.000$), age group ($p=0.360$), weight group ($p=0.323$), or fracture duration ($p=0.280$). (Table 3).

Table 3: Stratification of Functional Outcome Based on Different Variables

Categories	Excellent (%)	Satisfactory (%)	p-value
Male (n=101)	92 (90.7%)	9 (9.3%)	1.000

Female (n=44)	42 (94.7%)	2 (5.3%)	
5-8 (n=77)	68 (87.9%)	9 (12.1%)	0.360
9-12 (n=68)	66 (96.6%)	2 (3.4%)	
10-20 (n=35)	35 (100%)	0 (0%)	0.323
21-32 (n=110)	98 (89.4%)	12 (10.6%)	
1-6 (n=115)	108 (93.9%)	7 (6.1%)	0.280
7-18 (n=30)	25 (84.6%)	5 (15.4%)	

The patients recovered without encountering major postoperative medical issues. The nail insertion site caused brief pain for 4 patients (6.5%), but the symptoms disappeared within weeks. The study demonstrated no instances of infection, together with the absence of deep vein thrombosis and neurovascular injury.

DISCUSSIONS

Pediatric femoral shaft fractures commonly occur, and orthopedic specialists have developed several treatment approaches over the past years. Flexible intramedullary nailing (FIN) has become more popular because it offers minimally invasive procedures and achieves favorable results according to the prior study [8]. The authors researched to evaluate the functional results obtained from flexible intramedullary nails used to treat femoral diaphyseal fractures by applying Flynn's criteria as assessment measures. The patient sample consisted mainly of males who averaged 8.32 years in age among 145 participants. The research showed that flexible intramedullary nails delivered excellent functional results in 91.9% of patients, yet produced satisfactory results in 8.1% of cases. Similarly, another study found 80% excellent outcomes, besides a 20% satisfactory outcome through their equivalent investigation methods [10]. A previous study done in the year 2023 described that adequate axial and rotational stability from FIN treatment plays a key role in achieving success because it supports early mobilization and rapid healing without serious complications [15]. A meta-analysis was done in 2023 demonstrating superior treatment effectiveness based on its comparison against spica casting and external fixation methods for orthopedic care. Young children received spica casting in the past, but this treatment method caused malunion while delaying functional recovery, together with joint stiffness [16]. Another study identified that external fixation provides effective results in specific cases but comes with risks that involve pin tract infections and re-fractures, and prolonged periods of immobilization [17]. Early weight-bearing becomes possible with the FIN system while maintaining proper fracture stability, according to studies conducted by a prior study [18]. The current study established that demographic variables, including age, gender, weight, and fracture duration, were insignificantly associated with functional results ($p > 0.05$) [19]. This suggests that, within the studied population, the high success rate of FIN may be

consistent across different demographic subgroups. The influence of these specific factors on functional outcomes after FIN for femoral fractures has not been extensively detailed in existing literature, and our findings provide a baseline for future investigation. Moreover, the current study reported that no cases of infection, DVT, or neurovascular injury. This finding aligned with a previous case report, which states that none of the patients developed serious complications and also maintained good recovery and greater union rates with an acceptable rate of minor complications[20]. The evaluation of flexible intramedullary nailing requires additional patient-based outcome assessments combined with comparative studies of alternative treatment types to achieve a full evaluation. The treatment effect of flexible intramedullary nailing would benefit from more research into biomechanics along with improved surgical techniques. The study faces restrictions from a limited participant group, and a 12-week follow-up was sufficient for assessing early healing and mobilization; however, it was too short to evaluate long-term complications such as malunion and leg length discrepancy. Further examinations should utilize extensive follow-up phases and multiple research facilities for assessing prolonged treatment outcomes within larger-scale research.

CONCLUSIONS

Flexible intramedullary nailing (FIN) is considered a safe and effective procedure for managing femoral diaphyseal fractures in children aged 5-12 years, as it allows early mobilization, improves functional recovery, and is also associated with minimal complications. However, its application must be individualized, as spica casting is preferred in children under 5 years of age, and rigid trochanteric entry nailing might be suitable in adolescents (near to skeletal maturity). Furthermore, a longer follow-up is needed to investigate the potential late complications, including leg length discrepancy and malunion.

Authors' Contribution

Conceptualization: MA

Methodology: RA, MA, WA, IU

Formal analysis: RA, FS, IU

Writing and Drafting: MA, WA, FS, SA

Review and Editing: RA, MA, WA, FS, SA, IU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Brain Drain Perception Between Medical and Non-Medical Undergraduate Students in Lahore

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ABSTRACT

Brain drain is a serious issue for developing countries like Pakistan. Economic, political, and social determinants influence undergraduate students' intention to migrate. **Objectives:** To evaluate the perceptions and trends that would determine the intention of brain drain among medical and non-medical undergraduate students in Lahore. **Methods:** A stratified sampling strategy selected 300 participants from both medical and non-medical programmes. This cross-sectional study was carried out through a properly structured questionnaire from October 2024 to March 2025. Data were entered and analyzed using SPSS V-26; the Chi-square test and Cramer's V were applied for group comparisons. **Results:** A total of 300 undergraduates participated (47% male, 53% female; mean age 20.0 ± 1.4 years), with most in first (48.0%) or second year (29.7%). In general, 83.3% expressed willingness to migrate for foreign employment, while 90.3% cited poor working conditions and 76.7% long working hours as push forces. Employment safety abroad was perceived as better by 91.7% of respondents. Two significant discipline-based associations were observed: political instability was more frequently reported by non-medical students than medical students (16.7% vs. 5.3%, $p=0.003$, Cramer's $V = 0.17$), and lifestyle/safety concerns were also more common among non-medical students (31.3% vs. 20.7%, $p=0.03$, Cramer's $V = 0.13$). **Conclusions:** Brain drain intentions among medical and non-medical undergraduates are substantial overall, driven by workplace environment, as well as socio-economic factors. These systemic problems have to be resolved to ensure that skilled youth are retained.

INTRODUCTION

Brain drains, the movement of highly skilled people in search of better opportunities outside their home country [1]. It presents a great challenge to developing nations, and Pakistan is one of them. Undergraduate students represent the future professional workforce, and their aspirations are strongly shaped by economic, political, and social factors. Since they are at the beginning of their career paths, their perceptions and intentions provide an early indication of future brain drain trends [2]. It is important to understand the perception of these students towards brain drain for drawing policy measures to retain talent and create better conditions within the country.

According to recent studies, one of the leading causes of brain drain has been the desire by individuals to have a more favorable socio-economic setting. Pointing out the internationalization aspect of higher education, Alam et al. signify that such practice causes the outflow of talents, leaving their home countries vulnerable to a massive shortage of intellectual capital [3]. On the same note, Meo et al. argue that the lack of political and economic stability contributes to increasing the number of highly skilled professionals who fly out, even to the healthcare sector [4]. In this respect, undergraduate students may be especially vulnerable to these areas, because their career and



educational choices may usually depend on their beliefs of security and opportunity [5]. It is worthwhile giving more attention to the specific effect of the socio-economic situation on the intentions to brain drain among students. Nadir et al. found in a study that 72% of medical students expressed willingness to migrate after graduation due to socio-medical concerns [6]. More so, Kousar et al. assume that insufficient openings in the Pakistani job market force graduates to work in another country; therefore, there will always be a brain drain of educated people [7]. This is reiterated by the research, which pinpoints threats to human security as being one of the aggravating factors that give birth to brain drain [8]. The impact of brain drain varies across disciplines, influencing student migration intentions in distinct ways. For instance, 66.3% of nursing undergraduate students aspire to work internationally [9]. This pattern has a larger implication, as it indicates the gaps in educational and career structure with systematic issues like economic instability, limited institutional support, and political uncertainty, driving students to seek opportunities abroad [10]. Consequently, there is a need to eliminate the causes underlying brain drain, whose source factors include economic fluctuations, poor institutional support, and political instability, which influence student decisions negatively [11, 12]. Understanding the perceptions and attitudes of the undergraduate students towards the brain drain is important in coming up with specific measures to help the skilled graduates stay back. Determining the economic, social, and professional factors that affect their intentions to migrate can be used to influence policymakers to set up strategies that help in improving the job climate in their country, better career options, and lessen the drain of skilled personnel to foreign nations.

Understanding undergraduate students' perceptions of brain drain is essential to inform policies aimed at retaining future skilled professionals in Pakistan. Limited comparative evidence exists on differences in brain drain perceptions between medical and non-medical undergraduate students in Lahore. This study aimed to compare the perceptions of brain drain between medical and non-medical undergraduate students in Lahore, in order to identify discipline-specific differences and the factors influencing their views on migration.

METHODS

A quantitative, cross-sectional comparative design was used with a structured, closed-ended questionnaire. The duration of the study was six months from October 2024 to March 2025. The aim was to compare the perception and attitude to brain drain in medical and non-medical undergraduate students in Lahore, Pakistan. The study group included undergraduate students pursuing medical

and non-medical degrees (MBBS, BDS, Pharm-D, Allied Health Sciences) and non-medical (e.g., Computer Science, Aviation, Fashion Designing, Business Administration) in different departments of the University of Lahore. Participation was voluntary, anonymity was maintained, and no identifying information was recorded to ensure confidentiality. The Ethical Review Board of University College of Medicine and Dentistry, University of Lahore (No. ERC/52/24/09) gave the ethical clearance. Data collection was carried out in person by the principal investigator, who visited each participating department. The researchers personally visited classrooms and common student areas to distribute and collect self-administered questionnaires. The eligible students were first-year through final-year students. It was determined that the sample size was to be calculated by the following formula: $n = Z^2 \cdot p(1-p) / d^2$. Where: $Z = 1.96$, $Z = 1.96$, $Z = 1.96$ at 95% confidence level, $d = 0.05$, $d = 0.05$, $d = 0.05$ margin of error and $p = 0.78$ [10]. This gave a minimum required sample of 264 subjects. The provision of sample size was increased to 300 individuals (150 medical students and 150 non-medical students) to account for possible non-response and incomplete questionnaires. Stratified random sampling was used to ensure representation of the medical and non-medical groups. In each stratum, the students were randomly approached in between normal academic activities, and every n th student (systematic approach) who gave their consent was invited to take part until the target sample was reached. Students who are already living in foreign countries through scholarship programs were excluded from the study. The research survey was done using a structured, self-administered questionnaire, which had been designed specifically after scrutiny of the related literature on migration intentions and student perceptions. It was divided into two parts: the demographic (age, gender, and academic degree program) and the issues concerning migration intentions, reasons to leave, and perceived push and pull factors. Expert review was used to establish content validity, where three senior faculty members in the field of public health and medical education were involved. To ensure that the items were equally appropriate and understandable for non-medical undergraduate students, one faculty member from the Faculty of Social Sciences was later consulted. Refinement of uncertain items was done based on their feedback to make them clear and relevant. A pilot test was done with 20 students (who were not in the main study) before the data collection, and the questionnaire proved to be acceptable in terms of internal consistency, with a Cronbach's alpha of 0.78. The answers were mainly categorical (i.e., Yes/No or Agree/Disagree) and were coded in numeric form to undergo statistical analysis (Yes = 1, No = 0). In the case of multiple-choice questions, the best answer was obtained.

There were no composite scores, although the data were analyzed as individual items. To conduct this study, the operational definition of migration intention was the desire of a student to leave Pakistan to undertake postgraduate studies or seek jobs. The poor working conditions, political instability, long working hours, and the perception that it is better and safer in other countries were the predisposing factors of brain drain, and the preventive factors were the freelancing opportunities and supportive jobs in Pakistan that might have discouraged migrating. The Statistical Package of Social Sciences (SPSS) version 26.0 was used to analyze data. The Shapiro-Wilk test was used to examine the normalcy of continuous variables. The variables that were normally distributed were summarized by the value of mean with SD, whereas the non-normally distributed variables were summarized by the value of median with SD. Categorical variables were in the form of frequency (percentage). In the case of the group comparisons, the Chi-square test of independence was used, and the extent of the association was presented as the Cramer V. All proportions were given a 95% confidence interval (CI). A p-value of less than 0.05 was taken as significant.

RESULTS

There were 300 respondents; 141 (47.0%) men and 159 (53.0%) women. Most of them were in the first year (48.0%), second year (29.7%), third year (19.7%), and only a small proportion of them were in the fourth (2.0%) and fifth year (0.7%). The mean age of participants was 20.0 ± 1.4 years (range: 17–24 years). The Shapiro-Wilk test indicated that age was not normally distributed, $W(300) = 0.946$, $p < 0.001$. Therefore, both mean $\pm$ SD and median (IQR) are reported, with a median age of 20 years (IQR: 19–21) presented in table 1.

considerations have a stronger influence on determining the migration intentions of non-medical students, but medical students seem to have a more consistent motivation to migrate to foreign countries because of the professional opportunities that they have there, as shown in table 2.

Table 2: Migration Intentions and Perceptions among Medical and Non-Medical Students (n=300)

Variables	Medical (n=150)	Non-Medical (n=150)	Total (n=300)	χ^2 (p-value)	Cramer's V
Perceive the Scope in Pakistan	87 (58.0%)	96 (64.0%)	183 (61.0%, 95% CI: 55.3–66.5)	1.01 (0.32)	0.06
Willing to Leave for Foreign Employment	126 (84.0%)	124 (82.7%)	250 (83.3%, 95% CI: 78.7–87.2)	0.09 (0.76)	0.02
Poor Working Conditions Drive Brain Drain	139 (92.7%)	132 (88.0%)	271 (90.3%, 95% CI: 86.5–93.1)	2.10 (0.15)	0.08
Long/Exhausting Working Hours as a Factor	115 (76.7%)	115 (76.7%)	230 (76.7%, 95% CI: 71.5–81.2)	0.00 (1.00)	0.00
Prefer a Side Business With a Degree	94 (62.7%)	96 (64.0%)	190 (63.3%, 95% CI: 57.7–68.5)	0.04 (0.83)	0.01
Believe Employment Safety is Better Abroad	138 (92.0%)	137 (91.3%)	275 (91.7%, 95% CI: 87.8–94.6)	0.05 (0.82)	0.01
Reason for Working Abroad – Good Environment	100 (66.7%)	115 (76.5%)	215 (71.6%, 95% CI: 66.4–76.3)	3.37 (0.07)	0.11
Would Still Leave Under Better Work Conditions	89 (59.3%)	81 (54.0%)	170 (56.7%, 95% CI: 51.0–62.3)	0.84 (0.36)	0.05
Supportive Jobs Prevent Leaving	91 (60.7%)	83 (55.3%)	174 (58.0%, 95% CI: 52.3–63.5)	0.83 (0.36)	0.05
Reason for Leaving – Political Instability	8 (5.3%)	25 (16.7%)	33 (11.0%, 95% CI: 7.7–15.3)	9.13 (0.003)*	0.17
Reason for Leaving – Better Lifestyle & Safety	31 (20.7%)	47 (31.3%)	78 (26.0%, 95% CI: 21.1–31.5)	4.70 (0.03)*	0.13
Freelancing Prevents Leaving	76 (50.7%)	74 (49.3%)	150 (50.0%, 95% CI: 44.3–55.7)	0.05 (0.82)	0.01

*Significant at $p < 0.05$.

Table 1: Demographic Characteristics of Study Participants (n=300)

Characteristic	Frequency (%)
Gender	
Male	141 (47.0%)
Female	159 (53.0%)
Year of Study	
1 st Year (1 st –2 nd Sem)	144 (48.0%)
2 nd Year (3 rd –4 th Sem)	89 (29.7%)
3 rd Year (5 th –6 th Sem)	59 (19.7%)
4 th Year (7 th –8 th Sem)	6 (2.0%)
5 th Year	2 (0.7%)
Age (Years)	
Mean $\pm$ SD	20.0 ± 1.4
Median (IQR)	20 (19–21)*

*Normality assessed using the Shapiro-Wilk test: $W(300) = 0.946$, $p < 0.001$.

The study shows the difference in the migration perceptions and intentions of medical and non-medical students. Generally, no significant differences were found between the two groups on their intentions to emigrate to foreign jobs, their view on bad working conditions in Pakistan, tiring working hours, or even their safety in foreign working jobs (all $p > 0.05$). However, two significant associations were observed. Political instability was more frequently reported as a reason for leaving among non-medical students compared to medical students (16.7% vs. 5.3%), $\chi^2(1, N = 300) = 9.13$, $p = 0.003$, Cramer's V = 0.17. Similarly, lifestyle and safety concerns were more commonly cited by non-medical students (31.3% vs. 20.7%), $\chi^2(1, N = 300) = 4.70$, $p = 0.03$, Cramer's V = 0.13. These results indicate that, although the overall migration intentions seem to be fairly similar across academic backgrounds, political instability and lifestyle

DISCUSSIONS

Undergraduate brain drain in Lahore is a significant concern, considering its impact on personal ambition and socio-economic situation in Pakistan. Brain drain, defined as the emigration of skilled individuals from one country to another, is influenced by various factors, particularly working conditions and educational opportunities [13]. This discussion presents the synthesis of results of the latest investigations on the migration attitudes of students with a focus on the downtrodden local working environment and the charm of global opportunities. The study reveals that the gender distribution of the undergraduates in the survey is characterized by a significant number of female respondents (53%) relative to the male ones (47%). This observation demonstrates that women are becoming more active and needing higher education despite socioeconomic hardships and limiting social norms [14]. Most undergraduates were ready to go abroad to work, with 83.33% showing their willingness to abandon local employment opportunities, which translates to an increasing trend amongst Pakistani youth and especially women with intentions to seek foreign opportunities [15]. Perceptions of the local working conditions are also a critical factor in shaping migration intentions. Upon sampling the students, most of them, i.e., 90.3% of the total number of sampled students, identified poor working conditions as a major factor that would make them contemplate migration; 76.7% of the students identified long work hours as a reason [16]. These sentiments are associated with poor local environments act as major push factors in motivating students to pursue opportunities in countries that have better work environments [17]. With the improvement of local conditions, a significant % age (56.7%) of students even now remain willing to leave, which means that decisions on the issue of migration are in many cases made not only based on the existing situation but also with reference to long-term intentions of a higher quality of living [18]. The family structure also engages in matters of influences migration intentions. A significant (78%) proportion of respondents belong to nuclear families; similarly, the numbers are larger in medical students (84%) than in non-medical students (72%) [19]. Family influence in career aspirations implies that family context can be used to inform the move to pursue opportunities in foreign countries, as imminently resembled in other studies, which point out that the family plays a major role in determining the career choices and migration intentions of students [20]. Job security abroad is viewed positively by 91.7% of respondents, reflecting a sharp contrast with the instability of Pakistan's domestic labor market. This perception reinforces migration intentions, as many

students feel that sustainable income and career growth are more attainable overseas [21]. The fact that personal ambitions on the level of safety and professional growth overlap means the brain drain remains a highly complex phenomenon that expresses that migration is not a trade but frequently a need pursued by young people and focused on achieving a better future. The findings indicate that there is a high level of brain drain intentions among the Lahore undergraduate students, largely driven by poor local job conditions. The sentiments enable this great readiness to migrate because students are faced with the reality of the future of their disciplines in Pakistan. Brain drain has more implications than the personal dream of an individual, and possibly, there is a risk to the future of the country because it may lose the necessary skills and human capital needed for the development of the country. Gender relations, family background, and the situation in the region of work become the critical points in this persistent challenge.

The cross-sectional design limits causal inference between identified factors and migration intentions, while reliance on self-reported data may introduce response and social desirability bias. Additionally, conducting the study within a single private university may limit the generalizability of findings to other institutions or regions of Pakistan. Future multicenter longitudinal studies involving public and private universities are recommended to enhance representativeness and explore changes in migration intentions over time.

CONCLUSIONS

In conclusion, this study emphasizes that the perceptions of brain drain are common among the medical and non-medical undergraduates in Lahore, where poor working conditions, extensive working hours, and socio-economic instability are the most influential factors. Non-medical students were more likely to mention political instability and lifestyle issues as their motives to migrate. So, it is necessary to systematically address these issues in Pakistan to retain talented youth in the country.

Authors' Contribution

Conceptualization: AR

Methodology: MHT, MMA, MMI, MHA, MIB

Formal analysis: MMI

Writing and Drafting: AR, MMA

Review and Editing: AR, MHT, MMA, MMI, MHA, MIB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



A Comparative Analysis of Hypocalcemia Incidence in Patients Undergoing Thyroidectomy: LigaSure Versus Conventional Ligation of Vessels by Knot Tying

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ABSTRACT

Hypocalcemia is a frequent postoperative complication after total thyroidectomy. It usually arises from unintentional injury to the parathyroid glands or disruption of their blood supply during surgery. Advanced vessel sealing technologies like LigaSure aim to lower this risk by ensuring greater surgical precision and reducing thermal injury to adjacent structures, particularly the parathyroid glands. **Objectives:** To compare the incidence of postoperative hypocalcemia between LigaSure and conventional knot-tying techniques in total thyroidectomy patients. **Methods:** A randomized controlled trial was conducted at the Surgical Department of Gulab Devi Hospital, Lahore, from April 2024 to March 2025. Seventy-six patients who underwent total thyroidectomy for benign thyroid disease were randomly allocated to the LigaSure (n=38) and conventional knot-tying (n=38) groups. Serum calcium levels were measured preoperatively and at 24/48 hours postoperatively. For statistical analysis, SPSS v24 was used, and non-parametric tests like the Mann-Whitney U and chi-square tests were used. **Results:** Incidence of hypocalcemia was higher in the LigaSure group (10.5%) as compared to the conventional group (7.9%), but of no statistical significance (p=0.692). **Conclusions:** Both techniques demonstrated comparable safety profiles with no statistically significant differences in postoperative outcomes. LigaSure offers a comparable alternative to conventional methods of vessel sealing/ligation.

INTRODUCTION

Thyroidectomy is the surgical removal of all or part of the thyroid gland, which is located in the front of the neck. Depending on how much thyroid tissue is removed, thyroidectomy could be classified into Total thyroidectomy, subtotal thyroidectomy, near total thyroidectomy and lobectomy. Thyroidectomy is a routinely performed operation for managing various thyroid disorders, both benign and malignant. Conditions such as multinodular goitre, Graves' disease, and thyroid tumors often require surgical intervention [1]. Complications of thyroidectomy include hoarseness or

change in voice (33.3%), damage to parathyroid glands causing hypocalcaemia (54.4%), wound infection (3.4%), dysphagia (32.8%). Several risk factors may contribute to the occurrence of post-thyroidectomy complications, including age, gender, enlarged gland size, type of thyroid disease, presence of fibrosis and inflammation, extent of thyroidectomy, and lymph node dissection. Among these complications, hypocalcaemia and recurrent laryngeal nerve injury are the most frequently observed [2, 3]. This calcium imbalance typically arises from inadvertent injury, disruption of blood supply, or accidental excision of the



parathyroid glands, which are essential for regulating calcium levels in the body through parathyroid hormone (PTH) secretion [4, 5]. Reported rates of transient hypocalcemia following thyroid surgery vary considerably, with literature citing figures from 20% to 60%. In contrast, permanent hypocalcemia is less common but more impactful [6]. Symptoms can range from mild tingling and muscle cramps to severe manifestations such as seizures or laryngospasm, which may prolong hospitalization and delay recovery. Several factors influence the risk of this complication, including the surgical method, extent of gland removal, the presence of lymph node dissection, and the surgeon's experience [7]. To mitigate these risks, technological advancements have led to the introduction of energy-based hemostatic devices. Among them, LigaSure, a bipolar vessel sealing system, has gained traction for its ability to provide precise vessel control with limited lateral heat dispersion. This minimizes inadvertent damage to adjacent structures like the parathyroid glands and recurrent laryngeal nerves. In addition to improving intraoperative safety, LigaSure may also reduce operative time and blood loss when compared to traditional knot-tying techniques involving sutures and artery forceps. Post-thyroidectomy hypocalcaemia remains a common and clinically significant complication, necessitating evaluation of surgical techniques that may reduce its incidence. Limited local evidence exists comparing LigaSure with the conventional knot-tying technique regarding hypocalcaemia rates and perioperative outcomes after total thyroidectomy. This study aims to evaluate the incidence of hypocalcemia in patients undergoing total thyroidectomy using either LigaSure or the conventional knot-tying technique. Additionally, operative duration, intraoperative blood loss, and length of hospital stay were assessed to provide a broader perspective on the comparative effectiveness of the two methods.

METHODS

This study was a randomized controlled trial (RCT No. NCT06716632) carried out in the Department of Surgery at Gulab Devi Hospital, Lahore, from July 2024 to January 2025. Ethical approval was obtained from the Institutional Review Board (Approval No: AAMC/IRB/EA 41 2024). A total of 76 patients who were scheduled were recruited after obtaining written informed consent to undergo total thyroidectomy for benign thyroid disorders based on biochemical, radiological and cytological investigations. Neck dissection was not performed in any patient. Sample size calculation was performed using the WHO sample size calculator, incorporating a 95% confidence level, 5% margin of error, and 90% statistical power. The estimates were based on previously published data indicating

hypocalcemia rates of 6.7% in LigaSure procedures and 32.4% in those performed with conventional techniques [8]. This yielded a required sample of 76 participants, with 38 in each group who underwent total thyroidectomy. Participants were divided into two equal groups using a lottery-based randomization technique. During total thyroidectomy, a collar incision was given on the skin, subcutaneous tissue and platysma was dissected, strap muscles of the neck were retracted to expose the thyroid gland, superior and inferior thyroid veins were ligated or sealed, superior and inferior thyroid arteries were carefully ligated or sealed and divided near the gland after identifying recurrent laryngeal nerve, both of the lobes of thyroid gland along with the isthmus was removed after identifying and preserving parathyroid glands, no neck dissection was done, than hemostasis was secured and layers were closed in reverse order using sutures. In Group A, vessel sealing was performed using the LigaSure™ Precise device (Medtronic) that involved isolating the target vessel, positioning it between the device jaws, activating bipolar energy to create a secure seal, and dividing the vessel using the built-in cutter or another instrument. At the same time, Group B underwent conventional ligation using 3-0 Vicryl sutures. The same team of experienced surgeons performed all surgeries to ensure consistency in technique and minimize operator-dependent variability. Patients requiring neck dissection or those with malignant/recurrent thyroid disease, retrosternal goiter, preoperative hypocalcemia, low vitamin D levels, abnormal PTH levels or who were already on calcium or vitamin D supplementation were excluded from the study. The primary endpoint was the occurrence of postoperative hypocalcemia, which was defined as a serum calcium level of less than 8.0 mg/dL, assessed at both 24 and 48 hours following surgery. Additional outcomes observed included the total operative time, volume of intraoperative blood loss, duration of hospital stay, and any complications such as wound infection, voice changes, or bleeding. All data were captured using a standardized proforma. Quantitative variables such as patient age, serum calcium levels, and operative time were analyzed using the Mann-Whitney U test due to their non-parametric distribution. Categorical variables, including gender, incidence of hypocalcemia, and occurrence of complications, were assessed using either the Chi-square test or Fisher's exact test, where appropriate. Statistical analysis was conducted using SPSS version 24, with significance defined as $p < 0.05$ (Figure 1).

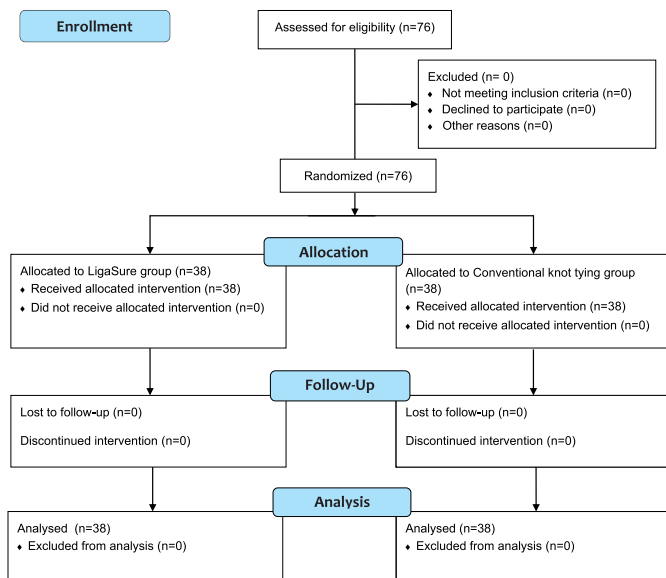


Figure 1: Consort Flow Diagram of Patient Recruitment and Allocation

RESULTS

A total of 76 patients were included in the study, with 38 patients in each group. In the LigaSure group, 4 patients (10.5%) developed hypocalcemia, compared to 3 patients (7.9%) in the conventional group. The difference was not statistically significant ($p=0.692$). A Chi-square test of association showed no statistically significant difference in hypocalcemia rates between the LigaSure and conventional knot-tying groups, $\chi^2(1) = 0.157$, $p=0.692$. Due to low expected cell counts, Fisher's exact test was applied and confirmed the result ($p=1.000$) (Table 1).

Table 1: Frequency of Hypocalcaemia in Each Group

Treatment Group	Hypocalcemia No	Hypocalcemia Yes	Total
Conventional Knot Tying	35 (92.1%)	3 (7.9%)	38
Ligasure	34 (89.5%)	4 (10.5%)	38
Total	69 (90.8%)	7 (9.2%)	76

The mean serum calcium levels at 24 hours postoperatively were 8.51 ± 0.21 mg/dL in the conventional group and 8.41 ± 0.28 mg/dL in the LigaSure group. At 48 hours, they were 8.49 ± 0.29 mg/dL and 8.47 ± 0.27 mg/dL, respectively. In addition, the mean operative time was 109.34 ± 24.88 minutes in the conventional group and 100.0 ± 24.82 minutes in the LigaSure group ($p = 0.106$). Median intraoperative blood loss was 92.37 ± 45.46 ml in the conventional group and 91.58 ± 36.13 ml in the LigaSure group ($p = 0.933$). Hospital stay was 5.18 ± 1.33 days in the conventional group and 5.0 ± 0.61 days in the LigaSure group ($p = 0.443$). No significant postoperative complications were noted in either group (Table 2).

Table 2: Postoperative Calcium Levels and Secondary Outcomes

Variables	Conventional Knot Tying (Mean $\pm$ SD)	LigaSure (Mean $\pm$ SD)	p-value
Time Postop			
24 Hours	8.51 ± 0.21 mg/dL	8.41 ± 0.28 mg/dL	0.106
48 Hours	8.49 ± 0.29 mg/dL	8.47 ± 0.27 mg/dL	0.411
Secondary Outcomes			
Intraoperative Blood Loss	92.37 ± 45.46 ml	91.58 ± 36.13 ml	0.933
Operative Time	109.34 ± 24.88 min	100.0 ± 24.82 min	0.106
Hospital Stay	5.18 ± 1.33 days	5.0 ± 0.61 days	0.443

The mean age in the conventional group was 39.29 ± 8.64 years, while in the LigaSure group it was 37.89 ± 8.14 years ($p=0.471$). There were 20 (52.6%) males and 18 (47.4%) females in the conventional group and 16 (42.1%) males and 22 (57.9%) females in the LigaSure group (Table 3).

Table 3: Age and Gender Distribution of Patients

Treatment Groups	Gender	n (%)	Age (Years) (Mean $\pm$ SD)
Conventional Knot Tying	Male	20 (52.6%)	39.29 ± 8.64 Years
	Female	18 (47.4%)	
Ligasure	Male	16 (42.1%)	37.89 ± 8.14 Years
	Female	22 (57.9%)	

One case of wound Infection occurred in the LigaSure group and none in the conventional group. This was not statistically significant ($p = 1.000$). One patient in the conventional group had a postoperative voice change, and none in the LigaSure group. No cases of RLN Injury occurred in either group. Due to the low frequency of complications, Fisher's exact test was used instead of the Chi-square. p -values > 0.05 indicate no statistically significant difference in complication rates between the groups (Table 4).

Table 4: Postoperative Complications

Complications	Conventional Group	LigaSure Group	p-value
Wound Infection	0 (0%)	1 (2.6%)	1.000
Voice Changes	1 (2.6%)	0 (0%)	(Fisher's)

This study consolidates the key statistical test results applied to categorical variables in the study. Chi-square test showed no significant difference in hypocalcemia Incidence between groups ($p=0.692$). Verified Gender Distribution balance between groups using Chi-square ($p=0.361$). Complication Frequency summarizes results, confirming with Fisher's test that no group had significantly more complications (Table 5).

Table 5: Statistical Comparison (Chi-Square Test Results)

Variables	Conventional Group, n (%)	LigaSure Group, n (%)	Test	p-value	Result
Hypocalcemia Incidence	3 (7.9%)	4 (10.5%)	Chi-square	0.692	Not Significant
Gender Distribution (Male) / (Female)	20 (52.6%) / 18 (47.4%)	16 (42.1%) / 22 (57.9%)	Chi-square	0.361	Not Significant

Complication Frequency	1(2.6%)	1(2.6%)	Fisher's exact	>0.050	Not Significant
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DISCUSSIONS

When it comes to thyroid surgery, there's still an ongoing debate about whether newer tools like LigaSure™ offer real benefits over the traditional method of tying knots with sutures. Our study aimed to explore this question by comparing both approaches in a clinical setting using a standardized surgical technique. Based on our results, it appears that while there may be minor differences, both methods are generally safe and effective in experienced hands. The study noticed a slightly higher rate of temporary hypocalcemia in patients operated on with LigaSure (10.5%) compared to those treated with conventional knot-tying (7.9%). However, this difference wasn't statistically significant ($p=0.692$), which means that both methods performed similarly in terms of preserving parathyroid function. Our findings are consistent with those reported by an earlier study, 12.5% versus 10% ($p=0.60$), that also found no significant difference in hypocalcemia rates between these techniques in a group of 80 thyroidectomy patients [9]. Looking at calcium levels more closely, both groups showed very similar trends in the immediate postoperative period. At 24 hours, the average serum calcium levels were around 8.4 to 8.5 mg/dL, and by 48 hours, they remained stable with very little variation between the two groups. Another study also reported comparable outcomes, reinforcing the idea that both approaches are equally reliable when it comes to preventing this common complication [10]. These findings suggest that neither method significantly disrupts calcium balance in the short term. Similar results were reported by an earlier study, 8.5 ± 0.3 mg/dL for both techniques at both time points, which also concluded that early postoperative calcium levels don't vary much depending on the sealing method used [11]. Some studies have indicated a lower incidence of hypocalcemia with LigaSure, which might be explained by variations in surgeon experience, technique consistency, or differences in the patient populations studied [12]. Similar trends were observed in other studies, which suggested that energy-based vessel sealing devices do not significantly impact early postoperative calcium levels [13]. This study also investigated how efficient each method was during surgery. While the LigaSure group showed a reduction in operative time. Still, this time saving has been echoed in larger studies like the meta-analysis conducted earlier, which found that energy-based devices could reduce operating time, a 34.1% reduction, particularly in high-volume surgical settings [14]. That said, the difference is modest and may not be enough to justify the higher cost of these devices on that basis alone. In terms of complications, both groups had very few issues.

Some patients in the LigaSure group developed a minor wound infection, while some in the conventional group had temporary voice changes. The low complication rates reported earlier, which highlighted the safety of both techniques when surgeries are done properly and on appropriately selected patients [15]. No study is without limitations. Our sample size of 76 patients was reasonable for a single-center trial but may not be large enough to detect rare complications like permanent hypocalcemia or RLN injury. This limitation is common in surgical studies and has been discussed in recent literature, which stressed the need for larger datasets to detect such events [16]. Also, since this study only followed patients for the first 48 hours after surgery, we can't say whether there might be longer-term differences in calcium levels or parathyroid function. From a practical point of view, these findings suggest that both techniques are good options, and the choice may come down to factors like availability, cost, and surgeon experience. In well-equipped hospitals where time efficiency is important, LigaSure might offer some benefit in terms of reducing operating time. However, in hospitals where cost is a bigger concern, conventional knot-tying remains a reliable, safe, and cost-effective method. While earlier studies have reported that LigaSure may help reduce operative time and blood loss due to better hemostasis. These study findings suggest that the surgeon's skill level may play a more decisive role in these outcomes than the choice of instrument [17, 18]. The nearly identical calcium levels we observed between the two surgical approaches make more sense when we consider some recent breakthroughs in parathyroid research. A fascinating 2023 study used advanced imaging technology to visualize blood flow to the parathyroid glands during surgery. Their findings showed that whether surgeons used LigaSure or traditional techniques, about 88–89% of parathyroid glands maintained good blood supply, as long as surgeons carefully preserved them during the procedure. This matches perfectly with what our patients experienced [19]. The similar calcium levels in both our groups (8.41 vs 8.51 mg/dL at 24 hours) tell the same story – the sealing method itself doesn't seem to make or break parathyroid function. A research team came to the same conclusion in their 2023 study of 84 patients [20]. Researchers tracked parathyroid hormone levels after surgery and found nearly identical recovery patterns regardless of which technique was used. By 24 hours post-op, both groups had regained about 70–80% of their normal PTH levels. In summary, both LigaSure and conventional knot-tying are safe and effective options for vessel sealing during thyroidectomy for benign disease. Our study shows that neither technique holds a clear advantage in terms of hypocalcemia rates or other perioperative outcomes. The

decision between them should be guided by local circumstances, available resources, and the surgeon's comfort with the technique.

The lottery-based randomization technique without mention of allocation of concealment may introduce selection bias. Furthermore, blinding of participants and outcome assessors was not described, which could increase the risk of performance and detection bias. Future studies should incorporate allocation of concealment and assessor blinding, along with larger multicenter samples, to strengthen methodological rigor and minimize potential bias.

CONCLUSIONS

This randomized trial found no significant differences in hypocalcemia incidence or other perioperative outcomes between LigaSure and conventional knot-tying techniques in total thyroidectomy for benign thyroid disease. Both methods appear equally safe when performed by skilled surgeons.

Authors' Contribution

Conceptualization: IA

Methodology: HBA, NP, IA

Formal analysis: ZH

Writing and Drafting: MM, UAR

Review and Editing: ZH, HBA, MM, NP, IA, UAR

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency of Raised Bedside Index for Severity in Acute Pancreatitis (BISAP) and Ranson Score in Patients of Acute Pancreatitis

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ABSTRACT

Acute pancreatitis is a growing abdominal disorder that presents a major surgical problem to general surgeons across the globe. **Objectives:** To identify the raised Bedside Index for Severity in Acute Pancreatitis (BISAP) and Ranson scores frequencies in patients with acute pancreatitis. **Methods:** The cross-sectional descriptive study was carried out on 120 patients in the Emergency Department of the Sheikh Zayed Hospital in Lahore. Patients who fit into the inclusion criteria were enrolled. Clinical histories, physical examinations, and laboratory investigations were conducted in detail. Each patient had their BISAP and Ranson scores calculated- BISAP on initial presentation and Ranson scores at admission and 48 hours. There were high levels of BISAP and Ranson scores that were stipulated based on the operational standards. The data analysis was done in SPSS version 23.0. **Results:** The average age of the participants was 44.92 ± 8.92 years; 46 (38.3%) were male and 74 (61.7%) female. It was seen that a high BISAP and Ranson scores occurred in 28 (23.3%) and 42 (35%) patients, respectively. The percentage of patients who had an increased BISAP was 23.3, and the percentage of patients who had an increased Ranson score was 35, which means that a higher percentage were classified as severe by the Ranson classification criteria. **Conclusions:** The BISAP score is a convenient, valid, and time-saving instrument to evaluate the severity of acute pancreatitis at an early stage and risk classification in clinical practice, although the Ranson might be more effective in this regard.

INTRODUCTION

Acute pancreatitis (AP) is an illness that has been experiencing a steady increase throughout the entire world, and has become one of the most significant gastrointestinal diseases subject to hospitalization. Epidemiological data further show the acute pancreatitis (AP) disease incidence in the United States to vary between 13 to 45 cases per one lakh individuals annually and the incidence of the disease in the United Kingdom to range from 4.8 to 24.2 cases per one lakh individuals annually [1-

3]. AP is a pancreatic inflammatory disease that is brought about by the destruction of the digestive enzymes that it produces. It is a sterile inflammation, i.e., it is not bacterially infected. The most common causes of AP are gallstones, which cause 54 percent of the cases, next comes consumer of alcohol and cases of unknown origin (idiopathic) [4]. Acute pancreatitis pathogenesis starts with the process of trypsinogen conversion to trypsin in acinar cells, in quantities that cannot be counteracted by



the active trypsin. This results in the activation of other proenzymes, such as trypsinogen in itself and other inactive precursors of elastase, phospholipase A2 (PLA2), and carboxypeptidase. Etiologically, the most common causes are gallstone disease (cholelithiasis) and alcohol use, which represent a large percentage of the cases [5]. Megafauna epidemiological studies provide the mortality rate related to pancreatitis, 1.5–4.2 percent, based on the severity of the disease. Nonetheless, the rate of mortality in the infected state of pancreatic necrosis increases significantly to 30% in this situation [6]. An incident of acute pancreatitis can result in several complications (both local and systemic), and, therefore, it should be diagnosed early so as to provide triage and effective treatment promptly to avoid the negative effects. Various scoring systems, such as the Ranson Scoring System, Acute Physiology and Chronic Health Evaluation (APACHE)-II, BISAP, Computed Tomography Severity Index (CTSI), and Sequential Organ Failure Assessment (SOFA) score systems, are based on different variables to measure the severity of acute pancreatitis [7]. Each scoring system has its own limitations, and the sensitivity and specificity range between 55 and 90% depending upon the cutoff values and timing of the score [8]. In one of the studies, the frequency of raised BISAP was 18.75% and that of Ranson score was 31.25% [9]. Ranson's criteria need to be calculated at admission and after 48 hours, while BISAP is easy to calculate, i.e., only at admission, these tools are equally effective in detecting patients at an elevated risk of mortality before organ failure develops [10, 11]. Similarly, the modified CT severity index demonstrated high diagnostic accuracy in evaluating severe acute pancreatitis [12]. AP is a serious condition with significant global health implications, leading to complications that contribute to both morbidity and mortality. The deaths are not uniform, and they are about 1 to 20 percent in mild and severe cases. Moreover, AP imposes quite a significant burden on healthcare resources because of the costs incurred with it [13]. Treatment of acute pancreatitis is difficult and aims at determining the etiology of the disease, assessing the severity of the disease, and identifying complications.

Early and accurate assessment of severity in acute pancreatitis is essential to reduce morbidity, mortality, and healthcare burden. Limited local data are available regarding the comparative frequency of elevated BISAP and Ranson scores in patients presenting with acute pancreatitis. This study aimed to establish the prevalence of an increase in BISAP and Ranson scores in patients with acute pancreatitis.

METHODS

This cross-sectional descriptive study was conducted on 120 patients at the Emergency Department of the Sheikh Zayed Hospital in Lahore, from 29 June 2019 to 28 December 2019, after ethical approval from the CPSP (CPSP/REU//GAS-2017-072-743). A total of 120 cases were included by a consecutive sampling technique. This was done by dividing 95% confidence level and 7 percent margin of error by an expected frequency of raised BISAP of 18.75 to come up with a sample size. The survey covered both male and female patients aged between 20 and 70 years with acute pancreatitis who gave written informed consent. Non-pregnant women, patients on hemodialysis, on anticoagulant therapy (aspirin, clopidogrel, warfarin, or heparin), and having COPD (FEV1 less than 70 percent of normal) were not excluded, however. A comprehensive history was taken on each patient. The same resident gathered all clinical tests, vital signs, and blood samples, and the laboratory results were obtained in the hospital laboratory to reduce bias. Two scoring systems were employed to measure the severity of AP, and were known as BISAP and Ranson. The BISAP score consists of five parameters, with blood urea nitrogen greater than 25mg/dl, impaired mental status, systemic inflammatory response syndrome (SIRS), age above 60 years, and pleural effusion being one point each (0–5). Ranson score was assessed at admission and 48 hours of admission on standard parameters and cutoff values defining severe acute pancreatitis. A BISAP score of 3 or more and a Ranson score of 3 or more were believed to be severe acute pancreatitis, which is in line with earlier published research. The data analysis was done using SPSS version 23.0. Numerical variables (age and serum amylase levels at admission) were also presented in the form of mean $\pm$ SD, and frequencies and percentages were filled on categorical variables (gender and raised BISAP and Ranson scores). The data were normally distributed by using the Shapiro-Wilk test, and the means plus SD were reported. Age, gender, BMI, symptom duration, and serum amylase levels at admission were used to stratify the data. Chi-square tests were post-stratified, where a p-value of <0.05 was taken as statistically significant.

RESULTS

The age distribution showed that 66 (55%) of patients were between 20 and 50 years, while 54 (45%) were aged 51 to 70 years, with a mean $\pm$ SD of 44.92 ± 8.92 years. Regarding gender, 46 (38.33%) were male, and 74 (61.67%) were female. The average serum amylase level at admission was 1341.14 ± 478.52 U/L (Table 1).

Table 1: Demographic Features of Patients

Variables	n (%)
Age (Years)	
20-50	66 (55%)
51-70	54 (45%)
Total	120
Mean $\pm$ SD	44.9 $\pm$ 28.92
Serum Amylase (U/L)	1341.14 $\pm$ 478.52
Gender	
Female	74 (61.6%)
Male	46 (38.3%)

Frequency of raised BISAP and Ranson score in patients of AP was calculated as 28 (23.33%) for BISAP and 42 (35%) for Ranson score (Table 2).

Table 2: Patients with Raised BISAP and RANSON Score (n=120)

Raised Scores	No. of Patients
BISAP	28 (23.33%)
Ranson	42 (35.0%)

Data stratification shows that out of 28 increased BISAP, 10 were male and 18 were female, p-value was 0.918, and of 42 increased Ranson score, 13 were male and 29 were female, p-value=0.819 (Table 3).

Table 3: Comparison of Gender with Raised BISAP and RANSON Score among Patients

Score	Gender	Raised (n)	Not Raised (n)	p-value
BISAP	Male	10	36	0.918
	Female	18	56	
Ranson	Male	13	23	0.819
	Female	29	45	

Out of the 28 individuals with higher BISAP scores, 19 were between the ages of 20 and 50, and 9 were between the ages of 51 and 70. The data stratification indicates that, of the 42 individuals with higher Ranson scores, 25 were between the ages of 20 and 50, and 17 were between the ages of 51 and 70 (Table 4).

Table 4: Comparison of Age with Raised BISAP and RANSON Score among Patients

Score	Age Group (Years)	Raised (n)	Not Raised (n)	p-value
BISAP	20-50	19	47	0.179
	51-70	9	45	
Ranson	20-50	25	41	0.590
	51-70	17	37	

DISCUSSIONS

Acute pancreatitis is an increasingly prevalent condition marked by pancreatic inflammation, presenting a significant challenge for general surgeons globally. It can range from a mild, self-resolving illness to a severe, rapidly worsening state that poses a serious risk to life. The

estimated incidence of acute pancreatitis is approximately 2.29% [14]. The severity of AP can be divided into three categories: acute hemorrhagic necrotizing, acute edematous, and acute persistent. For prompt therapeutic action and better results, patients at risk of severe disease must be identified early [15]. Each scoring system has its own sensitivity and specificity depend upon the cutoff values and timing of the score [16]. So there was a need to perform a local study to see the effectiveness of these scoring systems in our local population and prompt us in recognizing the patients who are at risk of developing severe morbidities or mortality, thus an early intensive treatment plan can be initiated. In this study, most patients were between 20 and 50 years old, while a slightly smaller proportion were aged 51 to 70 years. The average age was in the mid-40s. Females outnumbered males, making up a larger share of the study population. The frequency of elevated BISAP scores was observed in nearly a quarter of the cases, while an increased Ranson score was noted in over one-third of the patients with acute pancreatitis. While comparing the results with an earlier study where the frequency of raised BISAP was 18.75% and that of Ranson score was 31.25%, the findings agree with this study [9]. A study conducted at Dow University Hospital, Karachi, evaluated 206 patients with AP and found that the BISAP score predicted severe cases with 76.2% accuracy, whereas the Ranson score indicated that the accuracy of the Ranson score was higher at 82.2% [17]. The majority of the studies have shown that it is predominantly female, which correlates with the findings of this study [3, 18]. It is more prevalent among middle-aged people. Most of the patients in this study were in their 40s and 50s, which agrees with a previous study [19]. The BISAP and the Ranson scoring systems have been tested by Parimala and colleagues to determine their predictive value on the severity of AP, and came to the conclusion that BISAP is not less than the score of Ranson in this aspect. The BISAP scoring system is simple and affordable, and user-friendly, and it does not require long before results are generated. Ranson, however, takes at least 24 hours to score. BISAP is also an effective determinant of patient outcome in acute pancreatitis [20]. Local data on the prevalence of high BISAP and Ranson scores in acute pancreatitis are limited, so there is a need to conduct cross-centre research to corroborate the results. The work contributes to the useful evidence regarding the local prevalence and demographics, with the focus on the practicality of BISAP as a tool of simple bedside risk stratification in under-resourced settings.

Nevertheless, the study is cross-sectional, single-center, and small-sample, which cannot be generalizable. The imaging-based indices, such as the CT Severity Index and

long-term outcome, were not evaluated. It is suggested that future multicenter, longitudinal studies, including radiological and biochemical parameters, be used to improve prediction and best treatment of acute pancreatitis.

CONCLUSIONS

The scores of both BISAP and Ranson are important in determining the level of severity of AP. Timely clinical decision support because BISAP can be used to stratify risks early, and the score provided by Ranson, which incorporates both admission and 48-hour post-admission assessment, is a more holistic assessment of the disease course. The two scores are effective predictors of severe pancreatitis and useful in the early detection of high-risk patients. Nevertheless, these scores provide a more comprehensive prediction of the severity of the disease and the possible complications.

Authors' Contribution

Conceptualization: SJ

Methodology: UR

Formal analysis: UA, HW

Writing and Drafting: UR, SJ, HY, MHN, M

Review and Editing: UR, SJ, UA, HY, MHN, M, HW

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Current Status of Knowledge, Skill, and Attitude of Recent Medical Graduates Regarding Medicolegal Work in Lahore City

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ABSTRACT

Medicolegal responsibilities, including autopsy performance, injury documentation, and courtroom testimony, are essential components of clinical practice. In Pakistan, recent medical graduates often lack adequate preparation in these areas, raising concerns about their readiness for legal and ethical duties. **Objectives:** To assess the knowledge, skills, and attitudes of recent medical graduates in Lahore regarding medicolegal responsibilities, and to identify gaps to inform curriculum reform. **Methods:** This cross-sectional descriptive study was conducted from 1 January to 31 March 2025 in Lahore General Hospital, Lahore. A total of 394 medical graduates (within two years of graduation and having completed house jobs) were selected through stratified random sampling. A validated, self-administered questionnaire assessed knowledge, skills (self-reported), and attitudes (Likert-scale items). Data were analyzed using SPSS version 26.0 at a 95% confidence level. **Results:** Only 28% of participants demonstrated adequate knowledge ($\geq 70\%$ score), with better performance in informed consent (71.1%) and death certification (62.9%), and poor understanding of sexual-assault protocols (20.6%) and injury documentation (17.5%). Just 15.2% felt confident performing medicolegal tasks, and only 12.2% had observed an autopsy. While 78% agreed that medicolegal competence is essential, only 26% felt adequately trained during medical school. Notably, 71% expressed interest in further training. Graduates from public institutions had slightly better knowledge and exposure. **Conclusions:** Recent medical graduates in Lahore exhibit significant gaps in medicolegal knowledge and practical readiness. Structured medicolegal education and practical exposure must be integrated into undergraduate curricula to ensure competent and legally accountable practice.

INTRODUCTION

Medicolegal responsibilities such as autopsy performance, injury documentation, report writing, and legal proceedings are crucial aspects of clinical duties expected from new medical graduates. In Pakistan, despite the importance of these roles, the knowledge, practical competencies, and attitudes of young doctors toward medicolegal work are reported to be inadequate [1]. A study conducted in Lahore revealed that while most doctors acknowledged the importance of medical ethics, only 22%

showed interest in pursuing forensic specialties, and a significant portion lacked basic knowledge of medicolegal procedures [2]. Regular training to update the knowledge of medicolegal issues is necessary to ensure continuous improvement in healthcare delivery and administration of justice, including modules on consent, negligence, autopsies, and courtroom testimony [3]. To strengthen medicolegal capacity, the University of Health Sciences (UHS) Lahore recently introduced a one-month Certificate



in Medicolegal Examination for Medical Officers (MOs) and Women Medical Officers (WMOs) across Punjab [4]. Globally, studies have also reported similar deficiencies. In Italy, only 14% of medical students had observed autopsies or attended court proceedings, while in Saudi Arabia and Egypt, more than half were unfamiliar with legal reporting procedures [5-7]. Such global findings emphasize the universal challenge of integrating medicolegal competency into undergraduate medical training. Despite recent local initiatives, major gaps persist in medicolegal education and professional development. Professionalism, a core domain encompassing ethical and legal responsibilities, remains underemphasized in most medical curricula in Pakistan [8]. Studies indicate that medicolegal education receives limited hours, lacks structured assessments, and is often delivered without practical exposure [9]. Consequently, fresh graduates report deficiencies in communication, procedural skills, and confidence when handling real-world medicolegal cases [10]. Doctors are further required to comply with the regulations of the Pakistan Medical and Dental Council (PMDC) and the Punjab Healthcare Commission (PHC), both emphasizing ethical standards, documentation, and patient safety [11, 12]. Failure to meet these expectations may result in legal consequences, professional misconduct allegations, and even loss of licensure, highlighting the need for early medicolegal training. Given these challenges, the present study was undertaken with the aim of evaluating the current level of medicolegal competence among recent medical graduates in Lahore. Specifically, the study aims to assess their knowledge, skills, and attitudes toward medicolegal responsibilities, identify the educational and practical gaps in training, and provide evidence-based recommendations for curriculum enhancement and continuing professional development. Medicolegal competence is essential for medical graduates to ensure ethical practice, patient safety, and legal accountability. Despite its importance, recent graduates in Pakistan demonstrate inadequate knowledge, skills, and attitudes toward medicolegal responsibilities. This study aimed to assess the knowledge, skills, and attitudes of recent medical graduates in Lahore regarding medicolegal responsibilities and to identify gaps to inform curriculum reform.

METHODS

This cross-sectional descriptive study was conducted from January to March 2025 in major teaching hospitals and medical colleges of Lahore, including Lahore General Hospital, Mayo Hospital, Jinnah Hospital, and Services Hospital. Ethical approval was obtained from the Institutional Review Board of Postgraduate Medical Institute, Lahore (Ref. No. 7255/PGMI/AMC). Participation

was voluntary, and confidentiality was strictly maintained. The study population consisted of recent medical graduates who had completed their degrees within the past two years, who had completed their house job and were employed or seeking employment in public or private healthcare institutions. The sample size of 394 participants was determined using Cochran's formula: $n = \frac{Z^2 \times p \times (1-p)}{d^2}$, where $Z=1.96$ (95% confidence level), $p=0.5$ (assumed prevalence of adequate knowledge), and $d=0.05$ (margin of error). Stratified random sampling ensured representation from different institutions and genders. Graduates unwilling to participate, or those who had received formal medicolegal or forensic training beyond the undergraduate level, were excluded. A structured, self-administered questionnaire was used, developed through literature review and expert consultation. It comprised three sections assessing: Knowledge: Multiple-choice items on laws, consent, documentation, and postmortem procedures. Skills: Self-assessment and case-based questions on practical competence. Attitude: Five-point Likert-scale items evaluating perception, confidence, and interest in medicolegal work. The questionnaire was adapted from previously validated instruments [13]. The total possible score ranged from 0 to 30; scores $\geq 70\%$ were considered "adequate knowledge." Validity was confirmed through expert review (CVI = 0.87) and reliability through Cronbach's $\alpha = 0.82$. A pilot test on 30 participants (excluded from final analysis) ensured clarity and feasibility. Data were collected by trained data collectors after obtaining verbal informed consent. Data were analyzed using SPSS version 26.0 at a 95% confidence level.

RESULTS

A total of 394 graduates participated. The mean age was 25.3 ± 1.2 years. Among participants, 228 (58%) were female and 166 (42%) male. A majority (61%) graduated from public medical colleges and 39% from private institutions (Table 1).

Table 1: Demographic Characteristics of Participants (n=394)

Variables	Category / Unit	Frequency (n %) / Mean $\pm$ SD
Age	Years	25.3 $\pm$ 1.2
Gender	Female	228 (58%)
	Male	166 (42%)
Type of Institution	Public Medical College	240 (61%)
	Private Medical College	154 (39%)

*"n (%)" indicates frequency and percentage; show the % symbol once at the top of the column only.

Only 28% (108) of participants demonstrated adequate knowledge ($\geq 70\%$ score). The most familiar areas were informed consent (71.1%) and death certification (62.9%), while weaker areas included sexual-assault protocols

(20.6%) and injury documentation (17.5%) (Table 2).

Table 2: Knowledge of Medicolegal Topics Among Participants

Medicolegal Topic	Frequency (%)
Informed-Consent Procedures	280 (71.1%)
Death Certification	248 (62.9%)
Medicolegal Documentation of Injuries	69 (17.5%)
Sexual-Assault Case Protocol	81 (20.6%)
Police Information Handover (MLO Role)	114 (28.9%)
Legal Age of Consent and Liability	172 (43.7%)

Only 15.2% (60) of respondents felt confident performing medicolegal duties such as injury-report writing or court testimony. About 12.2% (48) had observed an autopsy, and fewer than 10% (38) had written any medicolegal report during their house job (Table 3).

Table 3: Self-Reported Skills Related to Medicolegal Practice

Medicolegal Topic	Frequency (%)
Confident in Writing Injury Reports	60 (15.2%)
Observed a Medicolegal Autopsy	48 (12.2%)
Attended Court Proceedings	22 (5.6%)
Wrote any Medicolegal Report	38 (9.6%)
Trained Formally in Medicolegal Procedures	51 (12.9%)

Regarding attitudes, 78% (307) agreed that medicolegal competence is essential for practice, while only 26% (103) felt adequately trained during medical school. About 71% (280) expressed interest in attending further training (Table 4).

Table 4: Attitudes Toward Medicolegal Education and Practice

Statement	Agree (%)	Neutral (%)	Disagree (%)
Medicolegal Competence is Essential	307 (78%)	59 (15%)	28 (7%)
The Undergraduate Curriculum Prepared me Adequately	103 (26%)	95 (24%)	196 (50%)
I Feel Confident Performing Medicolegal Duties	75 (19%)	130 (33%)	189 (48%)
I Would attend Medicolegal Workshops	280 (71%)	67 (17%)	47 (12%)
Medicolegal Work Should be a Compulsory In-House Job	252 (64%)	83 (21%)	59 (15%)

Graduates from public institutions showed higher mean knowledge scores (62.1%) compared to private ones (58.3%), though not statistically significant ($p=0.08$). However, public graduates reported significantly greater practical exposure ($p<0.05$) (Figure 1).

Would you Attend a Workshop or Training Course in Medicolegal Work?

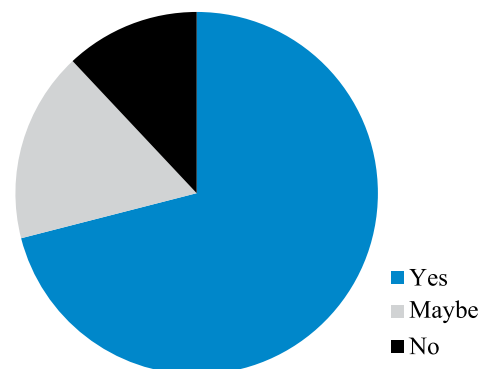


Figure 1: Interest of Participants in Attending Medicolegal Training Workshops

DISCUSSION

This study highlights a critical gap in the medicolegal preparedness of recent medical graduates in Lahore. Despite completing their house jobs, most participants lacked both knowledge and practical skills needed for core medicolegal duties. The demographic pattern shows a predominantly female cohort (58%) with a mean age of 25.3 years, similar to trends reported in South Asian medical institutions [9]. Inclusion of graduates from both public and private colleges provided a comprehensive understanding of institutional differences. Although public-sector graduates demonstrated slightly higher mean knowledge scores (62.1%) than private graduates (58.3%), this difference was not statistically significant ($p=0.08$) [1]. However, exposure to medicolegal cases was significantly higher among public-sector graduates ($p<0.05$), likely due to higher patient loads and more frequent legal referrals in government hospitals [14]. Overall, only 28% of respondents scored $\geq 70\%$ in medicolegal knowledge, indicating inadequate understanding of essential concepts. While awareness of informed-consent procedures (71.1%) and death certification (62.9%) was relatively satisfactory, familiarity with injury documentation (17.5%) and sexual-assault protocols (20.6%) remained alarmingly low [10]. Comparable studies from Lahore and other regions of Pakistan report a similarly weak grasp of documentation and trauma assessment procedures among young doctors [15, 16]. Practical competence was even more limited: only 15.2% felt confident writing an injury report, fewer than 10% had completed a medicolegal document, 12.2% had observed an autopsy, and just 5.6% had attended court proceedings [1, 9, 11]. Literature demonstrates that even in structured international systems, practical exposure is insufficient unless supported by targeted training interventions. Evidence from burn-case documentation in Lahore also indicates recurrent errors linked to poor undergraduate training and lack of supervised practice.

Participants' attitudes, however, were encouraging. Most graduates acknowledged the importance of medicolegal work 78% agreed that medicolegal competence is essential, and 71% showed willingness to attend further training [16-19]. Despite this interest, only 26% believed their undergraduate curriculum adequately prepared them for real-world medicolegal duties. This aligns with previous findings that lecture-based instruction alone is ineffective for developing clinical reasoning and documentation skills in forensic medicine [20]. Collectively, the combination of poor practical exposure, inconsistent institutional opportunities, and strong learner motivation highlights an urgent need for curriculum reform. Short-term strategies such as certificate-based workshops, case-based learning, structured simulations, and courtroom observation sessions could immediately enhance competence. Long-term reforms should adopt international best practices, including formal medicolegal rotations, simulation-based training laboratories, supervised documentation, and standardized assessment of skill-based competencies.

The cross-sectional design limits the ability to establish causality between education or training and medicolegal competency. Additionally, reliance on self-administered questionnaires may introduce reporting bias and overestimation of actual skills and knowledge. Future longitudinal studies with objective assessments of practical skills are recommended to better evaluate medicolegal competence over time. Long-term reforms should adopt international best practices, including formal medicolegal rotations, simulation-based training laboratories, supervised documentation, and standardized assessment of skill-based competencies.

CONCLUSIONS

Despite acknowledging the importance of medicolegal responsibilities, recent medical graduates in Lahore show critical deficiencies in both knowledge and practical preparedness. Immediate curriculum reforms, integrated training modules, and experiential learning are required to ensure that medical graduates can competently and confidently handle medicolegal responsibilities.

Authors' Contribution

Conceptualization: ZI

Methodology: ZI, MA

Formal analysis: AF

Writing review and editing: AZ, TAM, MH

Review and Editing: ZI, AZ, TAM, AF, MH, MA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency of Different Fracture Patterns of Acrylic Partial Denture in the Patients Visiting Sardar Begum Dental College

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ABSTRACT

Fracture of acrylic removable partial dentures (RPDs) is a major cause of prosthesis failure, often requiring repair or replacement. **Objective:** To determine the distribution of fracture patterns in acrylic RPDs and assess associations with demographic and clinical factors in patients at Sardar Begum Dental College. **Methods:** In this cross-sectional study (Sept 2023–Mar 2024), 96 patients with fractured acrylic partial dentures were enrolled consecutively. Fracture types (midline, clasp, connector, crack line, multiple) and variables including age, gender, reinforcement, parafunctional habits, and ridge resorption were recorded. Data were analyzed using chi-square tests and Cramer's V, with $p < 0.05$ considered significant. **Results:** Midline fractures were most frequent (57.3%), followed by clasp fractures (28.1%), multiple-site (12.5%), connector (1.0%), and crack line only (1.0%). Parafunctional habits were significantly associated with fracture pattern ($p = 0.042$, Cramer's V = 0.321). Reinforcement showed borderline significance ($p = 0.060$). Other factors showed no significant relationship. **Conclusions:** Midline fractures predominate in acrylic RPDs. Parafunction is a significant modifiable risk factor, and reinforcement may offer a protective benefit. Screening for parafunctional habits and implementing prudent reinforcement strategies could reduce fracture incidence.

INTRODUCTION

Fracture of acrylic removable partial dentures (RPDs) remains a common clinical problem, leading to functional disability, compromised esthetics, and repeated repairs. The inherent weakness of polymethyl methacrylate (PMMA) under cyclic loading makes it prone to fatigue and midline failure [1]. International reports consistently identify acrylic denture fractures as a major cause of prosthesis failure, with higher repair rates compared to cobalt-chromium frameworks. Mohamed et al. demonstrated that acrylic RPDs have significantly reduced service longevity relative to metal-based prostheses, underscoring their mechanical vulnerability [2]. PMMA

reinforcement has been explored to overcome this limitation. Studies report that metal mesh, glass fiber, carbon fiber, and nano-fillers can enhance flexural and impact strength, depending on their placement and bonding within the denture base [3-5]. Among these, metal mesh and glass fiber reinforcements are most commonly used in routine clinical practice and were considered in the present study when analyzing risk factors for denture fracture [6]. Recent reviews emphasize that while PMMA remains the material of choice, its low fracture toughness and fatigue resistance continue to challenge prosthodontic longevity. Alqutaibi et al. highlighted that



reinforcement strategies remain critical to improving PMMA's performance [3]. Similarly, Chen *et al.* showed that connector geometry and clasp design directly influence stress concentration in acrylic bases [6]. Finite element analyses and experimental models, such as those by Qin *et al.* demonstrate that optimized reinforcement placement significantly reduces displacement and fracture risk [4]. Despite global advancements, regional data remain limited. In South Asia, fracture frequency and pattern distribution have been insufficiently reported. An Iraqi study by Mohsen *et al.* noted frequent acrylic denture fractures but did not specify fracture types or associated factors [7].

In Pakistan, available studies are largely descriptive and lack a detailed evaluation of fracture locations and patient-related influences. This gap in local evidence highlights the need for region-specific research. Understanding the frequency and distribution of fracture patterns and their association with variables such as parafunctional habits, ridge resorption, and reinforcement can guide clinicians in adopting better preventive and reinforcement strategies. This study aimed to evaluate the fracture patterns of acrylic partial dentures among patients visiting Sardar Begum Dental College and to identify key demographic and clinical risk factors associated with these fractures.

METHODS

This cross-sectional descriptive study was conducted in the Department of Prosthodontics, Sardar Begum Dental College, Gandhara University, Peshawar, to evaluate the frequency and distribution of fracture patterns in acrylic partial dentures and their association with demographic and clinical factors. The study period extended from September 2023 to March 2024, following ethical approval from the institutional review board (Ref: GU/Ethical Committee/2023/210). Informed consent was obtained from all participants before data collection. The sample size ($n = 96$) was calculated using the World Health Organization (WHO) sample size calculator, assuming a previously reported denture fracture prevalence of 45% as reported by Mohsen *et al.* [7], with a 95% confidence level and 5% margin of error. To enhance the reliability and representativeness of the findings, the final sample was slightly increased beyond the minimum estimated value of 92 participants. A non-probability consecutive sampling technique was employed, whereby all eligible patients presenting during the study period were included until the sample size was achieved. Although consecutive sampling can potentially introduce selection bias, this was minimized by applying consistent inclusion and exclusion criteria throughout the six months and by recruiting patients from a diverse clinical pool to capture variability in demographics and prosthesis types. Patients aged 20

years and above presenting with fractured acrylic removable partial dentures (RPDs) were included, irrespective of gender. Exclusion criteria comprised patients with metal framework dentures, congenital craniofacial anomalies, systemic bone diseases (e.g., osteoporosis), and those with fractures resulting from laboratory errors before clinical use. Data were collected using a structured proforma that documented demographic details (age, gender, socioeconomic and educational status), prosthesis-related characteristics (arch involved, Kennedy classification, opposing dentition, and presence or absence of reinforcement), and clinical variables (ridge resorption, parafunctional habits, and previous denture repairs). Each denture was examined under standard illumination and magnification by the principal investigator. To ensure intra-examiner reliability, a subset of 10 dentures was re-examined after one week, yielding a kappa value of 0.86, indicating strong agreement. Fracture patterns were categorized into five operational groups adapted from Kamble *et al.* and Zheng *et al.* to ensure comparability with prior literature [8, 9]. The categories were as follows: (1) Midline fracture, a complete fracture along the mid-palatal line; (2) Clasp assembly fracture, involving the clasp, rest, or minor connector; (3) Connector fracture, through major or minor connectors excluding clasps; (4) Crack line only, referring to incomplete visible cracks without separation; and (5) Multiple fracture sites, representing dentures exhibiting more than one fracture type simultaneously. Residual ridge resorption was graded clinically as mild, moderate, or severe, in accordance with the Atwood (1971) classification, based on ridge contour and height on intraoral examination. Although no radiographic measurements were performed, a standardized clinical calibration protocol was followed to maintain consistency across all assessments. Reinforcement assessment was carried out by visually examining each denture base and reviewing clinical records to determine the presence of reinforcement materials such as metal mesh, glass fiber, or carbon fiber, which are most commonly used in the reinforcement of acrylic prostheses in the study region. All data were analyzed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including frequencies and percentages, were computed for categorical variables. The Chi-square test and Cramer's V were applied to examine associations between fracture patterns and selected variables. Due to the cross-sectional and descriptive nature of the study, no causal inference or multivariate regression analysis was conducted; however, potential confounders such as age, ridge resorption, and parafunctional habits were discussed in the interpretation of findings. A p -value < 0.05 was considered statistically significant.

RESULTS

Out of 96 patients, most were aged 41–50 years (29.2%) and over 50 years (29.2%), indicating that denture fractures occurred predominantly in mid-to-late adulthood. Females (54.2%) slightly outnumbered males (45.8%), and the middle socioeconomic class (43.8%) formed the largest group, followed by the lower (39.6%) and higher classes (16.7%). A sedentary lifestyle was more common (60.4%) than active occupations (39.6%). In terms of education, 33.3% had schooling up to the matric level, while 27.1% held graduate or higher qualifications. These trends suggest that socioeconomic and educational factors may influence denture maintenance and fracture risk (Table 1).

Table 1: Demographic Characteristics of Patients (n=96)

Variables	Category	Frequency (%)
Age (Years)	20–30	18 (18.8%)
	31–40	22 (22.9%)
	41–50	28 (29.2%)
	>50	28 (29.2%)
Gender	Male	44 (45.8%)
	Female	52 (54.2%)
Socioeconomic Status	Low	38 (39.6%)
	Middle	42 (43.8%)
	High	16 (16.7%)
Occupation	Sedentary	58 (60.4%)
	Active	38 (39.6%)
Education Level	Illiterate	12 (12.5%)
	Primary–Matric	32 (33.3%)
	Intermediate	26 (27.1%)
	Graduate+	26 (27.1%)

Maxillary dentures showed more fractures (60.4%) than mandibular dentures (39.6%). According to Kennedy's classification, Class III (37.5%) and Class II (27.1%) designs were most common. Over half of the cases (56.3%) had natural opposing dentition, while 25.0% had partial and 18.8% complete denture antagonists. Reinforcement was absent in 68.8% of dentures, suggesting that the lack of reinforcement may contribute to fracture risk (Table 2).

Table 2: Clinical and Prosthesis-Related Variables (n=96)

Variables	Category	Frequency (%)
Arch Involved	Maxillary	58 (60.4%)
	Mandibular	38 (39.6%)
Kennedy Class	I	22 (22.9%)
	II	26 (27.1%)
	III	36 (37.5%)
	IV	12 (12.5%)
Opposing Dentition	Natural Teeth	54 (56.3%)
	Partial Denture	24 (25.0%)
	Complete Denture	18 (18.8%)
Reinforcement	Present	30 (31.3%)

	Absent	66 (68.8%)
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Fractures occurred most frequently after 1–3 years (39.6%) and over 3 years (39.6%) of denture use, with 20.8% developing within the first year. Parafunctional habits were present in 29.2% of patients, indicating a key behavioral risk factor. Moderate ridge resorption (45.8%) was most common, followed by mild (29.2%) and severe (25.0%). Nearly one-third (31.3%) had a history of previous denture repairs, suggesting that repeated stress and prior structural weakness may predispose to recurrent fractures (Table 3).

Table 3: Distribution of Habits, Oral Condition, and Duration of Denture Use among Patients (n=96)

Variables	Category	Frequency (%)
Duration of Denture Use	<1 Year	20 (20.8%)
	1–3 Years	38 (39.6%)
	>3 Years	38 (39.6%)
Parafunctional Habits	Yes	28 (29.2%)
	No	68 (70.8%)
Residual Ridge Resorption	Mild	28 (29.2%)
	Moderate	44 (45.8%)
	Severe	24 (25.0%)
History of Previous Denture Repairs	None	66 (68.8%)
	≥1 Repair	30 (31.3%)

The most frequent fracture pattern was the midline fracture (57.3%), confirming its well-documented status as the most common site due to stress concentration and flexural fatigue. Fractures around the clasp assembly accounted for 28.1%, while 12.5% involved multiple fracture sites. Fractures around connectors (1.0%) and crack lines (1.0%) were rare. This distribution reinforces that design-related stresses and occlusal forces at the palatal midline and clasp regions are the most critical factors influencing fracture occurrence (Table 4).

Table 4: Distribution of Fracture Patterns among Patients (n=96)

Variables	Frequency (%)
Midline Fracture	55 (57.3%)
Around the Clasp Assembly	27 (28.1%)
Around Connectors	1 (1.0%)
Crack Line Only	1 (1.0%)
Multiple Fracture Sites	12 (12.5%)

Chi-square analysis showed a significant association between parafunctional habits and fracture pattern ($p = 0.042$, Cramer's $V = 0.321$), indicating a moderate relationship. Patients with bruxism were more prone to midline and clasp fractures. Reinforcement demonstrated a borderline association ($p = 0.060$), suggesting higher fracture susceptibility in unreinforced dentures. Other variables, gender, Kennedy class, duration of use, and ridge resorption were not significant. These results highlight the multifactorial nature of denture fracture, with

parafunctional habits as a key modifiable factor (Table 5).

Table 5: Association of Key Variables with Fracture Pattern (n=96)

Variables	χ^2 (df)	P-value	Cramer's V	Interpretation
Gender × Fracture Pattern	$\chi^2 = 4.72$ (df = 4)	0.318	—	Not Significant
Kennedy Class × Fracture	$\chi^2 = 6.63$ (df = 12)	0.881	—	Not Significant
Reinforcement × Fracture	$\chi^2 = 9.06$ (df = 4)	0.060	—	Borderline (Trend Toward Sig.)
Duration of Use × Fracture	$\chi^2 = 5.95$ (df = 8)	0.653	—	Not Significant
Parafunction × Fracture	$\chi^2 = 9.89$ (df = 4)	0.042	0.321	Significant (Moderate Association)
Ridge Resorption × Fracture	$\chi^2 = 6.78$ (df = 8)	0.560	—	Not Significant

$p < 0.05$ considered significant; Cramer's V values: 0.1 = weak, 0.3 = moderate, 0.5+ = strong

Midline fractures were the most frequent (57.3%), followed by fractures around the clasp assembly (28.1%). Multiple fracture sites accounted for 12.5%, whereas fractures around connectors (1.0%) and crack line only (1.0%) were rare. This highlights the midline as the predominant site of denture failure, consistent with the mechanical stress concentration in that region (Figure 1).

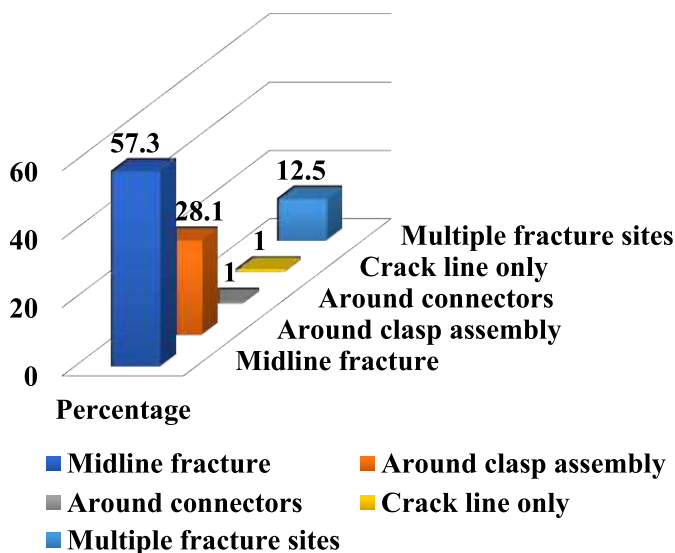


Figure 1: Distribution of Fracture Patterns among Patients with Acrylic Partial Dentures (n=96)

DISCUSSIONS

The present study identified midline and clasp-related fractures as the predominant patterns in acrylic partial dentures, consistent with previous literature describing midline failure as the classic fatigue path caused by flexural bending across the palatal vault. Mohamed *et al.* noted that denture fracture commonly arises from fatigue along high-stress zones such as the midline [2]. Similar findings by Kamble *et al.* and Iris *et al.* confirmed midline dominance due to repeated cyclic loading and stress concentration [8, 10]. Clasp-related fractures were the second most

frequent pattern, aligning with biomechanical evidence showing that junctions of clasps, rests, and minor connectors act as stress risers during function and insertion-removal cycles. Zheng *et al.* reported that cyclic loading and undercut depth influence clasp fatigue and adjacent acrylic failure [9], while Chen *et al.* demonstrated that clasp geometry strongly affects retention force and stress distribution [5]. A significant association was found between parafunctional habits and fracture pattern, supporting evidence that bruxism increases risk through greater occlusal forces and more frequent loading cycles. Chrcanovic *et al.* observed higher fracture incidence among bruxers, reinforcing the importance of behavioral screening [11]. Likewise, Ionfrida *et al.* emphasized preventive approaches such as night guards and occlusal adjustments for patients with parafunction [12]. Although reinforcement showed only a borderline association, its protective potential is supported by recent studies. Hussein *et al.* reported enhanced fracture resistance with metal mesh and glass fiber reinforcements [13], while Pavlin *et al.* found improved load tolerance with carbon fiber bases [14]. Other investigations also confirm that fiber or mesh reinforcement increases PMMA's flexural and impact strength [14-16]. These findings suggest that reinforcement remains beneficial, particularly for high-stress cases or long-span dentures. Advances in materials and design continue to reduce classical failure modes. Alqutaibi *et al.* reviewed PMMA modifications and substitutes to address fatigue limitations [3]. Digital frameworks using PEEK have demonstrated superior fit and reduced stress transmission compared to Co-Cr, as reported by Barbosa *et al.* [17]. Similarly, Naka *et al.* found digital fabrication to produce accurate RPD frameworks, potentially lowering fracture risk [18]. From a clinical perspective, proper repair protocols also contribute to denture longevity. Chladek *et al.* emphasized that surface treatments and standardized repair methods improve PMMA strength [19]. In addition, graphene-modified PMMA and nanocomposites offer promising improvements in flexural and impact performance, though further long-term studies are required [13, 20]. Overall, the current findings align with contemporary research: midline and clasp failures remain the most common, parafunctional habits are a major modifiable risk, and reinforcement and design optimization are crucial preventive strategies.

This study was limited by its cross-sectional design, which restricts causal inference, and by its single-center sampling, which may affect generalizability. Certain factors such as occlusal schemes, material variations, and laboratory processing techniques were not evaluated but could influence fracture risk. Additionally, multivariate analysis was not performed due to the descriptive design,

which limits the ability to control confounding variables. Future studies incorporating objective bruxism assessment, digital design accuracy, and standardized reinforcement protocols across larger cohorts could refine clinical recommendations.

CONCLUSIONS

This study evaluated the frequency and distribution of fracture patterns in acrylic partial dentures and their association with clinical and demographic factors. Midline fractures were the most frequent, followed by clasp-related fractures, reflecting areas of highest stress concentration. A significant link between parafunctional habits and fracture pattern indicates that behavioral factors play a key role in denture failure. Although reinforcement showed a borderline protective effect, other variables such as gender, Kennedy classification, duration of use, and ridge resorption were not significant. These findings underscore the need to screen for parafunctional habits and incorporate reinforcement strategies during denture fabrication to reduce fracture risk and enhance prosthesis longevity.

Authors' Contribution

Conceptualization: FI

Methodology: MAC, FH, AS, JA

Formal analysis: FH, AS

Writing and Drafting: FI, FH, SA, AS, JA

Review and Editing: FI, MAC, FH, SA, AS, JA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Association of Postoperative Hyperbilirubinemia and Infection Among Patients Undergoing Emergency Exploratory Laparotomy for Gastrointestinal Perforation at Tertiary Care Hospital Karachi

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ABSTRACT

Patients presenting to the surgery emergency room complaining of severe abdominal discomfort are often patients with gastrointestinal perforations. In the developing world, there are differences in incidence, site of perforation, aetiology, and demographics. Because of the distinct pathophysiologies associated with elevated levels of direct bilirubin (D-Bil) and indirect bilirubin (I-Bil), the consequences related to these two forms of bilirubin are likewise distinct.

Objectives: To determine the association of postoperative hyperbilirubinemia and infections among patients undergoing emergency exploratory laparotomy for gastrointestinal perforation at Tertiary Care Hospital, Karachi. **Methods:** This prospective cohort study utilized a non-probability convenience sample in a one-year cohort study that took place at the Department of Surgery, Dr. Ruth K.M. Pflua Civil Hospital in Karachi. The SPSS software (version 26) was used for data processing. The t-test was applied, and the p-value was determined to be less than or equal to 0.05. **Results:** Postoperative infection showed that in the patients who were in the exposed and unexposed groups, 24 (48%) and 15 (30%) had postoperative infection. P-value was 0.006 with a relative risk of 1.60. Mortality showed that in the patients who were in the exposed and unexposed group, 13 (26%) and 02 (4%) had mortality. P-value was 0.001 and a margin of relative risk 6.50. **Conclusions:** The results show that patients with GI perforation who experience postoperative hyperbilirubinemia are more likely to have persistent postoperative infection and have a worse prognosis.

INTRODUCTION

Perforation of the gastrointestinal tract (GIT) is a common medical emergency that is associated with a significant mortality rate (between 30 and 50%) [1]. Acute severe abdominal pain, odynophagia, and vomiting are some of the

symptoms that can accompany perforations of the oesophagus, gastric duodenum, and colon, respectively [2]. Perforations of the colon often develop more slowly and can lead to secondary bacterial peritonitis or localized



abscesses. Some individuals may have delayed symptoms, an abscess that looks like a lump in the abdomen, or sepsis, according to references. Enquire about past episodes of similar pain and any predisposing factors when reviewing a patient's medical history [3-5]. These include things like a history of stomach trauma, foreign bodies in the stomach, peptic ulcer disease, certain medications (especially NSAIDs), and previous surgeries or instrumentation [6]. Many factors can contribute to a bad prognosis, including lower GI tract perforation, advanced age, delayed diagnosis, organ failure, and the presence of comorbid conditions like diabetes and cancer [7]. When organ failure occurs alongside peritonitis or sepsis, the death rate for patients with these conditions increases. Infectious diseases account for the vast majority of ICU deaths [8]. Morbidity in patients with gastrointestinal perforation is also greatly impacted by it. Multiple organ failure may be a risk factor for this condition, which is believed to be partially mediated by inflammatory cytokines [9]. Additionally, bilirubin and bile acid output in the biliary system were both reduced due to biliary tract infection. Serum bilirubin levels tend to rise after invasive surgeries such as cardiopulmonary bypass and esophageal cancer surgeries, which are considered surgical insults [10]. The exact reason for postoperative hepatic injury is yet unknown, although factors such as reduced blood flow to the liver, infections, medications, anesthetic agents, and excessive inflammatory cytokines are thought to have a role [11]. Hyperbilirubinemia can develop after surgery for generalized peritonitis, although little is known about the causes or prognosis for this condition [12].

We aimed to fill the data gap by studying patients in our area who had emergency exploratory laparotomy for gastrointestinal perforation. We wanted to know if there was a correlation between postoperative hyperbilirubinemia and in-hospital outcomes. Early postoperative evaluation of hyperbilirubinemia is crucial since it is a risk factor for poor patient outcomes. This study aimed to determine the association of postoperative hyperbilirubinemia and infections among patients undergoing emergency exploratory laparotomy for gastrointestinal perforation at Tertiary Care Hospital, Karachi.

METHODS

This prospective cohort study utilized a non-probability convenience sample and was conducted at the Department of Surgery, Dr. Ruth K.M. Pua Civil Hospital in Karachi from July 2021 to July 2022. The study was approved by the Research Evaluation Unit of, College of Physicians and Surgeons of Pakistan (Ref. No. CPSP/REU/SGR/2017-183-9254). The study used a non-probability convenience sampling technique. The 95%

two-sided significance level (1-alpha) and 95% power were used for the computation of the sample size. Mortality in the exposed group was 59% and 4% in the unexposed group [13]. The total sample size calculated was 26 (13 in each group). To overcome non-responders and incomplete responses, we have added 50 patients in each group, for a total of 100 patients in this study. Inclusion criteria consisted of patients undergoing emergency exploratory laparotomy for gastrointestinal perforation were included, and patients developing hyperbilirubinemia were grouped into the exposed group, and those who did not develop hyperbilirubinemia were grouped in the unexposed group, either gender having age of 30-70 years. Participants who did not give their informed consent were not included in the study. Neither were patients who had a recent infection (such as pneumonia, UTI, or cellulitis), those who had hypothyroidism or hyperthyroidism in their medical history, anyone with a preexisting condition that can hinder thyroid function, such as a history of stroke, renal impairment, COPD, asthma, cirrhosis of the liver, heart failure, or any other similar illness. Each patient's signed informed consent was obtained before any data was gathered. We collected basic demographic information (gender, age, and residency status) from the past. When participants were first included in the study following surgery, A wall-mounted scale was used to measure their height in meters, and a weighing machine was used to measure their weight to the closest kilogramme. A person's BMI was subsequently determined. Patients with and without postoperative hyperbilirubinemia after emergency exploratory laparotomy for gastrointestinal perforation (confirmed on abdominal x-ray showing right upper quadrant sub diaphragmatic free air) were evaluated by the presence of any one or more of the following postoperative outcomes: Postoperative infection: Patients with deep infections affecting structures deeper than the fascial and muscular layers, organ/space infections affecting structures deeper than the skin and subcutaneous tissue, or superficial infections involving the skin and subcutaneous tissue infection that develops within seven days after surgery together with any of the following was classified as postoperative infection. Fever ($>38^{\circ}\text{C}$), Localized pain (VAS >2), Erythema (red area apparent on clinical examination) and purulent drainage from the skin incision site. Mortality: Patients were followed till discharge and if death occurred within 7 days of surgery it was labeled as mortality using Clavien-Dindo (CD) grades V. Patients undergoing emergency exploratory laparotomy for gastrointestinal perforation and developing serum bilirubin $\geq 5\text{mg/dl}$ within 48 hours of surgery were labeled postoperative hyperbilirubinemia. Patients undergoing emergency exploratory laparotomy for gastrointestinal

perforation and developing postoperative hyperbilirubinemia within 48 hours of surgery were labeled as the exposed group, and those who did not develop postoperative hyperbilirubinemia within 48 hours of surgery and during hospital stay were labeled as the unexposed group. Input and analysis were carried out using SPSS version 26.0. Means and standard deviations were computed for continuous variables such as age, height, weight, body mass index, and surgery time. Frequencies and percentages were calculated for categorical factors like gender. A statistically significant result was determined by comparing the two groups using a t-test, where a p-value less than 0.05 was employed. After stratification (with projected frequencies fewer than 5), a chi-square test was utilized; a $p \leq 0.05$ was deemed statistically significant, and the relative risk was calculated.

RESULTS

The present study showed descriptive statistics of the exposed and unexposed groups, whereas in both groups, patients' ages ranged from thirty to seventy years. With a standard deviation of ± 6.24 , the average age of patients in the exposed group was 47.21 years. In contrast, the average time spent in surgery was 2.28 ± 1.47 hours, the average body mass index was 29.58 ± 3.97 kg/m², the average height was 147 ± 4.21 cm, and the average weight was 71.7 ± 7.25 kg. Like the exposed group, the unexposed group had 50 patients with an average age of 52.48 years and a standard deviation of ± 8.41 . On the other hand, the average time spent in surgery was 2.16 ± 1.71 hours, the average body mass index was 30.14 ± 2.51 kg/m², the average height was 158 ± 5.28 cm, and the average weight was 78.7 ± 9.87 kg (Table 1).

Table 1: Descriptive Statistics of the Exposed and Unexposed Groups

Variables	Exposed Group (Mean $\pm$ SD)	Unexposed Group (Mean $\pm$ SD)	Range (Min-Max)
Age (Years)	47.21 $\pm$ 6.24	52.48 $\pm$ 8.41	30-70
Duration of surgery (Hours)	2.28 $\pm$ 1.47	2.16 $\pm$ 1.71	1-4
BMI (Kg/m ²)	29.58 $\pm$ 3.97	30.14 $\pm$ 2.51	26-34
Height (Cm)	147 $\pm$ 4.21	158 $\pm$ 5.28	138-172
Weight (Kg)	71.7 $\pm$ 7.25	78.7 $\pm$ 9.87	68-115

Out of 50 patients in the exposed group, 39 (78%) were male and 11 (22%) were female, according to the frequency distribution of gender. In the unexposed group, however, 41 (82%) were male and 09 (18%) were female. The results showed that out of 50 patients in the exposed group, 30 (60%) lived in an urban area, while 20 (40%) lived in a rural area. In contrast, 28 (56%) of the unexposed group's patients were from urban areas, and 22 (44%) were from rural areas. In the exposed group, 14 people (28%) had type

II diabetes mellitus, whereas 36 people (72%) did not; in the unexposed group, 8 people (16%) had type II diabetes, and 42 people (84%) did not. Similarly, 18 people (36%) in the exposed group experienced hypertension, while 32 people (64%) did not. Despite this, hypertension was present in 9 cases (18%) and non-existent in 41 cases (82%). In the exposed group, 19 people (or 38% of the total) smoked, while 31 people (or 62% of the total) did not. In contrast, 24 (48%) and 26 (52%), respectively, of the 50 patients in the unexposed group smoked and did not smoke (Table 2).

Table 2: Demographic Characteristics in Exposed and Unexposed Groups

Variables	Exposed Group	Unexposed Group
Male	39 (78%)	41 (82%)
Female	11 (22%)	09 (18%)
Urban Residence	30 (60%)	28 (56%)
Rural Residence	20 (40%)	22 (44%)
Diabetes Mellitus Type II (Yes)	14 (28%)	8 (16%)
Diabetes Mellitus Type II (No)	36 (72%)	42 (84%)
Hypertension (Yes)	18 (36%)	9 (18%)
Hypertension (No)	32 (64%)	41 (82%)
Smoking (Yes)	19 (38%)	24 (48%)
Smoking (No)	31 (62%)	26 (52%)

Assessment of postoperative infection showed that in the patients who were in the exposed and unexposed groups, 24 (48%) and 15 (30%) had postoperative infection. ($p=0.006$) and relative risk was 1.60. Frequency of mortality showed that in the patients who were in the exposed and unexposed group, 13 (26%) and 02 (4%) had mortality ($p=0.001$), where a relative risk was 6.50 (Table 3).

Table 3: Postoperative Infection and Mortality in the Exposed and Unexposed Groups

Variables	Exposed Group	Unexposed Group	p-value	Relative Risk
Mortality				
Yes	13 (26%)	02 (4%)	0.001	6.50
No	37 (74%)	48 (96%)		
Postoperative Infection				
Yes	24 (48%)	15 (30%)	0.006	1.60
No	26 (52%)	35 (70%)		

Stratification for age with respect to postoperative infection showed that in the patients who were in 30-50 years age group 18 (36%) and 13 (26%) had postoperative infection in the exposed and unexposed group accordingly (p -value 0.002) and relative risk was 1.91 and in patients who were in 51-70 years age group 06 (12%) and 02 (4%) in the exposed and unexposed group had postoperative infection respectively (p -value 0.034). with a relative risk of 0.56. Stratification for gender with respect to postoperative infection showed that in the patients who were in male group 17 (34%) and 10 (20%) had postoperative infection in

the expose and unexposed group respectively (p-value 0.006) and those who were in female group 07(14%) and 05 (10%) in the expose and unexposed group had postoperative infection respectively (p-value 0.071) having relative risk was 1.14 (Table 4).

Table 4: Postoperative Infection in The Exposed and Unexposed Groups According to Age and Gender

Variables	Exposed Group		Unexposed Group		p-value	Relative Risk
	Yes (%)	No (%)	Yes (%)	No (%)		
Age (Years) 30-50	18 (36%)	16 (32%)	13 (26%)	34 (68%)	0.002	1.91
51-70	06 (12%)	10 (20%)	02 (4%)	01 (2%)	0.034	0.56
Male	17 (34%)	22 (44%)	10 (20%)	31 (62%)	0.006	1.78
Female	7 (14%)	4 (8%)	5 (10%)	4 (8%)	0.071	1.14

The exposed group demonstrated higher postoperative infection (48% vs. 30%) and substantially higher mortality (26% vs. 4%) compared to the unexposed group. Relative risk estimates indicate a 1.60-fold increased risk of postoperative infection and a 6.50-fold increased risk of mortality among patients with hyperbilirubinemia (Table 5).

Table 5: Hyperbilirubinemia and Postoperative Outcomes

Group	Number of Patients	Postoperative Infection (%)	Mortality (%)	Relative Risk for Infection	Relative Risk for Mortality
Exposed Group	50	24 (48%)	13 (26%)	1.60	6.50
Unexposed Group	50	15 (30%)	02 (4%)	N/A	N/A

DISCUSSIONS

The results on the topic of postoperative hyperbilirubinemia and its relationship with poor outcomes are consistent with the findings of other clinical studies. Just like previous reports [14], postoperative hyperbilirubinemia is common in the aftermath of emergency gastrointestinal surgery and is more exaggerated among patients with sepsis or systemic inflammatory reactions. In those patients who developed postoperative hyperbilirubinemia, there were increased infections and increased length of stay, and this is consistent with findings in earlier clinical cohorts [3]. Gastrointestinal perforations cause a high number of acute abdomen emergencies, and may be secondary to a wide range of diseases, trauma, diagnostic or treatment procedures [15]. Gastrointestinal perforations have a high mortality and morbidity rate because of the various complications they may cause, such as septicaemia, diffuse peritonitis, metabolic and circulatory instabilities, renal failures, as well as pulmonary insufficiency. Such complications are aggravated by the variables, including old age and lag in the treatment procedures. Postoperative hyperbilirubinemia is one of the frequent postoperative complications and is associated with poor prognosis [16]. The total bilirubin is based on two factors: direct bilirubin

(D-Bil) and indirect bilirubin (I-Bil). Symptoms of hepatocyte excretory failure include cholestasis in the case of sepsis, hypoxic hepatocyte damage, and drug-induced hepatic injury, which is indicated by high D-Bil. The other ailments associated with high levels of I-Bil include haemolysis and blood transfusion reactions. D-Bil and I-Bil can be linked to clinical outcomes differently because they have different pathophysiologies [17]. Patients in the exposed group had 24 (48%) and those in the unexposed group had 15 (30) cases of postoperative infection (p=0.006). Death used in 13 (26%) out of the exposed group and 2 (4) out of the unexposed group. It has also been reported that the prevalence of postoperative infection (77% vs 9%) and mortality (59% vs 4%) in patients developing as opposed to not developing postoperative hyperbilirubinemia [18]. The potential causes of postoperative hyperbilirubinemia may include surgical injury, infection, too much bleeding, transfusion, and natural liver dysfunction after major surgery. Patients subjected to thoracic surgery on the esophagus even without infection can have an elevation in their levels of blood bilirubin and inflammatory cytokines post-surgery as a result of surgical shock. One trial demonstrated perioperative steroids as reducing this effect. It has been postulated that metabolism of bilirubin is altered and increased following major operations. Factors linked to postoperative hyperbilirubinemia in the scenario of generalized peritonitis as a result of gastrointestinal perforation included advanced age, poor nutritional condition, decreased base loss, postoperative infection, delay before surgery, greater serum total bilirubin level preoperative, and longer time delay preoperative [19]. The relationship between serum bilirubin level in the preoperative period and the time interval between perforation and surgery, and the fact that the incidence of predisposing liver illnesses in both groups was similar, provides evidence that the advanced form of peritonitis was the cause of elevated serum bilirubin level before surgery [11]. Poor nutrition before elective surgery predisposes one to the occurrence of complications following the surgery. This would result in a high morbidity and mortality rate in the form of relative increases in bacterial and surgical insults, poor nutrition, old age, and delays between perforation and surgical operation. Patients who experienced preoperative shock (P<0.001) had higher levels of lactic dehydrogenase and aspartate aminotransferase at the preoperative stage, which means that inadequate systemic circulation is the probable cause, but not the exact cause. These research findings support previous studies that relate postoperative infection to hyperbilirubinemia and mortality [20]. Hyperbilirubinemia patients suffered a higher mortality rate (59%) as

compared to their counterparts (4%). During the three to five days post-surgery, the level of blood bilirubin decreased in hyperbilirubinemia patients who survived, but it was stable in those who died. The following factors were found to increase the postoperative mortality probability: hyperbilirubinemia ($p < 0.001$), postoperative infection ($p = 0.005$), preoperative shock ($p = 0.003$), and decreased platelet count ($p = 0.015$) [21, 22]. The mortality rate of gastroduodenal perforation reported in most studies is approximately 5%-6% which has ranged between 0-18. The 30-day mortality rate of gastric cancer-induced perforation was between 7% and 20%, whereas that of colorectal perforation, the most adverse outcome, was between 12% and 22%. The outcomes of this research (16%) cannot be significantly different from these numbers [2]. Advanced age, postoperative shock, delayed surgery, and the conditions of comorbidity with severe illnesses like diabetes or renal failure are considered adverse prognostic factors of gastroduodenal and colorectal perforations. The use of a non-probability convenience sample may introduce selection bias and limit the generalizability of the findings. Additionally, the relatively short follow-up period restricted assessment of long-term postoperative outcomes and complications. Future studies with larger, randomly selected cohorts and extended follow-up are recommended to validate these findings and evaluate long-term postoperative effects.

CONCLUSIONS

Factors associated with hyperbilirubinemia in the setting of generalised peritonitis caused by gastrointestinal perforation include advanced age, poor nutritional status, a reduction in the base excess, a length of time until surgical intervention, and complications following surgery related to infection. There was an increased risk of complications and death for patients who developed postoperative hyperbilirubinemia. Improving surgical infection control is crucial, as these findings indicate a clear correlation between postoperative hyperbilirubinemia and infection and poor prognosis in patients with GI perforation. Postoperative hyperbilirubinemia was significantly associated with postoperative infection and prolonged hospitalization, suggesting its potential role as a marker of disease severity and postoperative stress response, rather than a proven independent predictor.

Authors' Contribution

Conceptualization: QUAA

Methodology: QUAA, MN

Formal analysis: QUAA, SSA

Writing and Drafting: SJ, MKL, ITK, DS

Review and Editing: QUA, SSA, MN, SJ, MKL, ITK, DS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Antibacterial Efficacy of Cinnamon Essential Oil Compared to Standard Antibiotics on Diabetic Foot Ulcer Isolates at Tertiary Care Units Karachi, Pakistan

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ABSTRACT

Lower limb complications associated with Type II Diabetes have become a serious public health issue in today's world. Diabetic patients with ulcers commonly experience infection due to Gram-positive, Gram-negative bacteria, as well as some anaerobes. **Objectives:** To investigate the antibacterial activity of Cinnamon essential oil on microbial isolates from diabetic foot ulcer. **Methods:** An experimental investigation was carried out on diabetic patients suffering from foot ulcers. A total of 115 pus swab samples from diabetic foot ulcer patients were acquired, who were recruited and processed at Baqai Institute of Diabetology and Endocrinology. Antibiotic sensitivity testing was performed by the Kirby agar Disc diffusion method. Antibacterial activity of cinnamon essential oil was checked by the Kirby agar well diffusion method. **Results:** Out of 115 samples, 138 bacteria were isolated. 80% of samples were mono-microbial and 20% were poly-microbial. *Pseudomonas Aeruginosa* was the most frequently encountered bacterium, followed by *E. Coli*, *S. Aureus*, *Klebsiella Pneumoniae*, *Proteus Mirabilis*, *Enterococcus* species, Coagulase-negative *Staphylococcus* Species, and *Proteus Vulgaris*. All the isolated bacteria showed different resistance patterns against commercially available antibiotics. Cinnamon essential oil showed antibacterial activity against all isolated bacteria. **Conclusions:** The study demonstrated a high bacterial isolation rate from diabetic foot ulcer. Antibiotic resistance varied among bacterial isolates, highlighting the challenge of treating bacterial infections. Cinnamon essential oil exhibited strong antibacterial activity against all isolated bacteria, suggesting its potency of being used as an alternative antimicrobial agent.

INTRODUCTION

Diabetes is a chronic illness that develops when insulin is not produced in an adequate amount in the body, or it becomes resistant to its effects, or a combination of both, and has serious health issues, affecting millions of individuals worldwide [1, 2]. The dysfunction of insulin action, whether due to insufficient production or resistance, results in the onset of Type I and Type II diabetes, respectively. In type II diabetes, Lower limb

complications are rising worldwide wide which include diabetic foot ulcers, infections, and even amputations, particularly in underdeveloped countries [3, 4]. Limited access to quality healthcare, poor diabetes management, and lack of awareness contribute to the increasing burden of these conditions. Without timely intervention, lower limb complications can significantly affect a patient's lifestyle and put the patient under financial strain for



affording higher expenses for management of lower limb complications [5, 6]. Peripheral neuropathy, along with macrovascular and microvascular complications, plays an important role in increasing the risk of diabetic foot ulcers. Additionally, the duration of diabetes and traumatic injuries further contributes to the development of these ulcers [7]. Most Gram-positive bacteria, *S. Aureus*, *Enterococcus* species, Gram-negative bacteria, including *Pseudomonas aeruginosa*, *E. coli*, *Klebsiella* species, *Proteus* species, as well as certain anaerobes are responsible for developing diabetic foot ulcers [8]. The delayed wound healing in Diabetic patients presents various complex pathological processes that interfere with the normal healing process, which tends to be a challenge for clinicians [9, 10]. In these patients, chronic hyperglycaemia causes microvascular damage, neuropathy, and immune dysfunction, all of which result in hindrance to the normal healing process [11, 12]. Specific features of diabetic wounds are associated with delayed healing, poor blood vessel formation, reduced collagen synthesis, and a high risk of infection, resulting in prolonged, non-healing ulcers. Current treatments for diabetic wounds mainly aim to control blood sugar, prevent infection, and relieve pressure on the wound area [13]. Despite the use of currently available antibiotics, diabetic foot ulcers often show poor response and repeated occurrence. Due to these facts, there is an urgent need for novel therapeutic approaches. Use of natural products with anti-inflammatory, antioxidant and healing and healing properties [14]. The quality of Cinnamon to cure wounds has already been studied in many recent studies, but none of them specifically demonstrate cinnamon's ability to heal wounds in diabetic conditions. It is observed that Cinnamon essential oil has strong antimicrobial and antioxidant effects, due to higher content of compounds like cinnamaldehyde. Cinnamon verum (commonly known as cinnamon) is a highly effective medicinal plant belonging to the Lauraceae family. Cinnamon essential oils can be extracted from leaves, fruits, and bark of the plants, which are known for their therapeutic and pharmacological properties [15]. Due to its multifaceted medicinal benefits, cinnamon continues to be explored as a natural remedy for various metabolic, infectious, and inflammatory conditions in both traditional and modern medicine [16]. Cinnamon extracts, essential oils, and their compounds have been reported to inhibit bacteria by damaging cell membranes; inhibiting cell division, membrane porins, and biofilm formation; and via anti-quorum-sensing effects. In view of the above-mentioned properties of cinnamon essential oil, the current study will be conducted to find out the antibacterial activity of cinnamon essential oil against isolated bacteria of DFU. Standard antibiotics refer to those antibiotics that are commonly used by physicians to

treat infection and are also used in microbiology laboratories for antibacterial susceptibility testing.

Diabetic foot ulcers are frequently complicated by resistant bacterial infections and delayed healing, highlighting the need for alternative antimicrobial agents. Limited evidence exists regarding the antibacterial efficacy of cinnamon essential oil specifically against bacterial isolates from diabetic foot ulcers. This study aimed to check the antibacterial activity of cinnamon essential oil against isolated bacteria from diabetic foot ulcer patients and compare it with standard antibiotics.

METHODS

This in vitro comparative experimental study was conducted at Baqai Institute of Diabetology and Endocrinology. The research work was conducted over a period of nine months (April 2023 to January 2024) on 115 active diabetic foot ulcer patients. The study was approved by the Ethics Committee (Ref: BMU-EC/01-2023) of Baqai Medical University, Karachi, and the Board of Advanced Studies and Research (BASR), Baqai Medical University, Karachi, in accordance with the international guidelines outlined in the 2008 WMA Declaration of Helsinki for Medical Research involving Human Participants. The samples were collected and processed by simple techniques used in microbiology studies. These individuals, having been diagnosed as diabetic foot ulcer patients with type II diabetes and who did not receive systemic and topical antibiotics or other medications, including steroids, from 24 to 72 hours, were included in this study. Pus samples were collected from these patients, bacteria were isolated and grown, and both different standard antibiotics and cinnamon essential oils were used to check their antibacterial activity against these isolated bacteria. Patients who had received systemic and topical antibiotics and other medicines, including steroids, for 24 to 72 hours were excluded from this study. Patients having diabetes other than type II were also excluded from this study. The calculated Sample size was 115 by using Open Epi Version 3.0.1, named as Open-Source Epidemiologic Statistics for Public Health [17]. Samples were collected from diabetic patients after obtaining their consent. A pus sample was collected from subjects by a sterile amine transport swab. The sample was inoculated on Sheep Blood Agar, McConkey Agar, and Chocolate Agar medium and incubated at 37°C for 24-48 hours according to Clinical Laboratory Standardization Institution (CLSI). After 48 hours, bacterial growth was observed. Identification was carried out by evaluating the appearance of colonies by Gram staining. Biochemical tests were conducted for the identification of isolated bacterial pathogens according to the protocol described by CLSI guidelines. All isolated bacteria isolated from Diabetic

Foot Ulcers were divided into two broad groups: mono-microbial isolates and poly-microbial isolates. They were further divided into Gram-positive and Gram-negative bacteria. Antibacterial activity of all the standard antibiotics and cinnamon essential oil was determined by measuring the zone of inhibition. By the disc diffusion method, Antimicrobial Susceptibility Testing (AST) was performed. 0.5 MCF suspension of bacterial colony was prepared and was made uniform by spreading on Muller-Hinton Agar (MHA) medium and incubated at 37°C for 24 hours. After 24 hours, the zone of inhibition was measured and compared with the standard zone of inhibition as described by CLSI guidelines. Commercially available Cinnamon essential oil was purchased and sent to the PCSIR Laboratory Karachi to check purity with the designated Sr No PCSIR KLC 5022069. Cinnamon essential oil was used in various dilution forms, from high to low dilution. Dilution forms of cinnamon essential oil used in the study were 2.5 mg/ml, 5.0mg/ml, 10.0mg/ml, 20.0mg/ml, and 40.0mg/ml. Cinnamon essential oil was diluted in Propylene glycol as done in a previous study [18]. Antibacterial sensitivity of Cinnamon essential oil was performed by the Kirby-Bauer agar well diffusion method. A diluted sample of Cinnamon essential oil was poured by an adjustable micro pipette into the wells designed in the MHA media plate. After adding cinnamon essential oil, the plates were incubated at 37°C for 24 hours. After 24 hours, the zone of inhibition was measured. The sensitivity of cinnamon essential oil was calculated by measuring the increase in zone of inhibition by serial dilution from a lower concentration to a higher concentration. No statistical analysis software was used to interpret the results; it was a simple comparative study in which the antibacterial activity was observed by measuring and comparing the zone of inhibition in which the zone of inhibition of the standard antibiotic with that of cinnamon essential oil against the bacteria isolated from diabetic foot ulcer patients.

RESULTS

All specimens showed growth of bacteria. Samples collected from 92 patients showed mono-microbial growth, and samples collected from 23 patients showed poly-microbial growth. Out of 115 collected specimens, a total of 138 bacterial species were isolated, of which 36 (25.94%) were gram-positive and 102 (73.73%) were gram-negative organisms. Gram-negative bacteria, *Pseudomonas Aeruginosa*, showed maximum prevalence in the isolates of DFU (Table 1).

Table 1: Distribution of Organisms Isolated from Diabetic Foot Ulcer Patients

Isolated Organism		Frequency (%)
Total Sample	—	115
Mono-microbial isolates	—	92 (80%)
Polymicrobial isolates	—	23 (20%)
Total bacterial Isolates	—	138
Gram Positive Bacteria	<i>Staphylococcus Aureus</i>	20 (14.4%)
	Coagulase-negative <i>Staphylococcus</i> Species (CONS)	02 (1.44%)
	<i>Enterococcus</i> Species	14 (10.1%)
Gram-negative Bacteria	<i>Pseudomonas Aeruginosa</i>	43 (31.1%)
	<i>E. coli</i>	29 (21.01%)
	<i>Klebsiella Pneumoniae</i>	19 (13.7%)
	<i>Proteus Mirabilis</i>	10 (7.2%)
	<i>Proteus Vulgaris</i>	01 (0.72%)
Methicillin-sensitive <i>Staphylococcus Aureus</i> (MSSA)	—	12
Methicillin-resistant <i>Staphylococcus Aureus</i> (MRSA)	—	08

Commercially available antibiotics show different sensitivity results. It is observed that Meropenem, Imipenem, and linezolid were the most sensitive antibiotics against isolated bacteria (Table 2).

Table 2: Antibiotic Profile of Gram-Negative Bacteria Isolated from Wounds of Diabetic Foot Ulcer

Antibiotics	P. Aeruginosa		P. Mirabilis		P. Vulgaris		E. Coli		K. Pneumoniae	
	S	R	S	R	S	R	S	R	S	R
Ampicillin	—	—	0	10	0	1	—	—	—	—
Amoxil/Clavulanic Acid	11	32	0	10	0	1	19	10	4	15
Piperacillin/Tazobactam	23	20	2	8	0	1	19	10	6	13
Ceftriaxone	39	4	0	10	0	1	19	10	4	15
Cefuroxime	39	4	0	10	0	1	19	10	4	15
Cefixime	25	19	0	10	0	1	19	10	4	15
Cefepime	25	19	0	10	0	1	—	—	—	—
Meropenem	25	19	9	1	1	0	1	28	19	0
Imipenem	10	33	9	1	1	0	1	28	19	0
Gentamicin	10	33	6	4	1	0	10	19	13	6
Amikacin	23	20	6	4	1	0	10	19	13	6
Tobramycin	11	32	6	4	1	0	10	19	13	6
Levofloxacin	23	20	4	6	0	1	13	16	10	9
Ciprofloxacin	39	4	4	6	0	1	13	16	10	9
Co-troximazole	39	4	4	6	0	1	13	16	10	9
Ceftazidime	25	19	4	6	1	0	—	—	—	—
Doxycycline	—	—	4	6	1	0	13	16	15	4
Polymyxin B	—	—	—	—	—	—	—	—	—	—
Colistin	4	0	1	0	—	—	1	0	—	—

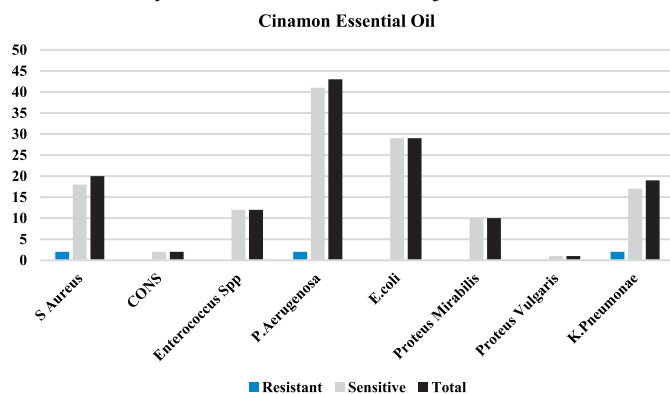
Commercially available antibiotics show different sensitivity results (Table 3).

Table 3: Antibiotic Profile of Gram-Positive Bacteria Isolated from Wounds of Diabetic Foot Ulcers

Antibiotics	S. Aureus		CONS		Enterococcus species	
	S	R	S	R	S	R
Ampicillin	—	—	—	—	11	3
Cefoxitin	12	8	2	0	—	—
Ciprofloxacin	12	8	2	0	—	—
Co-troximazole	12	8	2	0	—	—
Erythromycin	12	8	2	0	4	10
Clindamycin	12	8	2	0	4	10
Linezolid	20	0	2	0	—	—
Fusidic Acid	11	9	2	0	—	—
Doxycycline	12	8	2	0	—	—
Vancomycin	8	0	—	—	14	0

S= Sensitive, R= Resistant

Cinnamon essential oil shows a wide range of antibacterial activity against different isolated bacteria compared to commercially available antibiotics (Figure 1).

**Figure 1:** Antibacterial Potential of Cinnamon Essential Oil Against Bacteria Isolated from Diabetic Foot Ulcer Patients

DISCUSSION

Among the complications related to diabetes, Diabetic foot ulcer (DFU) is one of the most frequently occurring. Patients with peripheral neuropathy (PN) and peripheral vascular diseases (PVD) are more vulnerable to developing foot problems such as ulcers, infection, and if the condition is not managed properly, then it would lead to amputation. PN and PVD are one of the prevalent causes of non-traumatic lower limb amputation. DFU is influenced by several risk factors like neuropathy, vasculopathy, immunopathy, mechanical stress, and neuroarthropathy. These factors cause low blood flow and tissue hypoxia in various body parts, leading to a weak immune response toward pathogenic organisms, which then delays healing of tissues [19]. Various studies have conducted evaluations of the pathogenic profile of diabetic foot ulcer (DFU) patients, among which some have identified the presence of both mono-microbial and poly-microbial infections in the subjects included in those studies. The bacterial organisms isolated in previous studies include both Gram-

positive and Gram-negative organisms. The Gram-negative bacteria include species of *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus species*, *Klebsiella pneumoniae*, *Acinetobacter*, and *Enterobacter species* are among the gram-negative bacteria which have been frequently observed. Meanwhile, the Gram-positive bacteria identified include *Staphylococcus aureus* and various *Streptococcus species*. These findings highlight the diverse microbial landscape associated with DFU infections [20, 21]. In the present study, researchers collected a total of 115 samples from diabetic foot ulcers. Out of 115 samples, 92 samples (88%) were found to be mono-microbial, and 23 were found to be poly-microbial. A total of 138 bacteria were obtained from 115 patients. Different bacterial species were isolated from diabetic foot ulcer patients. Gram staining, colony morphology, and various biochemical tests were used to identify the bacterial isolates. The predominant bacteria isolated were *P. aeruginosa* found in 31.1% followed by *E. coli* 21.01%, *Staphylococcus Aureus* 14.4%, *Klebsiella Pneumoniae* 13.7%, *Enterococcus species* 10.1%, *Proteus Mirabilis* 7.2%, Coagulase-negative *staphylococcus species* 1.44% and *Proteus Vulgaris* found in 0.72%. Our findings are in alignment with the results reported by Singh et al. [15]. The authors reported a predominant prevalence of *P. aeruginosa* (27.3%) followed by *S. Aureus*, *E. coli*, *Proteus species*, and *Klebsiella species* in Diabetic Foot Ulcers (DFU). Our results are also supported by the findings of Naeem et al. and Miyan et al. which reported the presence of *S. aureus*, *S. epidermitis*, *Proteus species*, *Enterococcus species*, and *Klebsiella species* in the DFU samples [22, 23]. The antibiotic susceptibility profile of organisms isolated from diabetic foot ulcers exhibits varying resistance patterns. Previous studies have also reported the presence of methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant (MDR) bacteria. Among the antibiotics tested, linezolid (LZD) and vancomycin (VA) were found to be the most effective against Gram-positive bacteria, while meropenem (MEM) demonstrated the highest sensitivity against Gram-negative bacteria. Conversely, the most resistant antibiotics were penicillin G for Gram-positive isolates and amoxicillin-clavulanate (AMC) and trimethoprim-sulfamethoxazole (SXT) for Gram-negative isolates. These findings emphasize the need for continuous surveillance of antibiotic resistance patterns to guide effective treatment strategies for diabetic foot infections [24]. In the current study, antibiotic susceptibility testing showed different resistance patterns against these isolated bacterial species. Methicillin-resistant *Staphylococcus Aureus* (MRSA) and multidrug-resistant (MDR) organisms were found in 08 and 06 isolated organisms, respectively. All the bacterial isolates showed a

significant resistance pattern towards most of the antibiotics. *Pseudomonas Aeruginosa* showed high resistance rates toward Ciprofloxacin and Levofloxacin and was sensitive toward Meropenem and Imipenem. *E. coli* resistance rates were at the highest percent toward Amoxil/Clavulanic Acid, Piperacillin/Tazobactam, Ceftriaxone, Cefuroxime, and Cefixime, and were sensitive toward Meropenem and Imipenem. *Staphylococcus Aureus* shows a higher sensitivity rate toward Linezolid. Many traditional remedies have already been tested against different bacteria isolated from various infections to overcome the resistance of antibiotics against many bacteria. Considering these promising findings, the present research was conducted to assess the antibacterial activity of cinnamon essential oil. This investigation explored their potential as effective antimicrobial agents, which may contribute to the development of alternative therapeutic approaches for combating bacterial infections. In the present research project, Cinnamon essential oil was tested against bacteria isolated from diabetic foot ulcer patients in different dilutions. Cinnamon essential oil gives a maximum zone of 25mm against sensitive bacteria. Cinnamon essential oil inhibited the growth of *E. Coli*, *Proteus Mirabilis*, *Proteus Vulgaris*, *Enterococcus* species by 100%, *S. Aureus* was inhibited by 90%, *Pseudomonas Aeruginosa* by 95% and *Klebsiella Pneumoniae* was inhibited by 89%. Considering these promising findings, the present study was conducted to assess the antibacterial activity of cinnamon essential oil. This investigation explored their potential as effective antimicrobial agents, which may contribute to the development of alternative therapeutic approaches for combating bacterial infections. In the present study, Cinnamon essential oil was tested against bacteria isolated from diabetic foot ulcer patients in different dilutions. Cinnamon essential oil gives a maximum zone of 25mm against sensitive bacteria. Cinnamon essential oil inhibited the growth of *E. Coli*, *Proteus Mirabilis*, *Proteus Vulgaris*, *Enterococcus* species by 100%, *S. Aureus* was inhibited by 90%, *Pseudomonas Aeruginosa* by 95% and *Klebsiella Pneumoniae* was inhibited by 89%. This is also supported by a study conducted by Shu et al. and Radwan et al. [25, 26]. These results show the increasing challenge of antibiotic resistance in diabetic foot ulcers (DFUs), which can complicate treatment and lead to poor clinical outcomes if not effectively managed. The presence of multidrug-resistant (MDR) microorganisms, such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA), indicates that commercially available antibiotics may no longer be sufficient to treat these infections. In the present study, cinnamon essential oil (CEO) demonstrated even stronger antibacterial effects,

effectively inhibiting a broader range of pathogens, making it a more potent candidate for DFU treatment. Diabetic foot ulcers are frequently complicated by resistant bacterial infections and delayed healing, highlighting the need for alternative antimicrobial agents.

As an in vitro experimental study, the findings may not accurately reflect in vivo clinical effectiveness of cinnamon essential oil in diabetic foot ulcer management. Additionally, the absence of statistical analysis limits the ability to determine the significance and reproducibility of the observed differences in antibacterial activity. Future studies should incorporate robust statistical analysis and clinical trials to evaluate the safety and therapeutic efficacy of cinnamon essential oil in vivo.

CONCLUSIONS

The study demonstrated a high bacterial isolation rate from diabetic foot ulcer. Antibiotic resistance varied among bacterial isolates, highlighting the challenge of treating bacterial infections. Cinnamon essential oil exhibited strong antibacterial activity against all isolated bacteria, suggesting its potential as an alternative antimicrobial agent.

Authors' Contribution

Conceptualization: UU, KP

Methodology: UU, AK

Formal analysis: UU

Writing and Drafting: UU, SAR, KP, BZ, AK, AA

Review and Editing: UU, SAR, KP, BZ, AK, AA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Frequency of Cutaneous Allodynia among Patients of Migraine

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ABSTRACT

Cutaneous allodynia (CA) is considered a marker of central sensitization in migraine and is characterized by the perception of pain from non-painful stimuli. **Objective:** To determine the frequency of CA among migraine patients. **Methods:** This descriptive cross-sectional study was done between May and August 2025 at the Neurology Department of Pak Emirates Military Hospital, Rawalpindi, enrolling 194 patients diagnosed with migraine based on ICHD-3 criteria. CA was evaluated based on the validated 12-item Allodynia Symptom Checklist (ASC-12), on which the severity was determined as none, mild, moderate, or severe. The analysis of data was done using SPSS version 27.0. **Results:** Among 194 patients, the overall frequency of CA was 132 (68.0%). The severity was distributed as mild (29.9%), moderate (25.3%), and severe (12.9%). A statistically significant association was found between the presence of allodynia and female gender (73.8% vs. 48.9% in males, $p=0.004$) as well as migraine with aura (77.6% vs. 63.0% in migraine without aura, $p=0.024$). No significant associations were found with age or residence. **Conclusion:** CA is a frequent comorbidity among migraine patients in our region. Its significant association with female gender and migraine with aura highlights the need for routine clinical assessment. Early identification can guide targeted treatment strategies to mitigate central sensitization and improve patient outcomes.

INTRODUCTION

Migraine is a common neurological disease affecting about 15–20% of the population worldwide. It is characterized by periodic episodes of moderate to severe headache intensity and is often associated with other symptoms such as nausea, vomiting, and sensitivity to light and noise. It can be divided into two categories: migraine with aura and migraine without aura. The distribution is highly weighted towards females and the working population, with a great socioeconomic burden [1]. CA is defined as pain produced by stimuli that are usually non-painful, such as light touch or brushing against the skin. This symptom has been considered an important marker of central sensitization resulting from the repeated activation of nociceptive pathways, mainly including the trigeminovascular system. In the context of migraine, it is believed that the

development of central sensitization may be due to prolonged activation of second-order neurons in the trigeminal nucleus caudalis and thalamic regions, leading to abnormal pain processing [2, 3]. The presence of CA could point toward a higher burden of disease, longer duration of migraine, and higher attack frequency [4]. Research has shown that 60% of all migraine patients report CA, and the frequency can be as high as 92.5% among chronic migraine sufferers [5]. Significant predictors of CA in migraine patients include female gender and elevated body mass index (BMI), while longer migraine duration is associated with increased severity of CA [6]. Additionally, the existence of CA is connected to a heightened risk of migraine chronification, thereby influencing treatment strategies. The use of confirmed



assessment tools like the Allodynia Symptom Checklist is indeed very crucial for accurate diagnosis and management of migraine [5, 7]. In the above-mentioned study in Pakistan, Shabir G et al. have stated that CA signs and symptoms were seen in 111 patients (55.5%), while in 89 patients (44.5%), no such symptoms were seen. In the 111 patients with CA, a mild degree was seen in 51 patients (45.9%), moderate in 38 patients (34.2%), and severe in 22 patients (19.8%) [8]. The frequency of allodynia among migraine patients remains understudied in our region, and very little local data is available for the guidance of clinical practice.

Allodynia, the painful perception of normal stimuli, is a common yet largely ignored symptom in migraineurs, where quality of life is severely affected. The study bridged this gap in the literature by determining the frequency of allodynia in migraine patients, thus aiding clinicians in their understanding and management of this debilitating symptom. The results contributed to migraine patients through better diagnosis, appropriate treatment strategies, and management to raise the quality of care provided to them in the region. This study aimed to determine the frequency of CA among migraine patients.

METHODS

This descriptive cross-sectional study was conducted from May to August 2025 at the Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, after getting approval from the IRB committee under Ref No. A/28/ERC/04/2025. A total number of 194 participants were included, which was calculated via the WHO sample size calculator at a 95% confidence level, 7% margin of error, and an anticipated allodynia frequency of 55.5% [8]. Inclusion criteria were patients of either gender, age ≥ 18 years, and diagnosed with migraine, with or without aura, according to ICHD-3 beta criteria. Patients presented with other headache disorders, neurological or chronic pain conditions that could interfere with pain assessment, psychiatric conditions influencing symptom reporting, current use of pain-modifying medications, and pregnancy or lactation were excluded. The eligible patients were included in the study after obtaining informed written consent. Baseline demographic information, such as age, gender, BMI, and residential status of each patient, was noted. CA was evaluated using the 12-item Allodynia Symptom Checklist (ASC-12), which is a valid self-report scale with high internal consistency (Cronbach's $\alpha=0.78$) [9], consisting of 12 items about the presence of pain or discomfort in response to normally non-painful stimuli during migraine attacks, such as combing hair, pulling hair back, shaving face, wearing glasses, lenses, earring, necklace, tight cloths, taking shower, resting face or head in pillow, and exposure to heat or cold. Each item was

scored as never (0), rarely (1), less than half the time (2), half the time or more (3), or all the time (4). The severity was categorized as none (0-2), mild (3-5), moderate (6-8), or severe (≥ 9). Migraine types were classified as either migraine with aura or migraine without aura as per ICHD-3 diagnostic criteria [10]. All the patients were assessed and diagnosed by consultant neurologists trained in headache disorders, while taking a thorough clinical history and symptom profile. SPSS version 27.0 was used to carry out the statistical analysis. Normality of numerical variables such as age and allodynia scores was evaluated by the Shapiro-Wilk test; for this purpose, the results are presented as mean $\pm$ standard deviation or median (IQR). Categorical variables include gender, residence, migraine type, and allodynia severity, which are summarized as frequencies and percentages. The frequency of allodynia is also summarized in the same manner. Allodynia categories are stratified according to age, gender, residence, and migraine type. Associations were assessed using the Chi-square or Fisher Exact Test, considering a p-value ≤ 0.05 as significant.

RESULTS

This study includes 194 migraine patients with a mean age of 38.5 ± 11.2 years, and a median age of 36 years (IQR: 29-47 years). The majority were female, 149 (76.8%). The mean body mass index (BMI) was 26.4 ± 4.1 kg/m². Regarding residence, most participants were from urban areas, 132 (68.0%). As for migraine type, 127 (65.5%) had migraine without aura, whereas 67 (34.5%) had migraine with aura. The frequency of CA among migraine patients was found to be 132 (68.0%). The distribution of allodynia severity among these 132 patients is detailed (Table 1).

Table 1: Frequency and Severity of Allodynia

Allodynia Status	n (%)
No Allodynia	62 (32.0%)
Any Allodynia (Total)	132 (68.0%)
Mild	58 (29.9%)
Moderate	49 (25.3%)
Severe	25 (12.9%)

The presence and severity of CA were stratified across key demographic and clinical variables. A chi-square test of independence revealed a statistically significant association between gender and the presence of allodynia ($\chi^2 = 8.41$, $p = 0.004$), with a higher frequency observed in females (73.8%) compared to males (48.9%). Similarly, migraine type was significantly associated with allodynia ($\chi^2 = 5.12$, $p = 0.024$), with a higher frequency in patients with migraine with aura (79.1%) than in those without aura (63.0%). No significant associations were found between allodynia status and age group or residence ($p > 0.05$). The results of these stratifications are presented (Table 2).

Table 2: Stratification of CA Status by Participant Characteristics

Characteristic	Category	No Allodynia n (%), (n=62)	Allodynia Present n (%), (n=132)	p-value
Gender	Male	23 (51.1%)	22 (48.9%)	0.004*
	Female	39 (26.2%)	110 (73.8%)	
Age Group	18-30 Years	18 (30.0%)	42 (70.0%)	0.451
	31-50 Years	32 (35.6%)	58 (64.4%)	
	>50 Years	12 (27.3%)	32 (72.7%)	
Residence	Urban	45 (34.1%)	87 (65.9%)	0.209
	Rural	17 (27.4%)	45 (72.6%)	
Migraine Type	Without Aura	47 (37.0%)	80 (63.0%)	0.024*
	With Aura	15 (22.4%)	52 (77.6%)	

Note: p-value calculated using the Chi-square test. A p-value ≤ 0.05 was considered statistically significant.

A statistically significant association was observed between cutaneous allodynia (CA) severity and gender, BMI, and migraine type ($p < 0.05$). Moderate and severe allodynia were more frequent among female participants compared to males. Similarly, individuals with higher BMI (≥ 25 kg/m²) showed a greater proportion of moderate to severe allodynia. Patients with migraine with aura also demonstrated higher frequencies of mild and moderate CA compared to those without aura (Table 3).

Table 3: Association between CA Severity and Participant Characteristics

Characteristic	Category	Mild, n (%)	Moderate, n (%)	Severe n (%)	p-value
Gender	Male (n=45)	8 (17.8%)	8 (17.8%)	4 (8.9%)	0.041*
	Female (n=149)	41 (27.5%)	41 (27.5%)	21 (14.1%)	
BMI (kg/m ²)	<25 (n=60)	10 (16.7%)	10 (16.7%)	5 (8.3%)	0.043*
	25-29.9 (n=75)	20 (26.7%)	20 (26.7%)	10 (13.3%)	
	≥ 30 (n=59)	19 (32.2%)	19 (32.2%)	10 (16.9%)	
Migraine Type	Without Aura (n=127)	30 (23.6%)	30 (23.6%)	17 (13.4%)	0.047*
	With Aura (n=67)	19 (28.4%)	19 (28.4%)	8 (11.9%)	

Note: p-value calculated using Chi-square/Fisher Exact test. A p-value ≤ 0.05 was considered statistically significant.

DISCUSSION

In this study, the high frequency of CA (68.0%) points out the importance of this condition as a common comorbidity of migraine, mainly among females and those with migraine with aura. These data confirm the well-documented role of central sensitization in migraine pathophysiology and support the necessity for routine assessment of CA in clinical practice. In fact, the early identification of allodynia could affect therapeutic choices, particularly those targeting sensitization pathways, which might improve treatment outcomes for a significant proportion of migraine sufferers. Our findings (68.0% frequency; 29.9% mild, 25.3% moderate, 12.9% severe) are thus in line with previous studies that reported a similar frequency and severity distribution (55.5% frequency; 45.9% mild, 34.2%

moderate, 19.8% severe) [8]. Similar rates have also been described for other cohorts, at 74.6% [4] and ~70% [11, 12], further establishing CA as a very frequent characteristic of migraine. However, our frequency was somewhat lower than that seen in some populations, at 81.3–92.5% [11], and much lower than the 93.3% frequency among young adults with headache disorders as described by [13], in whom migraineurs showed higher severity than the tension-type headache sufferers. Regarding severity, our distribution is mainly mild-to-moderate, as in some previous studies [8], and corroborates previous reports that the overall degree of CA is usually mild to moderate but more pronounced in migraine patients compared with other headache types [13]. This pattern speaks further to the clinical importance of CA in distinguishing migraine phenotypes. Female gender and migraine with aura also emerged as strong predictors of CA in the current study, consistent with previous reports [2, 12]. A more recent investigation observed that females are more prone to both migraine and CA [14]; indeed, migraine frequency can be as high as 18% among women compared to men. Hormonal factors have been cited as the major forces underlying these gender differences due to their influence on migraine pathophysiology. In concert, the presence of aura has been consistently associated with a higher frequency of CA, reflecting the stronger contribution of central sensitization in this subgroup [15–17]. On the other hand, although migraine chronicity has been seen by various studies to be a major determinant of CA [7, 18], our results did not support this. Instead, we found stronger associations with gender and aura, indicating possible population-specific effects. High BMI and family history of migraine have also been mentioned as contributing factors or predictors of CA [6]. Furthermore, CA has been associated with higher disability and related symptoms such as kinesiophobia and gastrointestinal disturbances [19, 20], underlining the impact of CA on the multifaceted quality of migraine patients.

The cross-sectional and single-center design of this study limits generalizability, and self-reported data is susceptible to recall bias. Large-scale, longitudinal designs in the future will be required to confirm these findings and investigate mechanisms underlying. Routine screening for cutaneous allodynia is recommended to guide personalized migraine management and improve outcomes.

CONCLUSIONS

This study confirms that CA is a frequent comorbidity among migraine patients in the studied region. The severity of CA varied, with mild cases being most common, followed by moderate and severe presentations. Significant associations were identified between the presence of CA

and both female gender and migraine with aura, underscoring the role of demographic and clinical factors in the manifestation of allodynia. These findings highlight the importance of routine assessment of CA in migraine management, as it may inform treatment strategies aimed at reducing central sensitization and improving patient outcomes. Further research is warranted to explore longitudinal trends and therapeutic interventions tailored to allodynia-positive migraine patients.

Authors' Contribution

Conceptualization: AH

Methodology: TK¹, AH

Formal analysis: WR

Writing and Drafting: MBM, TK², AR

Review and Editing: TK¹, AH, MBM, TK², AR

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Positive Attitude Toward Health, Health-Related Concerns, Psychological Distress, and Quality of Life among Patients with Kidney Failure Disease

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ABSTRACT

Individuals' mental health and overall quality of life are affected by kidney disease. Patients' stress and belief about health upset their psychological worry and life satisfaction. **Objectives:** To examine the connection between quality of life, psychological discomfort, health-related anxieties, and positive health attitudes among patients with kidney failure. **Methods:** 250 patients with renal failure were identified by the Nephrology Departments for analytical cross-sectional quantitative research. These people finished a lot of standardized tests. The Depression Anxiety and Stress Scale (DASS-21), Health-Related Concerns Scale, Positive Attitude Towards Health Scale, and Quality-of-Life Scale (QOL) were used. **Results:** In this analytical cross-sectional study, a positive attitude about one's health was significantly associated with quality of life ($r=0.42$, $p<0.01$) and less psychological distress ($r=-0.36$, $p<0.01$). Stress, anxiety, and depression were favorably connected with health-related concerns ($r=0.40$, $p<0.01$), whereas QOL was negatively connected with them ($r=-0.33$, $p<0.01$). Simple linear regression analyses revealed that a positive attitude toward obtaining medical attention was a significant predictor of reduced psychological distress ($\beta=-0.38$, $p<0.01$), fewer health-related concerns ($\beta=-0.31$, $p<0.001$), and higher quality of life ($\beta=0.44$, $p<0.001$). **Conclusions:** Patients who have a positive attitude toward their health have a much higher quality of life, fewer worries about their sickness, and less psychological anguish.

INTRODUCTION

Psychiatric disorders and chronic illnesses are typically accompanied by psychological distress, notably health anxiety and depression, which can greatly damage a patient's functionality and quality of life [1]. Individuals with chronic kidney disease (CKD) and psychological issues have chronic difficulties related to health. This leads to adverse patterns such as over- or avoidant health-seeking behaviors [2]. The connection between physical and mental health is progressively acknowledged, but no one knows how psychological issues such as depression,

stress, and anxiety affect an individual's life, such as one's overall quality of life [3]. CKD is a public health worry that impacts individuals all over the world, like more than 850 million, globally [4]. The WHO estimates that it impacts more people than diabetes (422 million), osteoarthritis (528 million), and depression (264 million) [5]. Worldwide Disease Study (2017) showed that the incidence of CKD is 697.5 million globally. The incidence of CKD is high in low and middle-income countries due to numerous reasons, such as insufficient management of risks and less access



to medical care [6]. In Asian, such as in Pakistan, approximately 12% to 18% of adults suffer from CKD, which is higher in women, the elderly with numerous health issues, such as people with diabetes, heart disease, and high blood pressure [7]. The study looks at these interrelated groups to uncover common and distinctive psychological traits that affect behaviors related to health. Chronic kidney disease is highly prevalent and often accompanied by psychological distress, which may adversely influence patients' quality of life and health-seeking behaviors. Limited local evidence exists regarding the interrelationship between psychiatric symptoms, quality of life, and health-seeking behaviors among patients with CKD. This study aims to investigate the links among CKD patients with psychiatric problems, their QOL, depressive, and health-seeking behaviors.

METHODS

An analytical cross-sectional quantitative research approach was utilized in this study to evaluate the relationships between kidney failure patients' quality of life, psychological distress, health-related anxieties, and positive attitudes toward health. Following the Itefaq Hospital Lahore's Institutional Review Board (IHT/Adm/30). The data were gathered from Lahore dialysis facilities between May 2024 and May 2025. These locations were chosen because they offer patients with end-stage renal disease (ESRD) and chronic kidney disease (CKD) specialized therapy and follow-up care. Purposive sampling was used to find 250 people with a renal failure diagnosis. This study calculated sample size using G-Power software, estimating effect size (f)=0.20, α =0.05, power (1- β error prob.)=0.95, with actual power=0.96, which structured the sample size of 244, and we had 250 participants meet the criteria for eligibility [8]. Exact - Correlation: Bivariate normal model. Options: exact distribution (Table 1).

Table 1: A Priori: Compute Required Sample Size

Variables		Values
Input	Tail (s)	1
	Correlation ρ H1	0.21
	α err prob	0.05
	Power (1- β err prob)	0.95
	Correlation ρ H0	0
Output	Lower Critical r	0.12
	Upper Critical r	0.12
	Total Sample Size	241
	Actual Power	0.95

Patients range from 18 to 70. The patients are either receiving hemodialysis or peritoneal dialysis now, or they have a clinical diagnosis of chronic kidney disease (stage 4 or 5). To guarantee a stable course of treatment, the

disease must last at least six months. They can read and comprehend English. Patients with severe mental illnesses (such as bipolar disorder or schizophrenia) may have an impact on responses; for this reason, they were not included in the study. Also excluded are people who suffer from neurological disorders or cognitive impairment (e.g., dementia, stroke with cognitive decline). Individuals who have recently received a kidney transplant (within the last six months). The study also eliminated patients who were unable to fill out the questionnaires on their own or who refused to participate. The Positive Attitude Toward Health Scale evaluated patients' propensity to take an active and upbeat approach to health management [9]. Cronbach's alpha for this scale is frequently 0.82, indicating that it is typically reliable. This scale is built on a 5-point Likert-type scale, where a higher score denotes a more optimistic outlook on health. The Health-Related Concerns Scale assessed how anxious and concerned patients were about their health, course of treatment, and outlook [10]. The internal consistency of this tool was shown by alpha, which was larger than 0.7. In the scoring method, the higher score is linked to a high level of health-related concerns among patients. Depression Anxiety Stress Scale (DASS-21) [11]. This scale was used to assess Depression, Anxiety, and Stress among individuals. This scale was based on three subscales, and each of the subscales has seven items by using the 4 Likert scales. In this scale, the height scale was linked to a high level of dysfunction. The Cronbach's alpha of this scale ranges between 0.85 and 0.95. The environment, social relationships, psychology, and physical health were all assessed using the Quality-of-Life Scale (WHOQOL-BREF) [12]. A higher quality of life was associated with a higher assessment score. Strong internal consistency was indicated by the scale's score of 0.86. The Cronbach's alpha scores for every instrument used in this study ranged from 0.78 to 0.91 overall, indicating strong internal consistency. The patients were identified based on their medical records, and lately they were approached for outpatient care. All the patients have completed informed consent for participation in the study. By using SPSS (version 26.0), the data were analyzed. Statistics such as descriptive analysis such including mean, standard deviation, frequencies, and percentages, were applied. To study links between variables, Pearson correlations were obtained. Simple linear regression analyses were undertaken to investigate whether a positive health-seeking attitude may predict health-related worries, psychological discomfort, and overall quality of life. Furthermore, multiple regression analysis was utilized to analyze the combined impact of a positive attitude and psychological distress on quality of life. A statistical significance threshold was chosen at $p < 0.05$.

RESULTS

An analytical cross-sectional quantitative research approach was utilized in this study to evaluate the relationships between kidney failure patients' quality of life, psychological distress, health-related anxieties, and positive attitudes toward health. Following the Ittefaq Hospital Lahore's Institutional Review Board (IHT/Adm/30). The data were gathered from Lahore dialysis facilities between May 2024 and May 2025. These locations were chosen because they offer patients with end-stage renal disease (ESRD) and chronic kidney disease (CKD) specialized therapy and follow-up care. Purposive sampling was used to find 250 people with a renal failure diagnosis. This study calculated sample size using G-Power software, estimating effect size (f)=0.20, α =0.05, power (1- β error prob.) =0.95, with actual power=0.95, which structured the sample size of 244, and we had 250 participants meet the criteria for eligibility [8]. Exact - Correlation: Bivariate normal model. Options: exact distribution (Table 1).

Table 2: Sample Demographic Characteristics

Variables	Total Sample (n=250), n (%)	Male Patients (n=121), n (%)	Female Patients (n=129), n (%)
Age			
Years	42.6 ± 12.8	46.2 ± 11.5	39.3 ± 13.2
Gender			
Male	122 (48.8%)	73 (60.3%)	49 (38.0%)
Female	128 (51.2%)	48 (39.7%)	80 (62.0%)
Education Level			
Primary (≤5 Years)	52 (20.8%)	36 (29.8%)	16 (12.4%)
Secondary (6–12 Years)	111 (44.4%)	54 (44.6%)	57 (44.2%)
Graduate and Above	87 (34.8%)	31 (25.6%)	56 (43.4%)
Marital Status			
Married	186 (74.4%)	102 (84.3%)	84 (65.1%)
Unmarried	64 (25.6%)	19 (15.7%)	45 (34.9%)
Income Group (Monthly)			
Low (<PKR 30,000)	97 (38.8%)	51 (42.1%)	46 (35.7%)
Middle (PKR 30,000–70,000)	112 (44.8%)	53 (43.8%)	59 (45.7%)
High (>PKR 70,000)	41 (16.4%)	17 (14.0%)	24 (18.6%)
Family System			
Nuclear	136 (54.4%)	62 (51.2%)	74 (57.4%)
Joint/Extended	114 (45.6%)	59 (48.8%)	55 (42.6%)
Duration of Illness			
<1 Year	63 (25.2%)	22 (18.2%)	41 (31.8%)
1–5 Years	122 (48.8%)	59 (48.8%)	63 (48.8%)
>5 Years	65 (26.0%)	40 (33.0%)	25 (19.4%)
Period of Treatment			
<6 Months	58 (23.2%)	20 (16.5%)	38 (29.5%)
6 Months–2 Years	108 (43.2%)	50 (41.3%)	58 (45.0%)
>2 Years	84 (33.6%)	51 (42.1%)	33 (25.6%)

Results illustrate the Pearson correlation analysis; a good attitude regarding one's health is considerably linked to a

higher quality of life ($r=0.44$, $p<0.01$). This optimistic view, on the other hand, relates to decreased psychological distress ($r=-0.38$, $p<0.01$) and health-related concerns ($r=-0.31$, $p<0.01$). Mental distress was favorably connected with health-related concerns ($r=0.40$, $p<0.01$), whereas quality of life was adversely correlated with them ($r=-0.33$, $p<0.01$). There was also a negative link between quality of life and psychological distress ($r=-0.41$, $p<0.01$) (Table 3).

Table 3: Inter-Correlation among Variables

Variables	Mean ± SD	1	2	3	4
1. Positive Attitude Toward Health	34.52 ± 6.21	—	—	—	—
2. Health-Related Concerns	27.83 ± 5.94	-0.31**	—	—	—
3. Psychological Distress (DASS)	30.14 ± 8.72	-0.038**	0.40**	—	—
4. Quality of Life (WHOQOL-BREF)	65.47 ± 11.05	0.44**	-0.33**	-0.41**	—

Note: n=250, (*) indicates statistical significance at $p\leq 0.05$, $p\leq 0.01$ (**), PATH = Positive Attitude Toward Health; HRC = Health-Related Concerns; DASS = Depression, Anxiety, and Stress Scale-21; WHOQOL-BREF = World Health Organization Quality of Life-BREF.

Independent samples t-tests were conducted to examine gender differences in the study variables. Results indicated that male patients reported significantly higher positive attitude toward health (35.12 ± 6.34) than female patients (33.78 ± 6.01), $t(228) = 2.14$, $p=0.034$, $d=0.28$. Female patients reported significantly greater health-related concerns (28.71 ± 6.14) compared to male (27.01 ± 5.72), $t(228) = -2.03$, $p=0.044$, $d=0.27$, as well as higher psychological distress (31.41 ± 9.01) compared to males (29.02 ± 8.41), $t(228) = -2.11$, $p=0.036$, $d=0.29$. Quality of life was significantly higher among male patients (66.89 ± 11.24) than female patients (63.92 ± 10.71), $t(228) = 2.45$, $p=0.015$, $d=0.32$ (Table 4).

Table 4: Independent Samples t-Test Comparing Male and Female Patients on Study Variables (n=230)

Variables	Gender	n	Mean ± SD	T	df	p-value	Cohen's d
PATH	Male	121	35.12 ± 6.34	2.14	228	0.003**	0.28
	Female	129	33.78 ± 6.01				
HRC	Male	121	27.01 ± 5.72	-2.03	228	0.004**	0.27
	Female	129	28.71 ± 6.14				
DASS	Male	121	29.02 ± 8.41	-2.11	228	0.003**	0.29
	Female	129	31.41 ± 9.01				
WHOQOL	Male	121	66.89 ± 11.24	2.45	228	0.001***	0.32
	Female	129	63.92 ± 10.71				

Note: (*) indicates statistical significance at $p\leq 0.05$, $p\leq 0.005$ (**), $p\leq 0.001$ (***), PATH = Positive Attitude Toward Health; HRC = Health-Related Concerns; DASS = Depression, Anxiety, and Stress Scale-21; WHOQOL = World Health Organization Quality of Life.

Simple linear regression analyses revealed that a positive attitude toward health significantly predicts lower health-

related concerns ($B = -0.28$, $p=0.002$, $R^2 = 0.10$) and lower psychological distress ($B = -0.53$, $p<0.001$, $R^2 = 0.14$). Furthermore, a positive attitude was a predictor of higher quality of life ($B=0.72$, $p<0.001$, $R^2=0.19$) (Table 5).

Table 5: Simple Linear Regression Analyses Predicting Health-Related Concerns, Psychological Distress, and Quality of Life from Positive Attitude Toward Health ($n=230$)

Variables	B	SE-B	β	t	p-value	R^2
Health-Related Concerns	-0.28	0.09	-0.31	-3.12	0.002**	0.10
Psychological Distress (DASS-21)	-0.53	0.14	-0.38	-3.79	0.001***	0.14
Quality of Life (WHOQOL-BREF)	0.72	0.16	0.44	4.55	0.001***	0.19

Note: (*) indicates statistical significance, $p \leq 0.05$, $p \leq 0.05$, $p \leq 0.005$ (**), $p \leq 0.001$ (***), p = significance level; SEB = standard error; B = unstandardized coefficient; β = standardized beta; t = t-value; R^2 = coefficient of determination.

DISCUSSION

This current study investigated the relationships between patients with renal failure's quality of life, health-related anxieties, and psychological discomfort. The findings of the study suggested that individuals who have a good and positive attitude towards their health have a high level of quality of life, less health-related anxiety, and stress. Based on this analysis, individuals with chronic kidney disease (CKD) get assistance from well-being-related evaluation in terms of happiness and ability to adjust [13]. Likewise, a positive attitude towards health is linked to better QOL; on the other hand, distress is associated with health-related anxieties [14]. This finding is like previous literature, which showed that positive psychology, such as positive attitude, healthy coping, is related to QOL and well-being among individuals with chronic illnesses [15, 16]. Hence, when an individual goes through the process of renal failure and must take care of medical care as dialysis, then the positive coping strategies helped them to deal with body pain and cope with the situation [17]. Additionally, the data also showed a significant difference in the level of stress and duration of the disease, as well as their coping strategies also different between them. Women, are more sensitive and they are easily to vulnerable to the diseases and stress, similarly, in this case they are more vulnerable to stress and they more worry about the issues, on the other hand, Men, have more positive towards the life and they try to remain busy in the world activities and they have reported the good QOL and less stress about life. Similarly, this is similar to previous research, which indicated that women with chronic illnesses experience more emotional issues and mental health concerns [18]. Caregiving, cultural norms, standards, and different coping mechanisms can all affect one's results. Therefore, it is essential to take gender into account while developing treatments for individuals. Furthermore, regression analysis showed how important it is to have a positive outlook on health. Optimism is a

predictor of less health-related anxiety, decreased stress, and an enhanced standard of living in general. This is a thing that a positive attitude towards health makes an individual more motivated, strong, capacity to recover, and different coping strategies for managing disease as well as enhancing their health. However, positive attitudes towards health improve the patient's active role in care, act listen their doctor's instructions, and adopt stress reduction, exercise, and a balanced diet. The findings of this study showed significant evidence that psychological well-being and QOL are linked to patients in enhancing a positive attitude toward health-seeking. Although it is crucial to highlight that other factors, such as social support, treatment compliance, and the existence of concomitant diseases, all have a major impact on quality-of-life outcomes [19, 20]. Notably, the optimistic attitude explained 10% to 19% of the variance. Firstly, Psychological interventions such as cognitive-behavioral therapy and educational activities may help to take more positive steps. Secondly, based on screening, it will be very helpful in enhancing mental health care. After this, individuals will treat mental health as a normal treatment. Lastly, therapies might be required to report the evident challenges encountered by female patients, who often have a high level of discomfort and lower QOL.

A limitation of this study is that the findings may not be broadly applicable due to the dependence on purposive sampling. Future research should consider applying longitudinal methodologies, utilizing bigger and more representative samples, and incorporating intervention-based strategies to enhance the reliability and application of the results.

CONCLUSIONS

It was concluded that patients who report positive concerns and attitudes towards health tend to endure much less problems associated with sickness, experience reduced levels of psychological pain, and enjoy a dramatically improved quality of life.

Authors' Contribution

Conceptualization: ASH

Methodology: ASH, AU

Formal analysis: AU

Writing and Drafting: ASH, NN

Review and Editing: ASH, AU, NN

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of the Effectiveness of Tramadol and Dexmedetomidine as Adjuvants in Spinal Anesthesia for Prolonging Postoperative Analgesia in Patients Undergoing Hysterectomy (TAH & Vaginal Hysterectomy)

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ABSTRACT

TAH is a major procedure with significant postoperative pain, managed through various anesthetic techniques. Intrathecal dexmedetomidine offers consistent, opioid-sparing analgesia, whereas tramadol provides analgesic and anti-shivering effects but shows more variable and less established efficacy. **Objectives:** To evaluate the effectiveness of dexmedetomidine and tramadol in spinal anesthesia for extending postoperative analgesia in hysterectomy. **Methods:** A quasi-experimental study was conducted at M. Islam Medical and Dental College Teaching Hospital on two equal groups of 110 elective hysterectomy patients who were randomly assigned. Group T was given tramadol, and Group D was given dexmedetomidine. Clinical and demographic baselines were documented. Time to first rescue analgesia and total rescue analgesic intake were the main results. Patient satisfaction, incidence of adverse effects, and postoperative pain intensity were evaluated at multiple intervals. Data analysis was conducted by SPSS version 26.0 with statistical significance set at $p < 0.05$. **Results:** The dexmedetomidine group's patients consumed less rescue analgesic overall ($p < 0.001$) and had a considerably longer duration to initial rescue analgesia ($p < 0.001$) than the tramadol group. Additionally, the dexmedetomidine group had considerably higher patient satisfaction ($p = 0.002$). At every time point, the dexmedetomidine group's VAS pain scores were consistently lower ($p < 0.001$). There was no discernible difference in the frequency of side effects between the groups. **Conclusions:** Dexmedetomidine resulted in improved postoperative pain control and greater patient satisfaction and reduced analgesic consumption compared to tramadol, with a comparable safety profile. It represents an effective option for multimodal postoperative pain management following hysterectomy.

INTRODUCTION

A total abdominal hysterectomy (TAH) is a large-scale operation that is associated with significant risk of postoperative pain and associated morbidity. Different methods of anesthesia have been used in the management of pain in TAH, including general, epidural, spinal anesthesia, abdominal blocks, and local infiltration. It is

amazing that despite these alternatives, postoperative pain is still a major issue: the proportion of women reporting moderate to severe pain in the first 24 hours is as high [1]. Such a significant pain burden is evident in the patterns of opioid use, as women having a benign hysterectomy receive an average of 143.5 morphine



milligram equivalents (MME) of opioids as part of the perioperative process, and 83% of them are given opioids at the time of hysterectomy [2]. A large systematic review similarly found that patients undergoing abdominal hysterectomy consume approximately 108 MME (equivalent to about 14.5 tablets of 5-mg oxycodone) in the first 14 days post-discharge, compared to only around 35 MME after vaginal hysterectomy. Persistent opioid use, although relatively rare, affects around 5% of patients following benign hysterectomy procedures [3]. These figures collectively highlight the substantial analgesic demands and opioid exposure after hysterectomy, reinforcing the imperative for strategies that effectively prolong analgesia while reducing opioid requirements. Both vaginal and TAH frequently result in moderate-to-severe nociceptive pain during the first 24 hours, which increases the need for opioids, delays movement, and lengthens hospital stays [4]. Subarachnoid anesthesia is a common choice in lower abdominal and gynecologic procedures, and it is frequently supplemented with intrathecal adjuvants to extend analgesia without causing systemic opioid effects. One of the most effective adjuvants is dexmedetomidine, which is a highly selective 2-agonist that consistently prolongs sensory and motor block and deferrals the necessity of rescue analgesia [5, 6]. Nevertheless, dexmedetomidine can lead to dose-dependent bradycardia, hypotension, and sedation, with the most common dosage range now set on microgram levels [7-9]. Tramadol is a non-canonical opioid, which has analgesic effects because of low-affinity μ stimulation and reuptake inhibition of norepinephrine and serotonin. Doses up to approximately 20mg have demonstrated the potential of prolonging sensory block and counteracting shivering in infra-umbilical surgeries when administered intrathecally. Evidence is, however, limited and harsh against that of dexmedetomidine, with a significant number of studies investigating tramadol using alternative routes. There is also limited experience on the intrathecal use of tramadol, with most studies either using different categories of surgery or assessing anti-shivering effects, but not the analgesic effect duration [10, 11]. Higher doses of tramadol have been associated with side effects like nausea, vomiting, and risk of seizures, which restrict the widespread intrathecal use of tramadol. The relevance of this gap is that analgesic requirements and hemodynamic reactions differ across procedures, and generalization across specialties is invalid [12]. Postoperative pain management is a critical issue related to the hysterectomy of women because insufficient analgesia may slow down the process of mobilization, extend the time spent in the hospital, increase the level of opioid consumption, and lead to decreased patient satisfaction. Dexmedetomidine is reported to lengthen

sensory and motor blockage in the presence of opioid-sparing effects, but with a risk of sedation and hemodynamic alterations. Tramadol has an intrathecal analgesic and anti-shivering effect, although the effect is less reliable.

Effective postoperative analgesia in total abdominal hysterectomy remains challenging, with high opioid consumption and associated adverse effects necessitating safer and longer-acting intrathecal adjuvants. Limited comparative evidence exists regarding the analgesic efficacy and safety of intrathecal tramadol versus dexmedetomidine specifically in patients undergoing hysterectomy. This study aimed to determine the efficacy of intrathecal tramadol and dexmedetomidine when used as adjuvants to the spinal anesthesia in patients undergoing hysterectomy.

METHODS

This quasi-experimental research involved a comparison of the effectiveness of intrathecal tramadol and dexmedetomidine in extending postoperative analgesia in women who underwent a hysterectomy. It was done in the Department of Anesthesiology at the M. Islam Medical and Dental College Teaching Hospital during a period of more than six months, from 1 February 2025 to 31 July 2025. The Institutional Research and Ethics Committee was consulted and provided ethical approval (Approval No: RC/020/2025), which was in compliance with the Declaration of Helsinki. The open-ended Open Epi two means formula was used to calculate the sample size (180 minutes (SD) = pooled and 101 minutes = mean difference based on previous literature) and used 0.05 and 80 percent as the α and power, respectively. This provided 50 patients in each group; a 10% rate of attrition brought up the final sample of 110 patients (55 patients each) [10, 13]. Written informed consent was taken. Non-probability consecutive sampling was used to recruit participants. The inclusion criteria were a group of women between the ages of 35 and 65 years who were to undergo an elective TAH or vaginal hysterectomy under spinal anesthesia. The exclusion criteria were severe cardiovascular disease, neurological conditions, long-term opioid or sedative use, severe organ dysfunction, pregnancy, and unsuccessful spinal anesthesia. Pre-anesthetic and routine intraoperative assessment were done on all the patients. The spinal anesthesia was administered at L3-L4 or at L4-L5 with the 25G Quincke needle. Assigning patients to one of two groups was done according to the adjuvant to be used: Group D was put on 3 mL of 0.5% hyperbaric bupivacaine and 5 μ g dexmedetomidine, and Group T was put on 3 mL of 0.5% hyperbaric bupivacaine and 20mg tramadol. The intraoperative and postoperative hemodynamic parameters have been measured at specific times every

five minutes and at fixed times. The main outcome was time to first rescue analgesia, and this is a ratio of the time between intrathecal injection and VAS pain score 4 or greater [14, 15]. The secondary outcomes were VAS scores at 2, 4, 6, 12, and 24 hours, total rescue analgesic consumption at 24 hours, adverse effects (hypotension, bradycardia, nausea, vomiting, pruritus, shivering, sedation, urinary retention), and patient satisfaction at 24 hours. IV diclofenac and /or tramadol were used as rescue analgesia. The structured proforma was used to gather the data. SPSS version 26.0 was used to assess the data. The Shapiro-Wilk test was used to test the normalcy of continuous variables. Continuous data were presented as mean, SD, or median (IQR), whereas categorical variables were presented in the form of frequencies and percentages. These independent variables were age, ASA status, type of hysterectomy, baseline hemodynamics, and type of intrathecal adjuvant. The independent samples t-test was applied to compare groups that had normally distributed variables, and the Mann-Whitney U test was applied to compare non-normally distributed variables. The p-value of less than 0.05 was statistically significant.

RESULTS

Participants in both groups were primarily in their mid-forties, and the mean age was comparable. Additionally, there was no discernible variation in the average Body Mass Index (BMI) between the groups. More than half of the patients in both groups had ASA I physical status (56.4% in the Dexmedetomidine group and 60.0% in the Tramadol group), with the remaining patients in both groups having ASA II physical status (43.6% and 40.0%, respectively) (Table 1).

Table 1: Clinical and Demographic Features of Patients

Variables	Dexmedetomidine (n=55)	Tramadol (n=55)	p-value
Age (Years)			
Mean ± SD	46.8 ± 7.2	47.5 ± 6.8	0.623*
BMI (kg/m ²)			
Mean ± SD	26.9 ± 3.4	27.1 ± 3.6	0.789*
ASA Physical Status, n (%)			
ASA I	31(56.4%)	33(60.0%)	0.712**
ASA II	24(43.6%)	22(40.0%)	
Type of Hysterectomy, n (%)			
TAH	29(52.7%)	28(50.9%)	0.846**
Vaginal	26(47.3%)	27(49.1%)	
Baseline MAP (mmHg),			
Mean ± SD	92.5 ± 8.1	91.7 ± 7.9	0.645*
Baseline HR (beats/min)			
Mean ± SD	78.2 ± 6.9	77.6 ± 7.1	0.721*

Mann-Whitney U test and Chi-square test **p-value<0.001, *p-value<0.05

Strong statistical significance (<0.001) was indicated by the

p-value, which showed that the Dexmedetomidine group had a significantly longer time to first request rescue analgesia. Similarly, the Dexmedetomidine group consumed considerably less rescue analgesics overall within the first 24 hours than the Tramadol group (p-value <0.001). Dexmedetomidine recipients had higher patient satisfaction levels on a 24-hour Likert scale; this difference was statistically significant (p=0.002) (Table 2).

Table 2: Comparison of Outcomes of the Study Participants (n=110)

Outcomes	Dex-medetomidine (n=55)	Tramadol (n=55)	p-value
Time to First Rescue Analgesia (min)	420.6 ± 50.2	310.4 ± 55.3	<0.001 ^a
Total Rescue Analgesic Consumption (mg)	74.8 ± 14.6	119.6 ± 19.8	<0.001 ^a
Patient Satisfaction (Likert 1-5), Median (IQR)	5 (4-5)	4 (3-4)	0.002b ^{**}

^aIndependent sample t test & b Mann Whitney test **p-value<0.001, *p-value<0.05

When the Visual Analogue Scale (VAS) was used to compare the two groups' postoperative pain severity, the Dexmedetomidine group consistently scored lower at all time periods. Patients who received Dexmedetomidine reported considerably lower levels of pain at 2, 4, 6, 12, and 24 hours than those who received Tramadol; all comparisons showed p-values <0.001. These findings suggest that Dexmedetomidine maintained greater analgesic efficacy over the first 24 hours after hysterectomy, in addition to delaying the onset of substantial postoperative pain (Table 3).

Table 3: VAS Pain Scores at Different Time Points Reported by the Study Participants (n=110)

Time Point (Hours)	Dexmedetomidine VAS, Mean ± SD	Tramadol VAS, Mean ± SD	p-value
2 Hours	2.1 ± 0.5	3.2 ± 0.6	<0.001 ^a
4 Hours	2.4 ± 0.5	3.5 ± 0.6	<0.001 ^a
6 Hours	2.7 ± 0.6	3.8 ± 0.7	<0.001 ^a
12 Hours	3.1 ± 0.5	4.2 ± 0.6	<0.001 ^a
24 Hours	3.6 ± 0.6	4.6 ± 0.7	<0.001 ^a

^aIndependent sample t test **p-value<0.001, *p-value<0.05

There were no statistically significant variations in the incidence of negative effects, which were spread evenly across the two groups. Bradycardia was seen in 4 (8%) of patients in the Dexmedetomidine group versus 1 (3%) in the Tramadol group (p=0.365), and hypotension was seen in 3 (6%) of patients versus 2 (4%) in the Tramadol group (p=0.651). Compared to 8 (15%) of patients in the Tramadol group, 5 (10%) of patients receiving Dexmedetomidine had nausea and vomiting (p=0.424). Compared to 1 (2%) and 2 (5%) of patients in the Dexmedetomidine group, pruritus and shivering were more common in Tramadol users, occurring in 4 (8%) and 6 (12%) of patients, respectively

($p=0.173$ and $p=0.145$). Rarely, urinary retention was observed in 2 (3%) of Tramadol patients and 2 (4%) of Dexmedetomidine patients ($p=0.756$). In contrast to 3 (5%) in the Tramadol group, 5 (9%) of those on Dexmedetomidine experienced sedation ($p=0.467$) (Table 4).

Table 4: Incidence of Adverse Effects

Adverse Effects	Dexmedetomidine (n=55), n (%)	Tramadol (n=55), n (%)	p-value
Hypotension	3 (6%)	2 (4%)	0.651
Bradycardia	4 (8%)	1 (2%)	0.365
Nausea/Vomiting	5 (10%)	8 (15%)	0.424
Pruritus	1 (2%)	4 (7%)	0.173
Shivering	2 (5%)	6 (12%)	0.145
Urinary Retention	2 (4%)	2 (3%)	0.756
Sedation	5 (9%)	3 (5%)	0.467

Fisher's Exact test, * p -value<0.05

DISCUSSION

In this prospective comparative cohort of 110 hysterectomy patients, intrathecal dexmedetomidine produced a clinically and statistically significant prolongation of postoperative analgesia, reduced 24-hour rescue analgesic consumption, and yielded lower VAS pain scores across all time points compared with intrathecal tramadol. These findings are consistent with a growing body of literature demonstrating that intrathecal dexmedetomidine reliably prolongs sensory blockade and time to first analgesic request when added to local anesthetics. A comprehensive systematic review and meta-analysis by Paramasivan et al. reported significant prolongation of postoperative analgesia with intrathecal dexmedetomidine versus placebo across diverse surgeries, and cautioned that dose selection must balance efficacy against hemodynamic effects [7]. Similarly, Kumar et al. pooled randomized data and concluded that dexmedetomidine added to bupivacaine increases the duration of sensory and motor block and reduces early postoperative opioid requirements [9]. Our observed magnitude of benefit (≈ 110 minutes longer median time to first rescue analgesia and substantially lower 24-hour analgesic consumption) sits comfortably within the effect sizes reported for dexmedetomidine in these meta-analyses, supporting the external validity of our results. Dose-response and route-specific work help explain why dexmedetomidine produced consistent analgesic benefits in our cohort. Several dose-finding and randomized trials between 2020–2023 demonstrated that small intrathecal microgram doses (commonly 3–10 μ g) prolong analgesia in a dose-dependent manner without major neurotoxicity signals when administered with appropriate local anesthetic doses. Bao et al. and Zhang et al. reported faster onset and longer duration of block with low-microgram

intrathecal dexmedetomidine added to ropivacaine or bupivacaine, findings that align with the improved early and late VAS scores we observed [8, 16]. A study by Mo et al. further refined the ED50 for intrathecal dexmedetomidine in obstetric spinal anesthesia, reinforcing that small, precise doses maximize analgesia while limiting bradycardia/hypotension risk, a consideration reflected in our low but measurable rates of bradycardia and hypotension [17]. In contrast, intrathecal tramadol's data in the literature were more heterogeneous. Several recent randomized and comparative studies continue to show that tramadol can prolong analgesia when added to spinal bupivacaine and provides anti-shivering benefits, but the magnitude of analgesic extension is generally smaller and less consistent than that reported with dexmedetomidine. The trials assessing intrathecal or perioperative tramadol in abdominal and urological procedures reported reductions in early pain and anti-shivering effects, but variable effects on overall 24-hour opioid-sparing. [10, 18]. Current findings showed that tramadol produced shorter analgesic duration, higher rescue consumption, and higher VAS than dexmedetomidine, therefore align with this pattern of more modest and variable tramadol efficacy. A recent comparative study in a mixed surgical population reported superior block characteristics and longer analgesia with dexmedetomidine versus tramadol and other adjuvants, mirroring our results in the hysterectomy cohort [19]. Mechanistically, these differences are plausible: Dexmedetomidine produces spinal analgesia by α_2 -adrenergic receptor-mediated inhibition of nociceptive neurotransmission in the dorsal horn and by reducing C-fiber neurotransmitter release, whereas tramadol's multimodal action may provide analgesia but with less potent and shorter intrathecal effect at commonly used doses. This pharmacologic distinction likely explains both the longer duration and lower VAS in the dexmedetomidine arm of present study [20]. Current results are consistent with previous data demonstrating the better analgesic profile of dexmedetomidine, but these studies are difficult to compare due to the heterogeneity of surgical populations, the use of different doses, and even differences in the definition of outcomes. Despite these limitations, our data specific to hysterectomy supports the use of intrathecal dexmedetomidine as an adjuvant and highlights the need for procedure-specific, standardized trials to perfect dosage and safety.

The quasi-experimental design with non-probability consecutive sampling may introduce selection bias and limit the generalizability of the findings. Additionally, the absence of blinding and the relatively short 24-hour follow-up period may have influenced subjective outcomes such as VAS scores and patient satisfaction. Future double-

blinded, multicenter randomized controlled trials with longer follow-up are recommended to further validate efficacy and safety outcomes.

CONCLUSIONS

In patients having a hysterectomy, this study showed that dexmedetomidine offers better postoperative analgesia than tramadol. This is demonstrated by a significantly longer time to first rescue analgesia, lower overall analgesic consumption, lower pain scores at all time intervals observed, and higher patient satisfaction. Crucially, the safety profiles of the two medications were similar, with no statistically significant variation in the frequency of side events.

Authors' Contribution

Conceptualization: HFA

Methodology: HFA, MB, SA

Formal analysis: MB, NS

Writing and Drafting: SS, SA, ZK, ST

Review and Editing: HFA, MB, SS, SA, ZK, NS, ST

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Comparison of Polyfilament Suture (Vicryl Rapide-0) & Monofilament Suture (Monocryl 3-0) in the Repair of Mediolateral Episiotomies

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ABSTRACT

Episiotomy remains a common obstetric procedure, and the choice of suture material can influence postoperative pain, wound healing, and maternal satisfaction. **Objectives:** To compare Monocryl and Vicryl Rapide for mediolateral episiotomy repair in terms of pain, wound healing, complications, and patient satisfaction. **Methods:** A quasi-experimental study was conducted at the Gynecology Department, KRL General Hospital, Islamabad, from August 2022 to October 2023. Sixty women (18-45 years) undergoing spontaneous vaginal delivery were randomized into two groups (n=30 each). Skin closure was done with Monocryl 3-0 (study group) or Vicryl Rapide 3-0 (control group), while deeper layers were closed with Vicryl Rapide 0 in both groups. Pain was assessed using the Visual Analog Scale (VAS). **Results:** Baseline demographics were comparable between groups (p>0.05). The study group reported significantly lower pain at 1 hour (p=0.001), 3 hours (1.53 ± 1.41 vs. 3.30 ± 2.38, p=0.001), 6 hours (0.97 ± 1.59 vs. 2.63 ± 2.01, p=0.001), after defecation (0.63 ± 0.93 vs. 2.00 ± 1.46, p<0.001), after urination (0.53 ± 0.82 vs. 1.63 ± 1.35, p<0.001), and on day 7 (p<0.001). Wound healing was significantly better with Monocryl (p=0.005), and patient satisfaction was higher (p=0.001). No infections occurred in the Monocryl group, compared to 6.7% in the control. **Conclusions:** Monocryl demonstrated clear superiority over Vicryl Rapide for episiotomy repair, offering reduced pain, improved wound healing, and higher maternal satisfaction.

INTRODUCTION

Episiotomy is a surgical incision performed during the second stage of labor to enlarge the vaginal opening and facilitate delivery. Although once routinely practiced, its role has become increasingly debated, as clinical evidence suggests that routine use may not be justified and should instead be based on clear clinical indications [1, 2]. Perineal trauma remains a significant maternal health concern, with approximately 85% of women experiencing some form of perineal injury during spontaneous vaginal delivery, and over two-thirds requiring suturing [2]. Such trauma is

associated with considerable maternal morbidity, contributing to physical, psychological, and social challenges [3, 4]. Consequences may include urinary or fecal incontinence, dyspareunia, impaired mobility, and a disrupted maternal-infant bond [5]. Furthermore, perinatal events such as delivery mode, perineal injuries, and postpartum pain are closely linked with postpartum depression (PPD), while post-traumatic stress disorder (PTSD) affects 3-4% of women after childbirth [6, 7]. The quality of perineal repair plays a crucial role in reducing



morbidity. Prolonged second-stage labor increases the risk of severe perineal injuries, but appropriate repair techniques can minimize complications [8]. Continuous suturing has demonstrated advantages over interrupted methods, including reduced perineal pain, decreased analgesic use, improved wound healing, shorter repair duration, and lower material consumption [9]. However, outcomes are also influenced by the choice of suture material, suturing technique, and the skill of the operator [10]. Suture selection is particularly important [11]. The role of suture materials in wound repair is pivotal, as they provide a supportive framework that facilitates tissue healing [12]. Monocryl induces minimal tissue reaction due to its monofilament structure and maintains about 25% tensile strength by the 14th day [8]. Poliglecaprone-25 is an absorbable suture, completely absorbed within 91-119 days of application, with minimal inflammatory reaction [13]. Evidence therefore suggests that the choice between Monocryl and Vicryl Rapide should be guided by clinical priorities, including pain management, healing time, and risk of wound breakdown [13, 14].

Optimal suture material for episiotomy repair remains essential to minimize postpartum perineal pain, infection, and wound complications. Limited comparative evidence exists regarding maternal outcomes between monofilament and polyfilament sutures in mediolateral episiotomy repair. This study aims to compare monofilament and polyfilament sutures in mediolateral episiotomy repair following spontaneous vaginal delivery, focusing specifically on maternal outcomes of perineal pain, infection, and wound dehiscence.

METHODS

This study utilized a quasi-experimental design and was conducted among 60 pregnant patients visiting KRL Hospital in Islamabad, during the time period of October 2022 to April 2023. The study was duly approved by the ethical committee of the hospital. Ethical approval was obtained from the KRL Hospital Institutional Review Board (IRB) (Ref ERC: KRL-HI-PUB-ERC/Oct22/18). Women who had lived singleton pregnancies of 37 to 40+6 weeks' gestation were considered as part of this research. Among those who resulted in SVD with episiotomy, 75 women were selected as candidates for the study, and they were asked to participate. 15 women refused to participate in the study due to personal reasons in the beginning. The patients who had undergone an uncomplicated episiotomy after a vaginal delivery, either spontaneously or by the instrument, were included in the study. All the deliveries were conducted by 3rd and 4th-year resident obstetricians. An uncomplicated episiotomy was defined as one that was not associated with additional perineal tears and that did not involve the anal sphincter. The patients having known

coagulopathy, vulval or vaginal varicose veins, and 1st, 3rd, or 4th degree perineal tears were not made a part of this research. All participants gave verbal and written consent. Women were assigned to either the study (Monocryl) or control (Vicryl Rapide) group using convenience sampling, alternating enrollment to reduce bias. This single-blinded study ensured patients were unaware of their group. Episiotomies were performed under aseptic conditions by obstetricians following a standard protocol. Vaginal walls were sutured continuously with Vicryl Rapide '0', muscles with interrupted Vicryl Rapide '0', and skin with either interrupted Vicryl Rapide '0' or continuous subcuticular Monocryl 3-0, based on group. Monocryl used a 19mm curved needle; Vicryl Rapide used a 40mm taper point needle. Analgesia: 5-10 ml of 2% xylocaine. After perineal repair, participants received a questionnaire to record outcomes, preventing care provider influence. Demographic data (admission number, age, BMI, parity, gestational age) were collected from hospital records. Pain presence and severity were assessed at 1, 3, and 6 hours using the Visual Analog Scale (VAS), ranging from 0 ("no pain") to 10 ("unimaginable pain"), as proposed by the National Comprehensive Cancer Network, USA [15]. Pain after urination and defecation was also recorded as a primary outcome. Secondary outcomes included pain on day 7, dehiscence, infection, wound healing, and patient satisfaction. Wound healing was assessed on the 7th postpartum day using the Wound Healing Index, a validated scale evaluating erythema, edema, ecchymosis, discharge, and approximation of wound edges [16]. Patient satisfaction was measured using the Patient Satisfaction Questionnaire (PSQ) developed by Ware et al. which uses a Likert-scale format to assess satisfaction regarding pain, comfort, and overall experience [17]. All data were analyzed using SPSS version 22.0. Chi-square test was used to compare the qualitative data, whereas the independent t-test analysis was used to compare the quantitative data between the two groups. The p-value < 0.05 was considered significant.

RESULTS

In this research, 60 women were enrolled and were divided into two groups, consisting of 30 women in each group (study and control). The distribution of the demographic characteristics showed that the mean age of the study group (25.63 ± 4.08 years) was not significantly (p -value > 0.05) different from that of the (26.87 ± 3.78 years) control group. The mean parity (1.27 ± 1.23 vs. 1.77 ± 1.46 , p -value = 0.156) and the gestational age (38.58 ± 0.94 vs. 38.16 ± 1.20 , p -value = 0.132) were also similar in both the study and the control groups (Table 1).

Table 1: Baseline Characteristics of Study and Control Groups

Variables	Study Group (n=30)	Control Group (n=30)	p-value
Age of Patient (Years)	25.63 ± 4.08	26.87 ± 3.78	0.229
Parity of the Patient	1.27 ± 1.23	1.77 ± 1.46	0.156
Gestational Age (Weeks)	38.58 ± 0.94	38.16 ± 1.20	0.132

The distribution of body mass index (BMI) was also similar in both groups (Table 2).

Table 2: Distribution of Body Mass Index (BMI) in Study and Control Groups

BMI Category (kg/m ²)	Study Group (n=30)	Control Group (n=30)	p-value
Below 18.5	1 (3.33%)	1 (3.33%)	—
18.5–25.9	26 (86.67%)	26 (86.67%)	1.000
25–29.9	3 (10.00%)	3 (10.00%)	
Total	30 (100%)	30 (100%)	—

The majority, 28 (93.33%) of the patients in both groups delivered through spontaneous vaginal delivery (SVD). In our sample most common complication associated with delivery was perineal tear other than episiotomy in both the study group 3 (10.0%) and the control group 2 (6.67%), along with one case of cervical tear and PPH in both groups. Almost all the patients in both groups (83.3% vs. 96.67%) complained of pain in both the study and control groups. On the 7th day after the procedure, no case of infection was found among the participants in the study group. In the control group, 2 women (6.67%) presented with an infection on the 7th day, post-delivery. The comparison of wound healing shows that the rate of wound healing was significantly (p -value<0.05) better in a study group in which almost all the patients 30 (100%) showed good wound healing after 7 days, as compared to the control group in which 25 (83.33%) patients showed good healing at the 7th day. The comparison of patient satisfaction showed that 28 (93.33%) of patients in the study group were satisfied on the 7th day, in contrast with the control group, i.e., 17 (56.67%) of patients were satisfied on the 7th day. It specified that patients in the study group were significantly (p -value<0.05) more satisfied as compared to the control group, as shown in detail (Table 3).

Table 3: Comparison of Delivery and Postpartum Characteristics Between Study and Control Groups

Characteristics	Study Group (n=30)	Control Group (n=30)	p-value
Mode of Delivery			
SVD	28 (93.33%)	28 (93.33%)	1.000
Instrumental	2 (6.67%)	2 (6.67%)	
Delivery Complications			
Perineal tear	3 (10.00%)	2 (6.67%)	0.974
Cervical tear	1 (3.33%)	1 (3.33%)	
PPH	1 (3.33%)	1 (3.33%)	
No complications	25 (83.33%)	26 (86.67%)	

Pain Complaint			
Yes	25 (83.33%)	29 (96.67%)	0.085
No	5 (16.67%)	1 (3.33%)	
Infection on 7 th Day			
Yes	0 (0.00%)	2 (6.67%)	0.150
No	30 (100.00%)	28 (93.33%)	
Wound Healing on 7 th Day			
Very Poor	0 (0.00%)	2 (6.67%)	0.005
Poor	0 (0.00%)	3 (10.00%)	
Good	4 (13.33%)	11 (36.67%)	
Very Good	15 (50.00%)	12 (40.00%)	
Excellent	11 (36.67%)	2 (6.67%)	
Patient Satisfaction on 7 th Day			
Very Satisfied	17 (56.67%)	4 (13.33%)	0.001
Somewhat Satisfied	11 (36.67%)	13 (43.33%)	
Somewhat Dissatisfied	2 (6.67%)	8 (26.67%)	
Very Dissatisfied	0 (0.00%)	5 (16.67%)	

The comparison of pain showed that after 1 hour, the mean pain among study group patients (2.57 ± 1.55) was significantly less (p -value<0.05) than compared to the (4.30 ± 2.10) control group. Similarly, the pain was significantly (p -value<0.05) less in the study group after 3 hours post-delivery and was recorded to lessen after 6 hours in the control group. Similarly, after defecation, the pain was significantly (p -value<0.05) less in the study group (0.63 ± 0.93) as compared to the (2.00 ± 1.46) control group. The pain was also significantly less after urination among the study group patients (0.53 ± 0.82), in contrast to the (1.63 ± 1.35) control group patients. On the 7th post-partum day, the pain was also noted to be significantly (p -value<0.05) less in the study group (0.13 ± 0.43) as compared to the (1.70 ± 1.68) control group (Table 4).

Table 4: Comparison of Pain Based on Visual Analog Scale (VAS) Between Study and Control Groups (n=60)

Time Point / Activity	Group	Mean ± SD	p-value
After 1 Hour of Delivery	Study Group	2.57 ± 1.55	0.001
	Control Group	4.30 ± 2.10	
After 3 Hours of Delivery	Study Group	1.53 ± 1.41	0.001
	Control Group	3.30 ± 2.38	
After 6 Hours of Delivery	Study Group	0.97 ± 1.59	0.001
	Control Group	2.63 ± 2.01	
After Defecation	Study Group	0.63 ± 0.93	<0.001
	Control Group	2.00 ± 1.46	
After Urination	Study Group	0.53 ± 0.82	<0.001
	Control Group	1.63 ± 1.35	
On 7 th Postpartum Day	Study Group	0.13 ± 0.43	<0.001
	Control Group	1.70 ± 1.68	

DISCUSSION

Our study demonstrated significant differences in pain scores when comparing Monocryl (monofilament) and Vicryl Rapide (polyfilament) for intracutaneous closure of

mediolateral episiotomies. Kokanali et al. previously compared polyglycolide-co-caprolactone monofilament with Vicryl Rapide and found no difference in VAS pain scores at 24 hours or 10 days [18]. Similarly, the MOVE trial, conducted in primiparas, also reported no significant difference in pain between monofilament and Vicryl Rapide, although it did show a higher rate of dehiscence with Vicryl Rapide, consistent with our findings [5]. Importantly, the MOVE trial highlighted that analgesia use did not correlate with VAS pain scores ($r=1.10$, $p=0.22$), suggesting that analgesia can confound pain assessment [19]. To minimize this limitation, our study assessed VAS pain without perioperative analgesia, ensuring a more accurate evaluation of pain differences. These findings align with NICE guidelines, which recommend monofilament synthetic sutures for perineal repair [20]. In current study, while most women in both groups reported pain, its intensity was significantly lower in the monofilament group (83.3% vs 96.6%). By day 7, no infections were reported in the monofilament group, compared to 6.7% in the Vicryl Rapide group. Wound healing outcomes were also superior with Monocryl, with 36.7% of patients demonstrating "excellent" healing compared to only 6.7% in the control group ($p=0.005$). Dencker et al. compared monofilament (Biosyn) with multifilament (Dexon II) for perineal repair and reported no early differences in healing; however, at 8-12 weeks, complications were more common, and VAS scores were higher in the monofilament group [21]. Their results may have been biased by the use of different suturing techniques in the two groups. In contrast, we standardized the technique across both groups, thereby removing this source of bias and strengthening the validity of our findings. Overall, current results demonstrate that Monocryl was associated with reduced pain, improved early wound healing, and greater patient satisfaction at 7 days. However, larger randomized trials such as the MOVE trial and studies using standardized techniques have sometimes shown no long-term differences in pain, underscoring that outcomes are influenced by suture material, technique, operator skill, follow-up timing, and sample size [19]. Some studies compared vicryl Rapide and chromic catgut and found that vicryl Rapide has a better outcome as compared with chromic catgut in the repair of episiotomy in terms of pain and analgesic requirements [22, 23]. Despite historical data indicating potential advantages of Monocryl over Vicryl Rapide, contemporary research validating these findings is scarce, highlighting the need for updated trials. Therefore, our findings should be interpreted as evidence of early clinical advantages of Monocryl in this specific procedural context, rather than as definitive proof of superiority in all settings. A major

strength of our study lies in the evaluation of an under-researched monofilament material for perineal repair, with promising results that may reduce pain, discomfort, and dyspareunia in the long term. Nonetheless, the use of VAS to assess pain remains a limitation, as pain perception is subjective and can vary considerably between individuals. The limitation of the study was the pain measurement, as it was assessed using the VAS, which is subjective and varies between individuals, potentially affecting comparisons between the sutures.

Pain assessment was based on the Visual Analogue Scale (VAS), which is subjective and may vary between individuals, potentially affecting the accuracy of comparisons. Additionally, the relatively short follow-up period limited evaluation of long-term outcomes such as dyspareunia and late wound complications. Future large-scale randomized trials with longer follow-up and objective outcome measures are recommended to confirm long-term comparative effectiveness of suture materials.

CONCLUSIONS

Our research suggests that it is better to use Monocryl, i.e., monofilament suture, for perineal trauma, especially in cases of episiotomies. Monocryl causes less pain after episiotomy repair, even in the presence of complications, e.g., perineal tears other than episiotomy and cervical tears. Patients showed much more satisfaction with the use of Monocryl, and this suture helped in decreasing the rate of infection and dehiscence. Therefore, Monocryl is superior to Vicryl Rapide for the intracutaneous skin closure of the mediolateral episiotomies. However, further trials and research are needed to support these results.

Authors' Contribution

Conceptualization: MFZ

Methodology: MFZ, IS, HS, MR, SF

Formal analysis: MFZ, IS, HS, MR

Writing and Drafting: MFZ

Review and Editing: MFZ, IS, HS, MR, SF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Systematic Review


Anatomical Variations of Renal Arteries and Their Clinical Implications in Urological and Transplant Surgeries: A Systematic Review

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ABSTRACT

Anatomical variations of the renal arteries are frequent and can complicate urological and transplant procedures. However, contemporary evidence on their prevalence and clinical implications remains fragmented. **Objectives:** To systematically review studies published between 2019 and 2025 that report renal artery variants and evaluate their surgical impact in urology and transplantation. **Methods:** This review was conducted following PRISMA 2020 guidelines. A systematic search of PubMed, Scopus, and Cochrane identified original human studies reporting quantitative data on accessory arteries, early branching, or unusual origins. Fifteen eligible studies were included in the final synthesis. Risk of bias was assessed using the Joanna Briggs Institute checklist for imaging studies and the Newcastle-Ottawa Scale for surgical cohorts. Risk of bias across imaging and surgical studies was rated low to moderate based on JBI and NOS appraisal. **Results:** The prevalence of accessory renal arteries and early branching varied widely, ranging from 10% to over 30% across populations. A recent donor CTA study reported accessory arteries in 25.6% and early branching in 17%, while a contemporary Omani series found more than 30% of kidneys with multiple arteries. In transplant cohorts, grafts with multiple renal arteries achieved outcomes comparable to those with single arteries when appropriate reconstruction was performed. Microsurgical and vascular techniques have enabled the successful management of complex arterial anatomy without compromising graft function. **Conclusions:** Renal artery variations are common and clinically important. Preoperative CT angiography remains the gold standard for differentiating true multiple arteries from early branches, ensuring safe surgical planning.

INTRODUCTION

The anatomy of the renal arteries exhibits substantial variability beyond the classical single-artery paradigm, a fact that carries real implications for surgical and interventional management [1]. In many kidneys, accessory arteries or early branching patterns arise, altering surgical strategies in donor nephrectomy, kidney transplantation, partial nephrectomy, and endovascular

interventions. Despite advances in imaging technology, reporting of prevalence and morphometry remains inconsistent across populations, hindering the establishment of universal guidelines [2]. Recent studies reinforce the importance of high-resolution vascular mapping. For example, Çetinok *et al.* documented accessory renal arteries in 25.6% and early branching in

17% [3]. In Ethiopia, a computed tomography evaluation found that more than 30% of kidneys had supplementary arterial supply [4]. In the transplant setting, White *et al.* (2021) reported that grafts requiring arterial reconstruction in multiple-artery kidneys had comparable long-term outcomes to single-artery grafts [5]. Likewise, Rath *et al.* (2023) observed no significant functional disadvantage in recipients of multi-artery grafts through one year [6]. Microsurgical techniques to manage accessory arteries have shown durable success in living-donor settings [7]. Given this evolving landscape, a focused synthesis of post-2019 evidence offers an opportunity to clarify prevalence, compare surgical implications, and highlight best practices.

The research question guiding this review was: Among human populations undergoing imaging or surgical evaluation (Population), what are the frequencies and patterns of renal artery variations (Intervention/Exposure), and how do these variations influence surgical and transplant outcomes (Outcome)? This systematic review, therefore, aims to collate and interpret the latest data on renal artery variations, examine their clinical consequences, and propose standardized approaches for imaging and surgery in urology and transplantation.

METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A comprehensive literature search was performed across PubMed, Scopus, and the Cochrane Library to identify studies reporting anatomical variations of the renal arteries and their implications in urological and transplant surgery. The search covered publications from January 2019 to August 20, 2025. The Boolean and Medical Subject Headings (MeSH) search strategy was explicitly detailed as follows: ("Renal Artery"[MeSH] OR "Kidney Artery" OR "Renal Arteries" OR "Accessory Renal Artery") AND ("Variation" OR "Anatomy" OR "Anatomical Variation" OR "Anomalies" OR "Early Branching") AND ("Computed Tomography Angiography" OR "CTA" OR "Magnetic Resonance Angiography" OR "MRA") AND ("Transplantation" OR "Urological Surgery" OR "Living Donor" OR "Renal Surgery"). Search filters were limited to human studies, English language, and publications between 2019 and 2025. Reference lists of relevant articles were manually screened to capture additional eligible studies. Abbreviations were defined at first use as follows: CTA (Computed Tomography Angiography), MRA (Magnetic Resonance Angiography), DRA (Double Renal Artery), TRA (Triple Renal Artery), and EB (Early Branching). Studies were included if they reported quantitative data on renal artery variants such as accessory arteries, early branching, or unusual origins;

were conducted in human subjects using CTA, MRA, or direct surgical visualization; and described clinical or surgical implications relevant to donor nephrectomy or transplantation. Exclusion criteria comprised reviews, meta-analyses, case reports, pilot studies without quantitative data, and non-human research. Two reviewers independently screened titles and abstracts, followed by full-text evaluation using a standardized eligibility checklist. Disagreements between reviewers were resolved through discussion and consensus, and when disagreement persisted, a third senior reviewer adjudicated. Agreement between reviewers during study selection was quantified using Cohen's kappa statistic ($\kappa = 0.82$), indicating strong concordance. Data extraction was performed independently by two reviewers using a predesigned proforma capturing author, year, country, study design, imaging modality, prevalence, and clinical implications. Methodological quality was assessed using the Joanna Briggs Institute (JBI) checklist for cross-sectional imaging studies and the Newcastle–Ottawa Scale (NOS) for surgical or transplant cohorts. The overall risk of bias was graded as low, low to moderate, or moderate, based on sample representativeness, imaging clarity, and completeness of reporting (Figure 1).

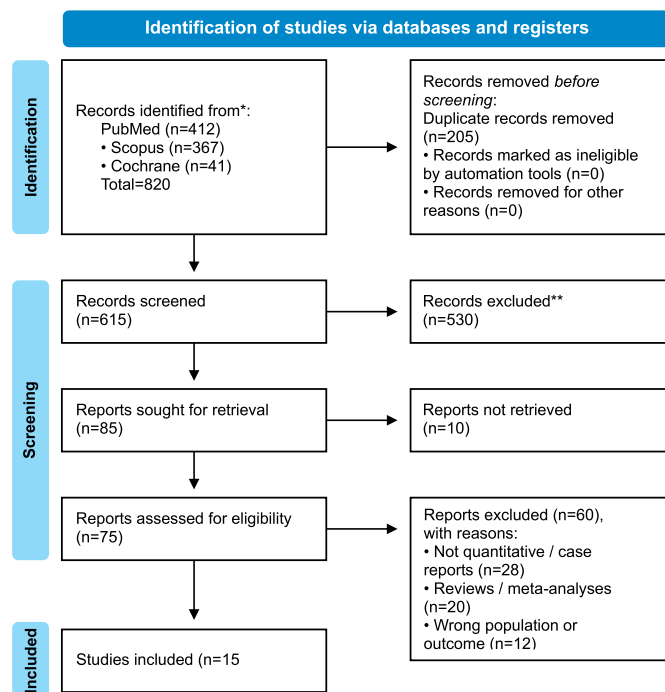


Figure 1: PRISMA 2020 Flow Diagram: PRISMA 2020 Flow Diagram of Study Selection for the Systematic Review of Anatomical Variations of Renal Arteries

RESULTS

The 15 included studies represented a diverse geographic distribution spanning Africa, Asia, Europe, and the Middle East. Most were cross-sectional radiological studies using Computed Tomography Angiography (CTA) or Multidetector CT (MDCT), while a subset involved surgical transplant cohorts. Sample sizes ranged widely, from 60 to 900 kidneys, reflecting heterogeneity in study design and population characteristics. Living-donor cohorts predominated, ensuring clinical relevance for

transplantation. Other studies focused on general hospital populations or specific patient groups, such as resistant-hypertension cohorts and renal-denervation candidates. The consistent use of high-resolution imaging across studies supports the reliability of anatomical mapping, though variability in cohort type and sample size may influence external validity. This distribution provides a strong foundation for understanding anatomical variation across different populations and clinical contexts (Table 1).

Table 1: Characteristics of Included Studies

Sr. No.	References	Country/Region	Study Design	Sample Size (Kidneys/Arteries)	Population Characteristics	Imaging / Method
1	[8]	Nigeria	Radiological (CTA)	100 donors (200 kidneys)	Living kidney donors	CT angiography
2	[9]	India	Radiological (CTA)	90 pts (180 kidneys)	Adult hospital cohort	CT angiography
3	[10]	Iran	Radiological (CTA)	129 donors (258 kidneys)	Living kidney donors	CT angiography
4	[11]	Türkiye	Radiological (MDCT)	450 pts (900 kidneys)	Adults undergoing abdominal CT	MDCT angiography
5	[12]	Sudan	Radiological (CTA)	400 pts	Adults (202 M / 198 F)	CT angiography
6	[13]	Sudan	Radiological (CTA)	160 donors (320 kidneys)	Potential kidney donors	CT angiography
7	[14]	Romania	Radiological (CTA)	185 scans	Archived angio-CT files	CT angiography
8	[15]	Oman	Radiological (CTA)	128 pts (256 kidneys)	Adults 2023-24	CT angiography
9	[16]	Bulgaria	Radiological (CTA)	240 pts	Resistant hypertension cohort	CT angiography
10	[17]	Germany	Surgical transplant cohort	212 grafts	LDKT recipients	Intra-op + preop imaging
11	[18]	India	Surgical transplant cohort	200 grafts	LDKT recipients	Intra-operative series
12	[19]	India	Radiological (CTA)	60 pts (120 kidneys)	Prospective adult cohort	CT angiography
13	[20]	Pakistan	Radiological (CTA)	61 donors (122 kidneys)	Living donor evaluation	CT angiography
14	[21]	Korea	Radiological (MDCT)	200 pts (NR kidneys)	Renal denervation candidates	MDCT angiography
15	[22]	Greece	Surgical transplant cohort	251 recipients	LDKT recipients (accessory polar artery sacrifice)	Surgical + imaging correlation

The prevalence of accessory renal arteries (ARAs) varied significantly, ranging from as low as 6 % to over 30 %, with an average rate of 20-25 % across studies. Laterality patterns often showed slightly higher prevalence on the left kidney, though some studies highlighted side-specific differences. The aorta was consistently identified as the dominant origin of ARAs, with rare variants arising from the iliac arteries. Anatomical subtypes included hilar arteries, which enter at the hilum, and polar arteries, which supply the upper or lower poles. Several studies reported early branching as an important variant, particularly relevant in donor surgery. Studies emphasized the critical distinction between “true” multiple renal arteries and false multiplicity caused by early short branching, underscoring the importance of precise radiological interpretation. Overall, these findings highlight wide anatomical variability across populations that must be considered during surgical and radiological planning (Table 2).

Table 2: Prevalence and Patterns of Renal Artery Variations

Sr. No.	References	Kidneys Examined	Single RA (%)	Multiple/ Accessory RA (%)	Laterality (R vs L)	Origin of Accessory Arteries	Type (Hilar / Polar)	Other Notable Variations
1	[8]	200	68	32	Slight ↑ left	Aorta	Hilar and polar reported	Early branching 18%
2	[9]	180	82	18	NR	Aorta	DRA 88.9%; TRA 11.1%	Pattern taxonomy detailed
3	[10]	258	83	R 15.5; L 17.1	L > R	Aorta	NR	NR
4	[11]	900	76	24	R 16.8; L 14	Aorta (rare iliac)	Hilar and polar	Early branching 7%
5	[12]	800	94	6	NR	NR	NR	Sex-stratified rates
6	[13]	320	57.5	25.6	Bilateral ARA 3.8%	Aorta	Hilar and polar	Early branching 17%; M > F
7	[14]	370	NR	“False MRA” from early short branching	NR	Aorta	Mimics hilar	Emphasizes distinction of true vs false MRA
8	[15]	256	76	24.22	NR	Aorta	Hilar and polar (incl. double unilateral)	NR

9	[16]	480	NR	Variants ↑ in resistant HTN	NR	Aorta	NR	Clinical correlation with HTN
10	[17]	212 grafts	71	29 (MRA grafts)	NR	Aorta	NR	Focus on VR outcomes
11	[18]	200 grafts	71	29	NR	Aorta	NR	Transplant outcomes by MRA vs SRA
12	[19]	120	NR	Correlates with the main RA diameter	NR	NR	NR	Diameter ↔ ARA presence
13	[20]	122	NR	Side-specific prevalence reported	R > L (example)	NR	NR	Also notes venous variants /incidental pathologies
14	[21]	200	NR	Anatomical variants quantified	NR	Aorta	NR	Variation impacts catheter positioning (RDN)
15	[22]	251 grafts	NR	Focus on accessory polar artery	NR	Aorta	Polar (sacrificed subset)	No adverse impact on long-term function when sacrificed judiciously

*RA – renal artery, ARA – accessory renal artery, DRA – double renal artery, TRA – triple renal artery, MRA – multiple renal artery, EB – early branching, HTN – hypertension, NR – not reported.

Across the included studies, anatomical variations of the renal arteries were consistently associated with increased surgical complexity rather than uniformly poor outcomes. In donor nephrectomy, the presence of multiple or early-branching arteries increased the need for additional anastomoses, potentially prolonging ischemic time. However, transplant outcome studies demonstrated that grafts with multiple renal arteries generally achieved comparable functional results to those with single arteries, provided that careful vascular reconstruction was performed. In urological and interventional contexts, the variants influenced operative strategy (Table 3).

Table 3: Clinical Implications (Urological and Transplant Relevance)

Sr. No.	References	Clinical Context	Reported Surgical Challenges	Reported Postoperative Complications	Authors' Recommendations
1	[8]	Donor nephrectomy	More anastomoses; potential ↑ ischemic time with MRA/early branching	NR	Pre-op CTA mandatory; map early branching/ARAs.
2	[9]	Urology & transplant planning	Complexities with DRA/TRA types during anastomosis	NR	Use clear taxonomy (DRA vs TRA; hilar vs polar) for planning.
3	[10]	Donor selection	Side choice influenced by ARA prevalence (L > R)	NR	Routine CTA mapping in donors.
4	[11]	Surgical/interventional	Early branching shortens the pedicle; bleeding risk	NR	Systematic MDCT survey (aorto-iliac to poles).
5	[12]	General urology	Lower ARA prevalence in females (cohort finding)	NR	Consider sex-based planning; CTA before major renal surgery.
6	[13]	Donor nephrectomy	ARA 25.6% and EB 17% affect graft selection/reconstruction	NR	Anticipate bilateral ARA (3.8%); plan reconstruction strategies.
7	[14]	Pre-op imaging QA	Early branching can be misread as "multiple RAs"	NR	Distinguish false MRA (short RA) vs true MRA on CTA.
8	[15]	General urology	24% ARA; double unilateral ARA examples	NR	Routine CTA characterization of variants.
9	[16]	Hypertension workup	Variants associated with resistant HTN (OR=4.7)	NR	Consider renal vascular variants in refractory HTN evaluation.
10	[17]	Transplant surgery	Multiple anastomoses in MRA grafts	Outcomes comparable to single-artery grafts	MRA kidneys not a contraindication; tailored vascular reconstruction.
11	[18]	Transplant surgery	Possible longer operative/ ischemia time	Similar DGF/stenosis/survival (per article)	Safe to use MRA kidneys with appropriate technique.
12	[19]	Surgical planning	Main RA diameter predicts likelihood of ARA	NR	Use RA diameter to anticipate complexity.
13	[20]	Donor evaluation	Variant mapping avoids intra-op surprises	NR	Standard CTA map in donors; note coexisting venous variants.
14	[21]	Interventional (RDN)	Arterial variants affect the catheter approach	NR	MDCT mapping before renal denervation.
15	[22]	Transplant surgery	Selective sacrifice of the accessory polar artery when needed	No adverse long-term impact on graft function	Judicious sacrifice is acceptable when reimplantation is not feasible.

*CTA – computed tomography angiography; MRA – multiple renal artery; EB – early branching; DRA – double renal artery; TRA – triple renal artery; DGF – delayed graft function; NR – not reported.

Most cross-sectional CTA studies were rated as low risk of bias due to robust imaging methodology and adequate sample

sizes. Moderate concerns arose in smaller or more selective cohorts, primarily related to limited generalizability or retrospective design. Studies focusing on special populations also carry a moderate risk, as their findings may not translate directly to general populations or donor cohorts. The transplant cohort studies (Roth, Modi, Panis) were generally rated as low to moderately low risk: although retrospective and single-center in nature, they demonstrated strong clinical follow-up and outcome reporting, which enhances reliability. Overall, the body of evidence can be considered of moderate to high quality, with its greatest strengths in consistent imaging methodology and real-world transplant outcomes, but with some limitations in representativeness and reporting detail (Table 4).

Table 4: Risk of Bias Assessment of Included Studies

Sr. No.	References	Study Design	Appraisal Tool	Risk of Bias	Main Concerns / Notes
1	[8]	CTA, cross-sectional	JB1 Prevalence	Low	Clear donor cohort, good imaging, adequate sample.
2	[9]	CTA, cross-sectional	JB1 Prevalence	Low-Moderate	Modest sample, single center, taxonomy strong.
3	[10]	CTA, cross-sectional	JB1 Prevalence	Low	Good sample size, donor population, reproducible CTA.
4	[11]	CTA, cross-sectional	JB1 Prevalence	Low	Large sample, robust MDCT, minimal bias.
5	[12]	CTA, cross-sectional	JB1 Prevalence	Low-Moderate	Sex distribution analyzed, but recruitment not detailed.
6	[13]	CTA, donor cohort	JB1 Prevalence	Low	Well-defined donor group, clear CTA methodology.
7	[14]	CTA, cross-sectional	JB1 Prevalence	Low-Moderate	Novel "false vs true MRA" distinction, but retrospective imaging.
8	[15]	CTA, cross-sectional	JB1 Prevalence	Low	Adequate sample, contemporary Omani population, clear imaging.
9	[16]	CTA, cross-sectional (HTN cohort)	JB1 Prevalence	Moderate	Resistant hypertension focus may limit generalizability.
10	[17]	Transplant cohort (surgical)	NOS Cohort	Low	Long-term follow-up, robust outcomes, strong validity.
11	[18]	Transplant cohort (surgical)	NOS Cohort	Low-Moderate	Single-center retrospective, but outcomes well reported.
12	[19]	CTA, prospective cross-sectional	JB1 Prevalence	Low	Prospective design, correlation analysis, small sample size.
13	[20]	CTA, donor evaluation	JB1 Prevalence	Low-Moderate	Small cohort, but donor selection well defined.
14	[21]	CTA, interventional planning	JB1 Prevalence	Moderate	Specific to renal denervation cohort; not general population.
15	[22]	Transplant cohort (surgical)	NOS Cohort	Low-Moderate	Retrospective single center, but large recipient sample.

DISCUSSION

The synthesis of fifteen primary studies confirms that renal artery variations are common and clinically significant. Several large imaging cohorts outside the included set support this high prevalence while highlighting population-specific and methodological effects. Karayağız *et al.* from Türkiye reported vascular variants in 59.4 % of 1,073 donors, with multiple renal arteries (MRA) in 35.4 % and early division in 21.4 % values at the higher end of the current review range and above those seen in non-donor hospital cohorts [23]. In contrast, Regmi *et al.* observed moderate, mixed-pattern frequencies, aligning with mid-range estimates [24]. Beyond donor cohorts, whole-abdomen CTA studies demonstrate a left-sided predominance and frequent polar arteries, echoing the laterality trend summarized in table 2. A Palestinian CT series reported arterial variants in 31 % of patients, again with a left-side bias, consistent with several included studies [24]. Kumaresan *et al.* in Indian donor data characterized peri-hilar branching in detail, noting accessory arteries in 39.4 % and early division in 21.2 %,

reinforcing that early branching must be distinguished from true multiplicity, the same interpretive caution raised by Jianu *et al.* [25, 14]. Kaushik *et al.* further supported broad morphological diversity and confirmed that such findings are not modality-specific but anatomically genuine [26]. Clinical implications are consistent across studies. In transplantation, MRA grafts have shown comparable outcomes to single-artery grafts when reconstruction is performed carefully. Garcia *et al.* reported similar patient and graft survival despite longer operative times [27]. Tabbara *et al.* detailed techniques to create a single inflow orifice in MRA grafts, emphasizing that meticulous vascular reconstruction underpins success [28]. Kurz *et al.* demonstrated that donors with remnant kidneys containing MRAs maintain normal long-term renal function and blood pressure, paralleling recipient outcomes [29]. Likewise, Colucci *et al.* found preserved renal and cardiovascular health in donors, supporting expansion of anatomical acceptance criteria in modern donor programs [30]. Outside transplantation, arterial

variants have procedural relevance across multiple specialties. In endovascular and ablative settings, Bartoli *et al.* proposed a semi-automatic CTA method for mapping perfusion territories to guide complex aortic procedures [31]. For oncologic surgery, Lv *et al.* linked accessory arteries to larger tumor size and higher Fuhrman grade, suggesting possible correlations between vascular anatomy and tumor biology [32]. Hypertension-related evidence also supports clinical importance. Wu *et al.* and Jing Li *et al.* found higher blood pressure and vascular remodeling among patients with ARAs, consistent with the resistant-hypertension signal in Naydenov *et al.* [16, 33]. Imaging advances continue to evolve: Liu *et al.* validated multimodal ultrasound for identifying accessory arteries in patients for whom contrast CTA is contraindicated [34]. Finally, Shi *et al.* reported individualized management strategies in robotic renal surgeries, reflecting the need for tailored arterial handling [35]. Across datasets, heterogeneity in prevalence reflects cohort composition and imaging rigor. Donor-only series (India, Türkiye) tend to report higher accessory and early branching rates due to detailed arterial-phase CTA protocols that detect smaller branches [25]. Large-field abdominal CT audits, such as Jalamneh *et al.* reveal mid-range prevalence with a persistent left-sided skew, compatible with the pooled findings here [36]. Technical studies further demonstrate how standardized reconstruction methods (e.g., pantaloons, Carrel patch, or side-to-side trunk creation) yield outcomes equivalent to single-artery grafts, underscoring that anatomical variation alone is not a contraindication for transplantation [28]. Overall, the evidence demonstrates that accessory renal arteries and early branching are frequent anatomical patterns with significant surgical implications. CTA provides the most reliable pre-operative assessment tool for differentiating true multiple arteries from early divisions, thereby improving surgical planning and reducing intra-operative risks. When such variations are accurately mapped and surgical techniques are appropriately adapted, patient outcomes are comparable to those with single-artery anatomy.

Most studies were single-center, cross-sectional, or retrospective, with variability in imaging protocols and sample characteristics. This restricts generalizability and prevents robust meta-analysis. Few datasets provided direct inter-regional comparisons or long-term non-transplant outcomes, representing an area for future improvement. Larger multicenter prospective studies using standardized imaging criteria are needed to refine prevalence estimates and improve risk stratification. Further research should explore the effect of vascular variants on minimally invasive and endovascular procedures, integrating tools such as 3D reconstruction,

AI-assisted segmentation, and automated morphometry to enhance accuracy and safety.

CONCLUSIONS

Renal artery variation is the norm rather than the exception. Evidence from recent donor, imaging, oncologic, and hypertensive cohorts demonstrates that accessory arteries and early branching patterns are frequent and clinically significant. Transplant and major urological surgeries can be performed safely when pre-operative vascular mapping and meticulous reconstruction are undertaken. Donors retaining kidneys with multiple arteries show stable long-term renal function, and recipients achieve comparable graft outcomes. For interventional and hypertensive cases, recognition and management of accessory vessels may influence procedural success and blood-pressure control. Future work should prioritize multicenter, prospective designs using standardized morphometric parameters such as diameter, ostial height, and branch angle to refine risk prediction and procedural algorithms.

Authors' Contribution

Conceptualization: SK

Methodology: MAJ, ASB

Formal analysis: SK, AHK

Writing and Drafting: SK, TM, MAJ, SMTS, AHK

Review and Editing: SK, TM, MAJ, SMTS, AHK, ASB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

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Systematic Review


Understanding the Goals of Service Learning and Community-Based Medical Education: A Systematic Review

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ABSTRACT

Service learning (SL) and community-based medical education (CBME) are increasingly integrated into undergraduate medical training to prepare students for socially accountable practice. While many programs report benefits for students and communities, the specific goals emphasized across contexts remain inconsistently defined. **Objectives:** To provide a comprehensive understanding of how SL and CBME contribute not only to student learning but also to community engagement and institutional development. **Methods:** Following the PRISMA 2020 guidelines, PubMed, Scopus, and the Cochrane Library were searched for English-language studies published between 2019 and 2024. Eligible studies included those involving undergraduate medical students participating in SL or CBME interventions. Data on study design, participants, interventions, and reported outcomes were extracted. Quality appraisal was conducted using the CASP, MMAT, and JBI tools. A thematic synthesis approach was used to categorize findings into educational, community, and institutional domains. **Results:** Sixteen studies were included, spanning Africa, Asia, North America, and the Middle East. Most studies reported educational outcomes such as improved clinical competence, empathy, reflective capacity, and professional identity formation. Community-level goals included increased access to care, health promotion, and stronger partnerships. Institutional goals, such as enhancing curricular relevance and social accountability, were less frequently documented. Few studies evaluated long-term sustainability or objectively measured community outcomes. **Conclusions:** SL and CBME consistently promote student growth while fostering community engagement. However, systematic evaluation of institutional impact and program sustainability remains limited. Future research should adopt longitudinal, multi-institutional approaches to capture durable outcomes and guide curricular reforms aligned with social accountability.

INTRODUCTION

Medical education worldwide is shifting from hospital-centered models toward approaches that emphasize population health and social accountability. Traditional training has been criticized for insufficiently preparing students to address inequities, thereby prompting the adoption of community-based strategies [1]. Globally, evidence shows that service learning (SL) and community-

based medical education (CBME) help medical students integrate academic learning with real-world service. In Australia, embedding community engagement early in curricula fosters reflective skills and strengthens readiness for underserved care [2]. In Japan, longitudinal SL electives promoted advocacy and sustained empathy among undergraduates [3]. Similarly, a Japanese study of

rural placements demonstrates growth in student accountability and community orientation [4]. The COVID-19 pandemic further accelerated innovation in SL and CBME. A U.S. study found that pandemic-modified SL projects preserved student leadership development and professional growth despite restrictions [5]. Comparable findings were noted in India, where virtual CBME activities maintained student community connections [6]. Local contexts also highlight the need for reform. In Pakistan, short-term community placements improved students' patient interaction skills but lacked long-term follow-up [7]. In Nepal, CBME has been linked with a greater interest in rural service, though challenges in sustainability remain [8, 9]. Across Africa, structured engagement in Uganda and Kenya fostered teamwork and social accountability but highlighted the need for institutional support [10, 11].

Despite these advances, critical gaps persist. Most published work focuses primarily on student perspectives, while systematic evaluation of institutional change and long-term community outcomes remains limited. Therefore, this systematic review was conducted to address these gaps by synthesizing existing evidence and clarifying the explicit goals of SL and CBME within undergraduate medical curricula. This review synthesizes evidence from 2019–2024 to clarify the explicit goals of SL and CBME programs for undergraduate medical students, categorizing them into educational, community, and institutional domains. Establishing evidence base is essential to inform future curriculum design, promote sustainability, and strengthen the social accountability of medical education programs globally. The review aims to provide a comprehensive understanding of how SL and CBME contribute not only to student learning but also to community engagement and institutional development.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The primary aim was to explore and synthesize the reported goals of service learning (SL) and community-based medical education (CBME) within undergraduate medical curricula. A comprehensive search was conducted in three electronic databases: PubMed, Scopus, and the Cochrane Library. The search covered studies published between 2019 and 2024, ensuring inclusion of the most recent and relevant evidence. Search terms included both Medical Subject Headings (MeSH) and free-text keywords such as "service learning," "community-based medical education," "undergraduate medical students," "professional identity formation," "empathy," "social accountability," and "community engagement." Boolean operators (AND, OR) were applied to refine the results. Searches were limited to

English-language studies, and the reference lists of included articles were screened to identify additional eligible papers. Studies were included if they focused on undergraduate medical students in preclinical or clinical years, reported on interventions involving SL or CBME (e.g., placements, medical camps, project-based courses, or student-run clinics), and described educational, community, or institutional outcomes as primary or secondary objectives. Studies were excluded if they were systematic reviews, meta-analyses, case reports, editorials, or conference abstracts, or if they focused solely on postgraduate trainees, faculty, or non-medical disciplines. Non-English publications and animal studies were also excluded. All identified records were imported into EndNote for reference management. Duplicates were removed before screening. Titles and abstracts were independently reviewed by two authors against the inclusion criteria. Full-text articles of potentially relevant studies were retrieved, and disagreements during selection were resolved through discussion until consensus was reached. Data extraction was performed using a structured proforma to maintain consistency. Extracted data included author, year of publication, country or region, study design, sample size, participants, intervention type, duration, and reported goals or outcomes. The methodological quality of the included studies was assessed using established critical appraisal tools. The Critical Appraisal Skills Program (CASP) checklist was applied to qualitative studies, the Mixed Methods Appraisal Tool (MMAT) to mixed-methods research, and the Joanna Briggs Institute (JBI) checklists to quantitative and cross-sectional designs. Each study was graded as high, moderate, or low quality based on clarity of aims, methodological rigor, appropriateness of analysis, and reporting standards. Given the heterogeneity in study designs and outcomes, a thematic synthesis approach was adopted. Findings were categorized into three overarching domains: educational goals for students, community goals, and institutional goals. Within these domains, subthemes were identified and supported with representative studies. A Venn diagram illustrates the overlaps between domains, highlighting shared outcomes such as professional identity formation, community engagement, and sustainability used consistently throughout to denote both community-level continuity and the long-term impact of educational programs. The database search covered PubMed, Scopus, and Cochrane Library for studies published between January 2017 and August 2025. After removal of duplicates and screening for eligibility, a total of 16 studies met the inclusion criteria and were included in the final synthesis (Figure 1).

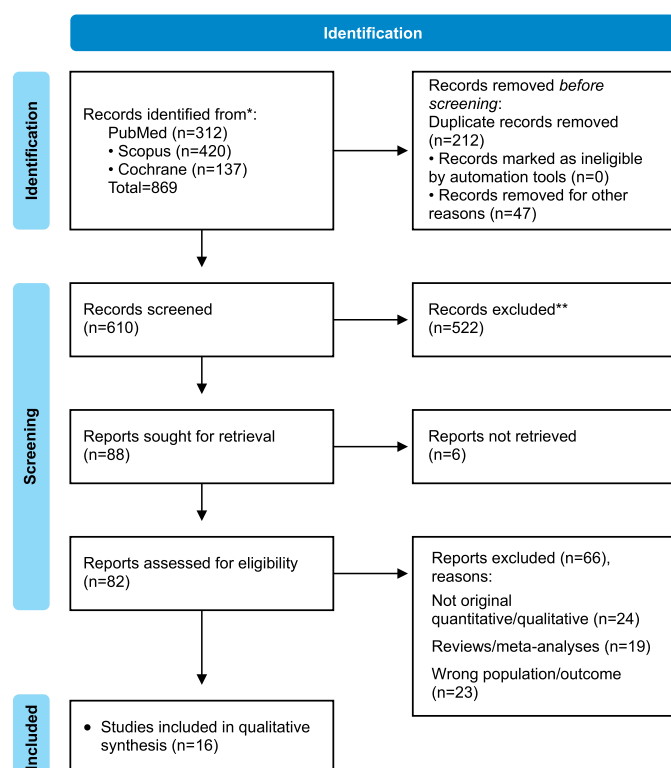


Figure 1: Flowchart of the Study Selection Process, Showing Identification, Screening, Eligibility Assessment, and Inclusion of Studies for Analysis

RESULTS

A total of 16 studies were included, spanning diverse regions, with strong representation from Asia (Japan, Taiwan, Singapore, Pakistan), North America (USA), Africa (South Africa, Ghana), and one study from the Middle East

(Pakistan). Study designs varied, including qualitative interviews and focus groups [12, 13], quantitative cross-sectional surveys [14-16], pre-post or quasi-experimental designs [17-19], and mixed-methods approaches [20-22]. Sample sizes ranged from small cohorts (22-45 students in Ohta's rural islands and Lu's study) to large multi-institutional surveys (over 200 students in Thomson and Burton). Across interventions, short-term rural CBME placements in Japan [23-25] consistently emphasized orientation to general medicine and rural practice, while project-based or hybrid service-learning courses in Taiwan, Singapore, and the USA [17, 18, 26] focused on empathy, reflective practice, and readiness to serve underserved communities. Community outreach models (Kamal in Pakistan, Burton and Rodriguez in the USA; Ampofo in Ghana) highlighted clinical skill development, patient engagement, and reciprocal benefits to communities [14, 22, 27, 28]. Programs introduced during the COVID-19 pandemic [24], underscored adaptability, professional identity formation, and communication skills in modified SL formats. Overall, the evidence shows that CBME and SL are consistently linked to student growth in clinical competence, empathy, and professional identity, while simultaneously fostering community engagement and health awareness. However, most studies were short-term and cross-sectional, limiting conclusions about long-term outcomes or sustainability. Institutional-level impacts such as curricular reform or reputation were rarely measured systematically, representing an important evidence gap (Table 1).

Table 1: Characteristics of Included Studies (Undergraduate Medical Students; 2017-Aug 2025)

Sr. No.	References	Country/Region	Study Design	Sample Size (n)	Participants	Intervention (SL/CBME)	Duration	Reported Goals/Outcomes
1	[12]	South Africa	Qualitative (Focus Groups)	54	Undergrad Medical Students	Community-Based Placements Integrated with 2 Curriculum	Rotation Block	Relevance of Cbme to Learning, Teamwork, and Community Orientation.
2	[13]	Japan (Rural)	Mixed-Methods	54	5 th -6 th Year Med Students	Two-Week Rural CBME Generalist Course	2 Weeks	Improved Attitudes Toward General Medicine, Rural Practice, and Community Health.
3	[14]	USA	Cross-Sectional	186	Med Students (Volunteers vs. Non-Volunteers)	Student-Led Vision Screening (Service-Learning)	Ongoing	Volunteers Gained Confidence in Ophthalmology Skills and Patient Engagement.
4	[15]	USA	Cross-Sectional (Multischool)	246	Med Students	Participation in Student-Run Free Clinics (SL)	Ongoing	Benefits in Service-Learning, Interprofessionalism, Early Patient Exposure.
5	[16]	Taiwan	Cross-Sectional	135	1 st -Year Med Students	Project-Based Service-Learning (Pandemic-Adapted)	1 st Semester	Improved Communication, Professionalism, and Learning Effectiveness.
6	[17]	USA	Pre-Post Quantitative	102	1 st -Year Med Students	Hybrid Service-Learning in Medical Humanities	1 st Semester	Increased Readiness for Underserved Care, Improved Community Attitudes.
7	[18]	USA	Quasi-Experimental	93	Early Med Students	Mandatory Team SL + Guided Reflection	1 st Semester	Significant Increases in Cognitive Empathy and Reflective Capacity.
8	[19]	Japan (Urban)	Pre-post Design	84	Undergrad Med Students	Urban CBME Placements	Course Block	Improved Understanding and Attitudes Toward Community Healthcare.

9	[20]	Singapore	Mixed-Methods	38	Medical Students	Service-Learning with Migrant Workers (6 Cycles)	Multi-Session	Nurtured Empathy, Peer Learning, and Collaborative Skills.
10	[21]	USA	Mixed-Methods	45	Med Students (UG Level)	COVID-19 SL Elective (Community Projects)	Elective Term	Professional Identity Formation, Leadership, and Partnership Skills.
11	[22]	Ghana	Cross-Sectional	303	4 th -year Med Students	Service-learning Embedded in Community Health Clerkship	Clerkship Block	>90% Valued Program; Improved Engagement Skills and Social-11 Determinants Awareness.
12	[23]	Japan (Islands)	Qualitative (Interviews)	22	Undergrad Med Students	Rural Island CBME Immersion	2 Weeks	Deeper Understanding of Local Resources, Interconnections, and Primary-Care Practice.
13	[24]	Japan (Rural)	Cross-Sectional Survey	128	Rural-Track Med Students	General Medicine CBME Exposure	Multiple Course Blocks	Identified Factors Shaping Perceptions of General 16 Medicine and Rural Practice.
14	[25]	Pakistan	Prospective (Non-Comparative)	64	Undergrad Med Students	CBME Via Ophthalmology Medical Camps	4-Hour Intensive	Gains in Focused History-Taking, Exam, Patient Counseling; Improved Confidence.
15	[26]	Taiwan	Longitudinal Quantitative	70	3 rd -Year Med Students	Preclinical Service-Learning Linked to Clerkship	1 st Year	Service-Learning Associated with Higher Empathy (perspective-taking, Compassion).
16	[27]	USA	Program Evaluation	79	Med Students	Student-Led Eye-Health Community Outreach	Multi-Event	Improved Eye-Health Knowledge and Reinforced Community Service Goals.

The synthesis of 16 studies highlighted three main domains of goals linked to SL and CBME: educational outcomes for students, community benefits, and institutional priorities. Educational goals for students were the most frequently reported. Several studies [14, 27, 28] report improvements in clinical competence, with students gaining confidence in history-taking, examination, and patient counseling through medical camps and vision screening programs. Other studies [12, 21, 25] emphasize professional identity formation, noting stronger student responsibility and community orientation after rural and urban placements. Programs integrating guided reflection [18, 20, 26] demonstrate measurable growth in empathy and reflective practice, while others [15, 17, 22] highlight the role of SL/CBME in fostering social accountability, particularly awareness of underserved populations and social determinants of health. At the community level, outcomes include improved healthcare access through vision care and outreach initiatives [22, 27, 28], as well as stronger partnerships with local organizations and community stakeholders [20-22]. Studies in rural Japan [24, 27] demonstrate how CBME contributes to trust-building and sustainability by preparing students for generalist and rural practice. At the institutional level, several studies [12, 16, 25] indicate that CBME and SL enhance curricular relevance, aligning medical education more closely with community needs. Others [15, 18] emphasize interprofessional collaboration, with students working in team-based and clinic settings. Institutions engaged in community programs [21, 22] also strengthen their reputation and social accountability, reinforcing their role as partners in public health. Overall, the evidence indicates that SL and CBME foster competent, empathetic, and socially responsible medical graduates, while simultaneously benefiting communities and strengthening institutional credibility (Table 2).

Table 2: Thematic Synthesis of Goals of Service Learning (SL) and Community-Based Medical Education (CBME)

Themes	Sub-Themes	Representative Studies	Reported Goals / Outcomes
Educational Goals for Students	Development of Clinical Competence	[27, 28]	Improved History-Taking, Examination, Patient Counseling, Ophthalmology/Vision Care, and Eye Health Knowledge.
	Professional Identity Formation	[21, 25]	Growth of Student Professional Roles, Understanding Community Healthcare Responsibilities, Sense of Accountability.
	Reflective Practice and Empathy	[26, 20]	Increased Empathy (JSPE), Compassion, Self-Reflection, and Bias Mitigation through Structured Reflection.
	Social Accountability Awareness	[15, 22]	Heightened Awareness of Underserved Needs, Social Determinants of Health, and Commitment to Service.
Community Goals	Improved Access to Healthcare	[14, 27]	Expanded Access to Vision Screening, Eye Care, and Ophthalmic Outreach; Enhanced Community Health Education.
	Strengthening Community Partnerships	[21, 22]	Collaborations with Community Organizations; Reciprocal Benefits for Both Community and Students.
	Building Trust and Sustainability	[23]	Trust-Building in Rural Communities; Sustainable Pipeline for General Medicine and Rural Practice.

Institutional/ Faculty Goals	Enhancing Curricular Relevance	[16, 25]	Demonstrated that Cbme/SL makes Curriculum more Applicable to Real-World Settings and Community Needs.
	Promoting Interprofessional Collaboration	[18, 15]	Student-Run Clinics and team Service-Learning Encouraged Collaboration across Disciplines.
	Building Institutional Reputation	[21, 22]	Institutions Seen as Socially Accountable and Engaged with Local Communities; Improved Visibility and Credibility.

The Venn diagram (Figure 2) illustrates how SL and CBME operate at multiple levels. Educational goals center on developing competence, empathy, and professional identity. Community goals emphasize healthcare access, reciprocity, and sustainability. Institutional goals focus on curricular relevance and social accountability. The overlaps demonstrate that these domains are interdependent, with outcomes such as social accountability benefiting both students and communities, while curricular relevance and partnerships connect institutional and community roles. Together, they underscore that SL and CBME not only prepare socially responsible graduates but also deliver tangible community impact and strengthen institutional credibility. Venn diagram illustrating the thematic synthesis of goals associated with SL and CBME. The three domains, educational goals for students, community goals, and institutional goals, overlap to highlight shared outcomes such as social accountability, curricular relevance, and partnerships and trust (Figure 2).

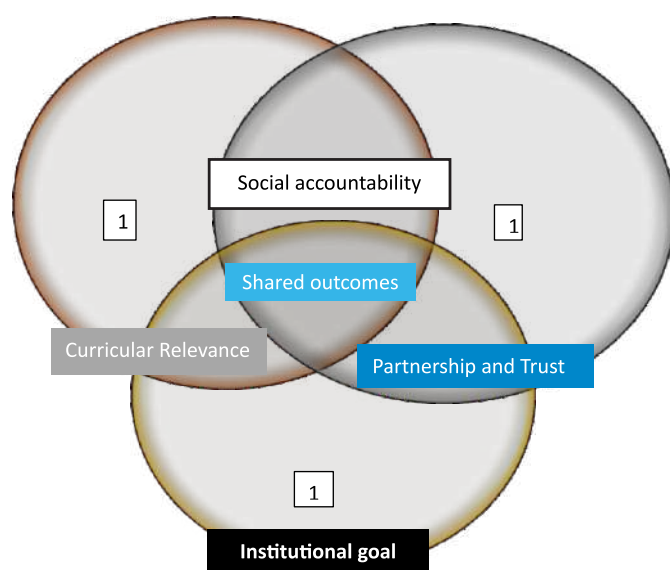


Figure 2: Venn Diagram Showing How SL and CBME Intersect Educational, Community, Institutional Goals, Highlighting Shared Outcomes Like Social Accountability, Partnerships, and Community Impact

The majority of included studies were rated as moderate to high quality, with none classified as low quality. Qualitative research [12, 29] generally demonstrated strong alignment with CASP criteria, though some had limited reflexivity, leading to moderate ratings. Mixed-methods studies [20, 21, 22] performed well on MMAT, showing methodological rigor and integration of qualitative and quantitative components. Quantitative and cross-sectional designs [14, 17, 24, 27] were more frequently rated as moderate, reflecting common limitations such as small sample sizes and limited generalizability. Overall, the quality assessment supports confidence in the thematic synthesis, though future studies would benefit from more robust designs and longitudinal evaluations (Table 3).

Table 3: Quality Assessment of Included Studies

References	Study Design	Appraisal Tool	Quality Rating
[12]	Qualitative (Focus Groups)	CASP	High
[13]	Mixed-Methods	MMAT	Moderate
[14]	Qualitative (Interviews)	CASP	Moderate
[15]	Longitudinal Quantitative	JBIC (Cross-Sectional/Longitudinal)	High
[16]	Mixed-Methods	MMAT	High
[17]	Pre-Post Quantitative	JBIC	Moderate
[18]	Quasi-Experimental	JBIC	High
[19]	Cross-Sectional	JBIC	Moderate
[20]	Prospective (Non-Comparative)	JBIC	Moderate
[21]	Cross-Sectional (Survey + Open-Ended)	MMAT	High
[22]	Mixed-Methods	MMAT	High
[23]	Pre-Post Design	JBIC	Moderate
[24]	Cross-Sectional	JBIC	High
[25]	Cross-Sectional (Multischool)	JBIC	High
[26]	Cross-Sectional Survey	JBIC	Moderate
[27]	Program Evaluation	JBIC	Moderate

High quality = clear aims, rigorous methodology, appropriate analysis, well-reported outcomes, Moderate quality = some limitations (e.g., small sample size, limited generalizability, unclear reflexivity), and Low quality (none in our included set) would indicate major flaws in design or reporting.

Analysis of the included studies shows that the majority emphasize educational outcomes for students, particularly gains in clinical competence, empathy, professional identity formation, and social accountability. Three studies [14, 27, 28] report measurable improvements in clinical skills such as history-taking, examination, and patient counseling through medical camps and community screenings. Others [12, 21, 25] describe professional identity growth and a stronger sense of responsibility after placements in rural or urban community settings. Studies by Yang, Van Winkle, and Sin consistently demonstrate

positive effects on empathy and reflective capacity, although the sustainability of these outcomes beyond training was not assessed [18, 20, 26]. Programs in Ghana, the USA, and Singapore further highlight the role of service learning in fostering awareness of social determinants of health and readiness to serve underserved populations. Community-level outcomes were also frequently described. Initiatives in Pakistan, Ghana, Singapore, and the USA report improved healthcare access and stronger partnerships with local organizations, though most rely on student perceptions rather than direct measures of community benefit. Studies from rural Japan uniquely emphasize trust-building and sustainability, suggesting that CBME may encourage future workforce distribution toward underserved areas. However, evidence from other regions on long-term community benefit remains limited. Institutional-level outcomes were the least studied. While some studies [12, 16, 25] show that SL and CBME improve curricular relevance and contextual learning, and others [15, 18] report enhanced interprofessional collaboration, few systematically address institutional reputation or accountability. Overall, findings indicate that SL and CBME consistently strengthen student learning and community engagement, but notable gaps remain in longitudinal evaluation, objective measures of community impact, and assessment of institutional change.

DISCUSSION

The present synthesis showing that SL/CBME most strongly targets student learning outcomes (competence, empathy, identity), with additional community and institutional benefits tracks closely with recent literature. For student-level gains, newer studies continue to report improved empathy, reflective capacity, and readiness for service when SL is structured with guided reflection and authentic community roles. A recent post-clerkship Health Systems Science course integrating service-learning reported meaningful professional development and highlighted the importance of distinguishing SL from community service or volunteering to maintain educational integrity, mirroring the emphasis on structured reflection in this review [28]. Likewise, a 2025 study of community-based problem-based learning (CB-PBL) in rural Japan showed improvements in students' understanding of community health, personal/professional growth, and engagement with rural needs paralleling the rural CBME effects observed in your included Japanese studies [29]. Evidence from student-run free clinics (SRFCs) further reinforces the pattern of skill gains and service orientation. A 2024 analysis found that SRFC participation bolstered confidence in clinical and interpersonal skills and preparedness for clerkships, aligning with findings from vision-screening and outreach models in your set [30].

Beyond self-reported learning, an education-economics evaluation estimated substantial educational value and an 8:1 benefit-cost ratio for an SRFC, suggesting institutional and learner returns that complement the competence gains you observed [31]. Newer community-engaged curricula also echo the dual-benefit model. In Ghana, a structured, course-embedded approach reported high student valuation and leadership/engagement gains consistent with your findings on social accountability and partnership building, though still short on population-level outcomes [32]. A 2024 mixed-methods SL curriculum report emphasized social justice awareness and durable service commitment through close work with community partners, reinforcing the partnership/reciprocity sub-themes in this review [33]. The COVID-era SL adaptations in the literature also align with this review's observations about adaptability and identity formation. A 2024 study of a SL elective documented positive effects on professional identity formation and learning, paralleling pandemic-adapted, project-based SL in your dataset [22]. Institutional-level outcomes remain under-measured; a gap echoed in contemporary sources. Recent program reports and surveys describe enthusiasm for CBME and explicit social accountability aims, yet identify structural barriers to faculty development, cross-sector collaboration, and curricular embedding as limiting sustained impact [34]. Emerging work does suggest institutional promise: for example, SRFC cost-value data imply a path to demonstrate return on educational investment, and health-systems SL courses frame SL as part of mission-aligned, system-aware training, but these remain exceptions rather than the rule [31]. Two cross-cutting issues in the recent literature mirror the gaps in this review. First, short-duration and cross-sectional designs dominate, limiting insight into the durability of empathy, identity, or community outcomes [33]. Second, community impact is commonly inferred from student self-reports rather than objective metrics (service utilization, disease control, longitudinal access indices). Some newer work begins to address community-facing education and empowerment within CBME, suggesting potential for measurable patient outcomes, but rigorous community indicators remain rare [35]. Finally, the scope is broadening geographically. Global CBME initiatives report growth in understanding of social determinants and community-driven approaches, consistent with the global South/North blend in your results; at the same time, national surveys (e.g., South Korea) reveal system-level needs to integrate CBME as a continuous curricular thread [32]. In summary, this review and the recent literature indicate that well-structured SL/CBME reliably advances student competence, empathy, and professional identity, while fostering community partnership and offering a

rationale for institutional relevance. The field now benefits from contemporary exemplars health-systems SL, CB-PBL in rural settings, and SRFC evaluations but still lacks longitudinal designs, objective community health metrics, and explicit institutional outcome tracking. Addressing these gaps will clarify sustainability, inform curriculum and accreditation, and help align medical education with social accountability goals. New studies should pair reflective pedagogy with robust evaluation frameworks that capture student trajectories, community outcomes, and institutional change overtime.

However, the current evidence base is limited by predominantly short-term and cross-sectional study designs, with insufficient emphasis on long-term community benefits or institutional transformation. Future research should adopt longitudinal, multi-institutional designs to evaluate program sustainability and broader systemic impact.

CONCLUSIONS

This systematic review demonstrates that service learning (SL) and community-based medical education (CBME) consistently foster key educational outcomes among undergraduate medical students, including enhanced clinical competence, empathy, reflective capacity, and professional identity formation. These interventions also promote meaningful community engagement and health awareness, while supporting institutional priorities such as curricular relevance and social accountability.

Authors' Contribution

Conceptualization: HW

Methodology: HW, FP

Formal analysis: HW, MAK

Writing and Drafting: MK, FP, PZ, MAK, SSF

Review and Editing: MK, HW, FP, PZ, MAK, SSF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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Systematic Review



Association of Oxidative Stress Biomarkers with Polycystic Ovary Syndrome (PCOS) and Its Metabolic Outcomes, Including Insulin Resistance and Dyslipidemia: A Systematic Review

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common endocrine metabolic disorder characterized by hyperandrogenism, ovulatory dysfunction, and insulin resistance. Increasing evidence suggests that oxidative stress (OS) contributes to its metabolic and reproductive complications. **Objectives:** To systematically review primary studies evaluating oxidative stress biomarkers in PCOS and their associations with metabolic outcomes. **Methods:** A comprehensive search was conducted in PubMed, Scopus, and Cochrane Library up to April 2024, following PRISMA 2020 guidelines. Eligible studies included case-control and cross-sectional designs reporting quantitative OS biomarker data in PCOS versus controls. Quality and risk of bias were assessed using the Newcastle Ottawa Scale (NOS). **Results:** Fifteen studies (2014–2024) involving over 1,000 participants were included. Malondialdehyde (MDA) was elevated in nearly all studies, indicating enhanced lipid peroxidation. Total antioxidant capacity (TAC/FRAP) and enzymatic antioxidants (SOD, CAT) were consistently reduced, while non-enzymatic antioxidants (GSH, vitamins A/C/E) were also lower. PON1 activity and sRAGE levels decreased, and 8-isoprostane in follicular fluid correlated with poorer oocyte quality. OS markers were positively associated with BMI, insulin resistance, and dyslipidemia. Five studies were rated low risk and ten moderate risk by NOS criteria. **Conclusions:** PCOS is characterized by increased oxidative stress and reduced antioxidant defense, closely linked to metabolic severity. Incorporating OS biomarkers into clinical evaluation and exploring phenotype-specific antioxidant interventions may improve metabolic and reproductive outcomes. Future longitudinal studies should standardize biomarker measurement to strengthen clinical applicability.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders among women of reproductive age, affecting 8–13% globally and up to 20% in South Asian populations [1]. Beyond menstrual irregularities and hyperandrogenic features, PCOS is

strongly linked with a cluster of metabolic abnormalities, including obesity, insulin resistance, dyslipidemia, and an increased lifetime risk of type 2 diabetes and cardiovascular disease, making it a major public health concern [2, 3]. Increasing evidence suggests that oxidative



stress(OS) plays a central role in the pathogenesis of PCOS, contributing to both metabolic dysregulation and impaired folliculogenesis [4]. Oxidative stress is known to influence key metabolic pathways involved in insulin signaling, lipid metabolism, and adipocyte function. Reactive oxygen species (ROS) can impair insulin receptor activity, promote lipid peroxidation, and trigger chronic low-grade inflammation, all of which exacerbate insulin resistance, obesity, and dyslipidemia in women with PCOS [5]. Recent international studies have highlighted that PCOS is characterized by elevated reactive oxygen species, higher malondialdehyde (MDA) levels, and reduced antioxidant defenses, even in non-obese phenotypes [6]. Studies like Yan *et al.* demonstrated that women with PCOS exhibit energy metabolism abnormalities with heightened OS independent of body mass index [7], while Padder *et al.* reported significantly reduced superoxide dismutase (SOD) and catalase (CAT) activity in hyperinsulinemic, hyperandrogenic PCOS phenotypes [8]. Granulosa-cell studies confirm that mitochondrial dysfunction parallels OS burden and negatively affects oocyte quality [9]. Similarly, Santander *et al.* observed downregulation of Nrf2-regulated antioxidant genes in PCOS, implying impaired cellular defense [10]. Furthermore, several interventional studies have demonstrated that reducing oxidative stress can improve metabolic profiles in PCOS. Interventional research supports these findings, showing that lifestyle measures such as yoga [10] and structured exercise [11] and structured exercise [12] can significantly lower OS indices and improve metabolic profiles. Locally, oxidative imbalance in PCOS remains underexplored despite the high prevalence of obesity and metabolic syndrome among South Asian women. Azim *et al.* reported significantly higher MDA and lower paraoxonase-1 (PON1) activity among Pakistani women with PCOS [13], and Zaki *et al.* documented reduced total antioxidant capacity in adolescents with PCOS, suggesting that OS is present early in the disease course [14].

However, heterogeneity in biomarker selection, assay methods, and reporting makes it difficult to compare results across populations and to establish clear links with metabolic severity. Taken together, these findings indicate that oxidative stress not only contributes to reproductive dysfunction in PCOS but also underlies its major metabolic manifestations, including insulin resistance, dyslipidemia, and obesity. This systematic review was therefore conducted to synthesize global and regional evidence on oxidative stress biomarkers in PCOS and explore their associations with insulin resistance, dyslipidemia, obesity, and reproductive outcomes. The study aimed to generate a consolidated understanding of the redox imbalance in PCOS and highlight its potential as a target for therapeutic intervention and risk stratification.

METHODS

This systematic review was conducted between 2014 and 2024, and in June 2024, following the PRISMA 2020 guidelines. The primary objective was to synthesize available evidence on oxidative stress biomarkers in women with polycystic ovary syndrome (PCOS) and their association with metabolic manifestations such as obesity, insulin resistance, and dyslipidemia. The review protocol was prospectively planned; however, it was not pre-registered in a public database but developed in advance to ensure methodological transparency, specifying the search strategy, eligibility criteria, and data extraction approach. A comprehensive electronic literature search was carried out in PubMed, Scopus, and Cochrane Library from database inception until April 2024. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords including "polycystic ovary syndrome" OR "PCOS" AND "oxidative stress" OR "malondialdehyde" OR "MDA" OR "superoxide dismutase" OR "SOD" OR "glutathione peroxidase" OR "GPx" OR "catalase" OR "total antioxidant capacity" OR "paraoxonase" OR "8-isoprostane" OR "sRAGE". Boolean operators (AND/OR) were used to maximize sensitivity. Reference lists of all eligible articles were also screened manually to capture additional studies not indexed in the databases. Studies were selected based on the following inclusion criteria: Population: Women of reproductive age diagnosed with PCOS (any diagnostic criteria acceptable, preferably Rotterdam), Design: Original primary research limited to cross-sectional and case-control designs, as no cohort or interventional studies meeting the inclusion criteria were available, Outcomes: Assessment of at least one oxidative stress marker (MDA, TAC, SOD, CAT, GPx, GSH, PON1, oxLDL, 8-isoprostane, sRAGE, or antioxidant vitamins) with or without metabolic parameter correlations and Language: Published in English and available as full text. Exclusion criteria included review articles, systematic reviews, meta-analyses, pilot or narrative studies, case reports, animal studies, and studies not reporting quantitative biomarker data or involving non-PCOS populations. All retrieved records were exported to EndNote and duplicates were removed. Two reviewers independently screened titles and abstracts for relevance, followed by full-text review of potentially eligible articles. Discrepancies were resolved by consensus. A total of 550 records were identified through database searching, of which 175 were removed before screening (duplicates and ineligible records). After screening 375 titles and abstracts, 270 records were excluded as irrelevant. Full texts of 105 articles were assessed for eligibility, leading to the exclusion of 84 studies (35 non-quantitative, 30 reviews/case reports, 20 with unrelated outcomes). Finally, 15 studies were included

in the qualitative synthesis (Figure 1).

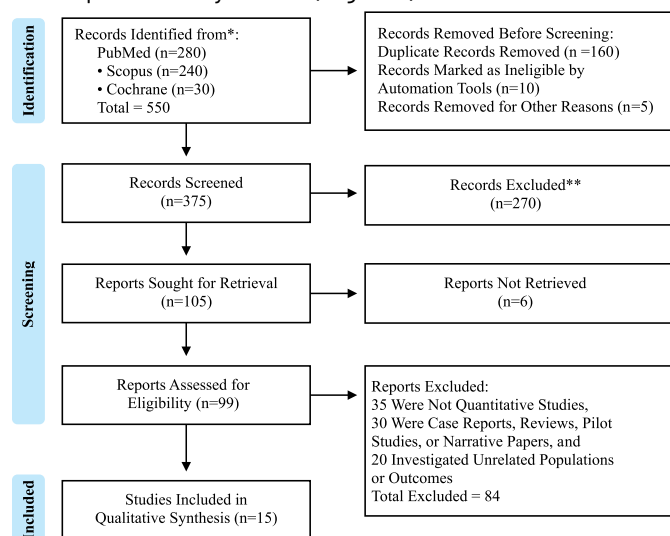


Figure 1: Selection of Studies for the Systematic Review

Data were extracted using a standardized data extraction sheet. Extracted variables included first author, year of publication, country, study design, sample size (PCOS vs controls), mean age, mean BMI, diagnostic criteria, biomarkers measured, and key findings (direction of change, correlations with metabolic parameters). Where available, information on assay type, sample type (serum, plasma, follicular fluid), and cycle phase was also recorded. Risk of bias for included studies was evaluated independently by two reviewers using the Newcastle-

Ottawa Scale (NOS) for case-control and cross-sectional studies. Each study was scored across three domains: selection (0–4), comparability (0–2), and exposure/outcome assessment (0–3). Studies scoring ≥ 8 were rated low risk, scores of 6–7 were considered moderate risk, and scores ≤ 5 were considered high risk. Disagreements were resolved through discussion.

RESULTS

This systematic review included 15 primary studies published between 2014 and 2024, collectively representing a wide geographic distribution across Asia, Africa, and Europe. Most were case-control studies, with one cross-sectional study in adolescents. Sample sizes ranged from 19 to over 300 participants. Where reported, mean age typically fell between 24–32 years, aligning with the reproductive age group, and most PCOS cohorts were in the overweight or obese range (e.g., Azim *et al.* reported mean BMI 28.5 kg/m² vs. 25.7 kg/m² in controls) [13]. All but two studies used the Rotterdam criteria for PCOS diagnosis. The most common biomarkers evaluated were malondialdehyde (MDA) and total antioxidant capacity (TAC/FRAP), with several studies measuring enzymatic antioxidants (SOD, CAT, GPx), non-enzymatic antioxidants (GSH, vitamins A/C/E), and advanced markers (PON1, oxLDL, 8-isoprostane, sRAGE). Together, this study highlighted the moderately heterogeneous but methodologically comparable evidence base (Table 1).

Table 1: Characteristics of Included Primary Studies on Oxidative-Stress Biomarkers in PCOS

Sr. No.	References	Country	Design	n (PCOS/ Control)	Mean Age (y) (PCOS / CTL)	BMI (kg/m ²) (PCOS / CTL)	PCOS Criteria	Biomarkers Measured	Main Findings (PCOS vs Control)
1	[5]	Poland	Case-control	63 / 53	NR	NR	NR	oxLDL-C, FRAP	Pro/antioxidant imbalance; subgroup patterns.
2	[13]	Pakistan	Case-control	70 Total (split per paper)	NR	28.5 ± 4.6 / 25.7 ± 4.5	Rotterdam	MDA, PON1	↑MDA; ↓PON1 in PCOS.
3	[14]	Egypt	Cross-sectional	50 / 50	17.15 ± 2.6 / 16.09 ± 1.6	20.50 ± 1.74 / 20.75 ± 1.50 (non-obese)	Rotterdam	TAC/FRAP + hormones	↓TAC; negative correlation with LH/FSH.
4	[15]	Nigeria	Case-control	50 / 50	28.18 ± 5.06 / 27.80 ± 5.11	26.58 ± 5.16 / 24.40 ± 2.86	Rotterdam	MDA, SOD, TAC, lipids	↑MDA; ↓SOD & TAC; adverse lipids.
5	[16]	Poland	Case-control	26 / 21	28.09 ± 6.68 / 32.84 ± 9.92	26.57 ± 6.68 / 24.53 ± 4.37	Rotterdam (in PCOS)	MDA, SOD, CAT, GPx	Group differences; patterns vs IR/obesity.
6	[17]	Turkey	Case-control (infertility clinic)	44 / 44	24.8 ± 4.8 / 31.3 ± 5.6	28.4 ± 6.7 / 25.9 ± 4.6	Rotterdam	PON1, Fetuin-A	↓PON1 more evident with higher BMI.
7	[18]	Oman	Case-control	100 / 100	29.9 ± 6.2 / 32.2 ± 6.3	NR (reported by obesity categories, not mean)	Rotterdam	Multiple OS indices (e.g., TOS/TAS, MDA)	PCOS linked to increased oxidative stress.
8	[19]	Sudan	Case-control	153 / 152	NR	NR	NR	GSH, SOD, LPO/MDA, Homocysteine	↑Lipid peroxidation, SOD, TG; associations with BMI /age.
9	[20]	India	Case-control (ART; follicular fluid)	90 / 90	NR	NR	Rotterdam	8-isoprostane (FF)	↑8-iso in PCOS FF; possible impact on ART outcomes.

10	[21]	Saudi Arabia	Case-control	NR	NR	NR	NR	SOD, GSH, metals	↓SOD & GSH; heavy-metal exposure links with OS.
11	[22]	Turkey	Case-control	51 / 50	NR (18-45 y)	NR	NR	TOS/TAS, inflammatory markers	OS and inflammation elevated in PCOS.
12	[23]	Iran	Case-control (IVF)	19 / 26	29.3 ± 5.54 / 37.4 ± 5.97	27.3 ± 4.40 / 24.9 ± 3.38	Rotterdam	sRAGE (serum & FF)	Altered sRAGE profile vs covariates; BMI influences FF sRAGE.
13	[24]	Turkey	Case-control (FF)	40 / 40	NR	NR	NR	TAC, TOC, 8-OHdG (FF)	Redox imbalance & DNA damage markers differ by PCOS phenotype.
15	[26]	Bangladesh	Case-control (pregnant PCOS vs controls)	NR	NR	NR	NR	MDA, vitamins A/C	↑MDA; ↓vitamins A/C in pregnant PCOS.

Among the 14 studies, MDA/LPO was the most consistently reported biomarker, appearing in nine studies and showing elevated levels in nearly all PCOS cohorts, strongly indicating increased lipid peroxidation. TAC/FRAP/TAS was assessed in five studies, with four reporting significant reductions, pointing to impaired antioxidant defenses. SOD activity was lower in four of four studies, whereas GPx findings were mixed, reflecting possible compensatory upregulation in select phenotypes. Non-enzymatic antioxidants (GSH, vitamins A/C/E) were uniformly decreased in all reporting studies, reinforcing the presence of systemic redox imbalance. Both studies measuring PON1 reported significantly reduced activity, while follicular fluid 8-isoprostane levels were consistently elevated. Overall, oxidative stress in PCOS was not isolated to one pathway but represents a broad imbalance between oxidants and antioxidants (Table 2).

Table 2: Oxidative-Stress Biomarkers with Number of Studies and References

Biomarkers	No. of Studies	Studies Reporting	Direction of Change in PCOS vs Control	Consistency of Evidence
MDA / LPO	9	[24-26]	↑ Significantly higher in nearly all studies	High
TAC / FRAP / TAS	5	[21, 22]	↓ Lower in PCOS in 4/5 studies	Moderate-High
SOD	4	[19, 24]	↓ Lower activity in most (4/4)	Moderate
GPx	2	[16, 24]	Mixed (1 ↑, 1 ↓)	Low
CAT	2	[16, 24]	↓ in both	High
GSH	2	[19, 24]	↓ in all	High
PON1	2	[13, 17]	↓ Lower activity across both studies	High
oxLDL-C	1	[21]	↑ Elevated vs controls	Single-study evidence
8-Isoprostane (FF)	2	[20, 24]	↑ Elevated in follicular fluid	High
sRAGE	1	[23]	↓ Lower serum & FF levels	Single-study evidence
TOC / TOS	2	[22, 24]	↑ Higher in PCOS	Consistent (2/2)
Antioxidant Vitamins (A, C, E)	2	[24, 26]	↓ Lower levels in both	High

↑ for increased, ↓ for decreased, and "mixed" where studies disagreed. Consistency is rated qualitatively High = ≥80 % of studies agree on direction, Moderate = 50-79 % agree, and Low = <50 % or highly mixed results.

Associations between oxidative markers and metabolic outcomes were evident in several studies. MDA showed positive correlations with BMI, HOMA-IR, fasting insulin, and dyslipidemia, indicating that oxidative stress burden parallels metabolic risk severity. TAC/FRAP and SOD were inversely associated with BMI and HOMA-IR, suggesting that lower antioxidant defense accompanies worsening insulin resistance. Markers such as GSH and PON1 consistently displayed negative correlations with BMI and HOMA-IR, indicating their depletion may contribute to cardiometabolic risk. Follicular fluid biomarkers (8-isoprostane, TOC) were linked to poorer oocyte quality and reduced fertilization rates, supporting the hypothesis that oxidative stress directly compromises reproductive potential in PCOS (Table 3).

Table 3: Association of Oxidative-Stress Biomarkers with Metabolic and Endocrine Parameters in PCOS

Biomarkers	Metabolic / Endocrine Parameter	No. of Studies	Direction / Key Findings	Studies Reporting
MDA / LPO	BMI / Obesity	4	Positive correlation – higher MDA in overweight/obese PCOS and rises with BMI category.	[21, 25]
	HOMA-IR / Fasting Insulin	5	↑MDA strongly associated with higher HOMA-IR, fasting insulin and IR prevalence.	[22, 26]
	Lipid Profile (TG, LDL, HDL)	3	↑MDA correlates with ↑TG, ↑LDL, ↓HDL (atherogenic pattern).	[18, 19]

TAC / FRAP / TAS	BMI / Obesity	3	↓TAC more pronounced in obese PCOS women.	[18, 21]
	HOMA-IR / Insulin	2	Inverse correlation lower TAC associated with worse insulin sensitivity.	[18, 22]
SOD	BMI / WC	3	Negative association lower SOD activity with higher BMI and WC.	[18, 19]
	HOMA-IR / Insulin	2	Lower SOD linked to higher IR indices.	[15, 19]
GPx	BMI / HOMA-IR	2	Mixed evidence ↑GPx in one study, ↓ in another; may depend on obesity status.	[16, 18]
CAT	BMI / WC	2	↓Catalase correlated with higher waist circumference.	[16, 18]
GSH	BMI / HOMA-IR	3	↓GSH consistently associated with obesity and IR severity.	[18, 21]
PON1	BMI / IR markers	2	↓PON1 activity inversely correlated with BMI and HOMA-IR.	[13, 17]
8-Isoprostane (FF)	Ovarian response / ART outcomes	2	↑8-iso associated with poorer oocyte quality, reduced fertilization rates.	[20, 24]
sRAGE	HOMA-IR / AMH	1	↓sRAGE associated with higher IR and altered ovarian reserve (AMH).	[23]
TOC / TOS	HOMA-IR / TG	2	↑TOS positively correlated with TG and IR markers.	[22, 24]
Vitamins A/C/E	BMI / HOMA-IR	2	↓Vitamin levels inversely related to BMI and IR indices.	[18, 26]

Quality assessment rated five studies as low risk (NOS score ≥8) and nine as moderate risk (NOS score 6–7). No study was considered high risk. Lower scores were mainly due to smaller control groups, incomplete reporting of BMI/age, or single-center design. Importantly, most studies used validated diagnostic criteria and standardized assays, lending confidence to the overall findings. These results suggest the evidence base is reasonably strong but would benefit from larger multicenter cohorts, standardized sample timing (fasting state, cycle phase), and consistent reporting of anthropometrics to enhance comparability (Table 4).

Table 4: Risk of Bias Assessment of Included Studies Using Newcastle–Ottawa Scale (NOS)

References	Selection (0–4)	Comparability (0–2)	Outcome/Exposure (0–3)	Total (0–9)	Risk Category
[5]	4	1	3	8	Low
[13]	4	1	3	8	Low
[14]	3	1	3	7	Moderate (adolescents only – generalizability limited)
[15]	4	1	3	8	Low
[16]	3	1	3	7	Moderate (control group smaller, single-center)
[17]	3	2	3	8	Low
[18]	3	1	3	7	Moderate (BMI data categorical only)
[19]	3	1	2	6	Moderate
[20]	3	1	2	6	Moderate
[21]	3	1	2	6	Moderate
[22]	4	2	3	9	Low
[23]	3	2	3	8	Low
[24]	3	1	2	6	Moderate
[25]	3	1	2	6	Moderate
[26]	3	1	2	6	Moderate

DISCUSSION

This systematic review of 15 primary studies provides strong evidence that women with polycystic ovary syndrome (PCOS) have significantly elevated oxidative stress (OS) and impaired antioxidant capacity. Lipid peroxidation markers such as malondialdehyde (MDA) were consistently elevated in nine studies, while total

antioxidant capacity (TAC/FRAP) was reduced in most studies. Enzymatic antioxidants, including superoxide dismutase (SOD) and catalase (CAT), were significantly lower in PCOS cohorts, whereas glutathione peroxidase (GPx) showed mixed results. Non-enzymatic antioxidants such as glutathione (GSH) and vitamins A, C, and E were universally reduced, indicating a systemic redox imbalance. These findings corroborate previous evidence that OS plays a central role in the pathophysiology of PCOS, influencing both metabolic and reproductive outcomes. Recent studies reinforce these observations. Sharma *et al.* reported significantly higher total oxidant status (TOS) and lower TAC in PCOS, confirming a pronounced redox shift [27]. Similarly, Sen *et al.* demonstrated elevated OSI and inflammatory markers, suggesting that OS and inflammation act synergistically in PCOS progression [22]. In non-obese adolescents, Zaki *et al.* observed reduced TAC with significant correlations to LH and FSH, indicating that OS is present early and independent of obesity [14]. These findings highlight that metabolic factors exacerbate oxidative stress but do not solely determine its presence, suggesting underlying genetic, hormonal, and environmental influences. The variability in GPx results observed across studies may reflect differences in PCOS phenotypes, body composition, ethnicity, and environmental exposures. Obese and hyperandrogenic PCOS phenotypes tend to display greater oxidative burden, while lean phenotypes may show compensatory increases in GPx activity. These differences underscore that oxidative stress is a heterogeneous process influenced by both intrinsic metabolic status and external factors such as diet, pollutants, and micronutrient intake. Understanding this variability is essential for interpreting biomarker data

and developing phenotype-specific interventions. Markers of lipid peroxidation also appear to be closely tied to metabolic dysfunction. MDA showed positive associations with BMI, HOMA-IR, and dyslipidemia in our synthesis, which was consistent with Nawrocka-Rutkowska *et al.* who reported that MDA and GPx were significantly higher in PCOS and correlated with triglycerides and insulin resistance [16]. Heavy-metal exposure has also been implicated in aggravating OS. Abudawood *et al.* found higher cadmium and lead levels with lower SOD and GSH in PCOS women, supporting the role of environmental triggers [28]. These environmental and metabolic modifiers highlight the multifactorial nature of oxidative imbalance in PCOS and its complex interplay with systemic inflammation and insulin resistance. The ovarian microenvironment is particularly vulnerable to oxidative damage. Our review showed that follicular fluid (FF) 8-isoprostane levels were elevated and associated with poorer oocyte quality. Similar results were reported by Ardehjani *et al.* where resveratrol supplementation significantly reduced TOS and OSI in FF and improved ART outcomes [29]. Growth hormone co-treatment has also been shown to attenuate FF oxidative stress and improve fertilization rates in PCOS undergoing IVF [30]. Proteomic studies by Pereira *et al.* revealed altered HDL-related proteins and antioxidant pathways in FF, further supporting that OS contributes to compromised folliculogenesis [31]. Therapeutic interventions targeting OS appear promising. Ildarabadi *et al.* demonstrated that green coffee supplementation increased PON1 activity without significantly lowering MDA [32], indicating selective improvement of antioxidant defense. Melatonin supplementation has consistently raised TAC and improved menstrual cyclicity [33]. Vitamin D replacement has been shown to improve TAC and reduce hs-CRP in infertile PCOS women, highlighting a potential adjunctive role for antioxidant-oriented therapy [34]. These findings suggest that individualized antioxidant interventions could be integrated into PCOS management, with treatment tailored according to metabolic phenotype, BMI, and oxidative biomarker profile. Phenotype-specific analyses reveal that obese and hyperandrogenic PCOS phenotypes exhibit the greatest OS burden. Mizgier *et al.* reported that MDA and CRP were significantly higher in obese PCOS women than lean counterparts [35]. Lifestyle factors also play a role, as Song *et al.* found that lower dietary TAC was associated with increased odds of PCOS [36], indicating that diet modification may help restore redox balance. Collectively, these insights reinforce the need for precision-based approaches that consider both phenotype and metabolic background when addressing oxidative stress in PCOS.

This review is limited by significant heterogeneity in study

design, PCOS diagnostic criteria, oxidative stress biomarkers, and participant characteristics, which may reduce comparability and limit quantitative synthesis. Additionally, most included studies were cross-sectional with relatively small sample sizes, restricting causal inference and generalizability of the findings. Future research should focus on longitudinal, phenotype-specific studies with standardized biomarker protocols to enhance comparability and clinical translation. Recognizing oxidative stress as both a diagnostic and therapeutic target may pave the way toward more personalized and effective management strategies for women with PCOS.

CONCLUSIONS

This review underscores oxidative stress as a central mechanism linking metabolic, endocrine, and reproductive abnormalities in PCOS. The consistent elevation of MDA and reduction of antioxidant capacity across diverse populations support the inclusion of oxidative biomarkers in risk assessment and clinical monitoring. Targeted antioxidant interventions, including melatonin, vitamin D, polyphenols, and lifestyle modification, hold promise for improving metabolic health, insulin sensitivity, and fertility outcomes.

Authors' Contribution

Conceptualization: HZ

Methodology: BI, AA, SK

Formal analysis: BI, AA

Writing and Drafting: HZ, SS, BI, AM, AA

Review and Editing: HZ, SS, BI, AM, AA, SK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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