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Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

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# Ensuring Support and Inclusion for Individuals with Autism Spectrum Disorder in Pakistan

OPEN ACCESS

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Autism Spectrum Disorder (ASD) is a lifelong neurodevelopmental condition characterized by differences in social communication, restricted or repetitive behaviors, and atypical sensory processing. The term "spectrum" reflects the wide variation in strengths, challenges, and levels of support required by individuals with autism, ranging from those who live independently to those needing substantial assistance. As understanding of ASD has expanded globally, it has increasingly been recognized not only as a clinical condition but also as a broader social and public health concern, particularly in countries where awareness, diagnosis, and support systems remain limited [1,2].

Autism Spectrum Disorder (ASD) is among the most urgent and yet least understood social health issues in Pakistan. It influences social communication, behavior, as well as sensory processing, and children and adults display a broad spectrum of skills and disabilities. Worldwide, ASD is found in approximately 1 per 160 children and research in Pakistan shows that prevalence is similar with 1.3% of children in Karachi (2017) and 1.45% of school going children in Lahore (2019) being diagnosed with ASD. In spite of the increased awareness around the world, Pakistan still has a lot of gaps in awareness, diagnosis and care of ASD individuals [1,2].

In Pakistan, the family of children with ASD have enormous challenges in accessing the qualified professionals and evidence-based interventions. Consequently, they are left to deal with complicated behavioral, sensory and co-occurring problems in many cases without much support. This is often postponed through inconsistent screening and lack of professional capacity as a result of early diagnosis, which may greatly improve the outcome. There are also misconceptions and a dependency on untested home remedies or expensive private care and low educational inclusion of children denies them special learning settings. All of these gaps demonstrate that ASD is not merely a medical problem, but a social and even a bigger social and public health problem that requires immediate intervention [1].

The Punjab Autism Act was passed and it has given official support and recognition to the specialized schools, resource centers, research, professional training, and public awareness campaigns. Recent researches emphasize psychosocial needs of families, sensory and behavioral characteristics of children, and the significance of structured and evidence-based interventions. The focus on the early detection of ASD in regular pediatric care and the development of telehealth, as well as on building community-based support networks, such as online parent communities, offering peer support and emotional assistance is growing. These advances are significant progress in the direction of inclusive education and holistic care, and the problems of awareness, early diagnosis, and professional training still exist [3].

Although these positive steps are made, there is still much to be done. To address the problem of stigma, Pakistan needs to invest in ongoing professional training of healthcare workers, implement screening of ASD at the primary pediatric stage, and initiate mass-scale public education programs. There is an urgent need to have robust support systems to families, better access to quality diagnosis and evidence-based therapy. Studies should emphasize on culturally appropriate interventions and experiences of Pakistani families to inform effective policies. Pakistan has the potential to shift the awareness into action by

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connecting healthcare, education, and social services and promoting community inclusion [3,4].
The developments anticipated in 2025 may represent a critical turning point for autism care and policy in Pakistan. However, sustained, coordinated efforts across healthcare, education, and social sectors will be essential to ensure that individuals with ASD are empowered to thrive and that their families receive the long-term support, inclusion, and dignity they deserve.

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**Original Article**

OPEN ACCESS

# Post Operative Outcomes of Acute Perforated Appendix During Index Admission

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## ABSTRACT

Acute perforated appendicitis is a serious condition associated with higher morbidity, prolonged hospital stays, and increased risk of complications. Understanding postoperative outcomes is crucial for optimizing patient care, improving clinical decision-making, and reducing healthcare burdens. **Objective:** To determine the postoperative outcomes of acute perforated appendicitis during index hospital admission. **Methods:** This descriptive study was conducted at the Department of Surgery, Khyber Teaching Hospital, Peshawar, from October 1, 2024, to July 31, 2025. Male and female patients aged 18 to 60 years diagnosed with acute perforated appendicitis were enrolled. The patients were evaluated for postoperative outcomes, recorded in terms of surgical site infection, wound dehiscence, hospital stay, and intestinal obstruction. Data analysis was carried out using SPSS version 26.0. **Results:** The Mean age of the participants was 33.91 ± 11.834 years, while the mean hospital stay was 7.12 ± 2.721 days. Most of the patients were male (n=101, 67.8%). Retrocecal position of the appendix was frequently recorded in 98 patients (65.8%). Hospital stay more than seven days was observed in 57 patients (38.3%), followed by surgical site infection (n=47, 31.5%). Wound dehiscence was the least frequently recorded in 21 patients (14.1%). **Conclusions:** Acute perforated appendicitis was associated with increased occurrence of postoperative complications and morbidities. Male patients with advanced age were more likely to experience prolonged hospital stay and surgical site infection.

## INTRODUCTION

Acute appendicitis represents the most common clinical condition in emergency surgical departments. Diagnosis is largely clinically supported by various laboratory and imaging tools. Early diagnosis and prompt surgical intervention are the key treatments and prevent complications related to acute appendicitis [1]. Male patients have a slightly higher complication rate than female [2]. Luminal occlusion is the fundamental underlying mechanism for acute appendicitis and perforation. A fecolith is considered the most common cause of such blockage, implicated in approximately 90% of perforation cases. However, other etiologies of luminal obstruction exist, including lymphoid hyperplasia, parasitic infestations (e.g., worms), neoplasms, and foreign bodies [3, 4]. Complications related to acute appendicitis are common at the extreme of ages. The probability of appendicular perforation is twenty percent in the first and after the fourth decade of life [5]. Pre-existing medical conditions like diabetes increase the likelihood of complications and mortality. Among female, the complication rate increases during pregnancy [6-8]. While surgical intervention is the cornerstone in the management of acute appendicitis and perforation, conservative management with broad-spectrum antibiotics or minimal invasive techniques and supportive care may be considered in certain cases, such as very sick

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patients unfit for surgery or anesthesia. Nevertheless, irrespective of the management approach, perforated appendicitis is associated with increased morbidities and mortality [9]. In a study, 76 individuals (25.5%) experienced postoperative complications. The perforated appendicitis and non-perforated appendicitis groups had respective overall rates of complications of 38.02% and 15.49% ($p<0.001$). In the non-perforated group, the median length of hospital stay was statistically substantially less than in the perforated group (3 vs. 5 days; $p<0.001$) [10]. Despite advances in surgical techniques and perioperative care, perforated appendicitis remains a critical condition that often leads to increased risk of postoperative complications, which are seldom studied in the context of local settings. By analyzing these factors, the study identified potential areas for intervention to enhance postoperative recovery. The findings contributed to existing literature by providing updated evidence on the clinical course of perforated appendicitis in the contemporary surgical setting, ultimately guiding healthcare providers in delivering better patient-centered care.

Several risk factors for perforation have been identified, still postoperative outcomes of perforated appendicitis are infrequently evaluated in local clinical settings. Limited contextual data hinders the development of targeted strategies to reduce complications and hospital stay. Therefore, this study aims to determine the postoperative outcomes of patients with acute perforated appendicitis during the index hospital admission to inform improved perioperative management and patient care.

## METHODS

This descriptive study was carried out at the Department of Surgery, Khyber Teaching Hospital (KTH), Peshawar, during the period 1st October 2024 till 31st July 2025, after taking approval from the hospital IRB vide no: 713/DME/KMC. Male and female patients aged 18 to 60 years diagnosed with perforated appendix were enrolled and evaluated for postoperative outcomes. Patients with intestinal perforation, severely cardiopulmonary compromised patients, immune-compromised patients, patients with appendicular mass, and pregnant patients were excluded. Perforated appendix was confirmed by clinical findings such as fever (core body temperature more than 38°C on thermometer) and pain (visual analogue scale score more than four), laboratory features including raised white cell count (total leucocyte count more than 10,000cells/mm3), positive inflammatory markers such as CRP, and an abdominal ultrasound abdomen confirming the presence of appendicular perforation. Post operative outcomes were assessed in the immediate postoperative period till 15 days after surgery, in terms of surgical site infection (defined by the appearance on redness and erythema of 1cm around the wound margin with seroanguinous discharge and culture of discharge revealing growth of microbes), wound dehiscence (defined as the total or complete separation of the wound margins leading to visible window in the wound on clinical examination), hospital stay (number of days spent at the hospital), intestinal obstruction (defined as presence abdominal pain, nausea/vomiting and X ray erect abdomen showing multiple air fluid levels). Sample size was 149, calculated using the WHO sample size calculator, taking the anticipated proportion of complications as 25.5%, 7% margin of error, and 95% confidence level [10]. The sampling technique was non-probability consecutive sampling. Participants were enrolled after approval from the hospital research review committee. Informed consent was obtained from enrolled participants after explaining the study, risks, benefits, and purpose. Baseline clinical and demographic data were gathered. All patients underwent exploratory laparotomy under general anesthesia. A midline incision was given, and the intra-abdominal cavity was exposed. A 10-cc sample was collected from an intra-abdominal collection, which was sent for culture and sensitivity. The collection was drained, and the abdominal cavity was thoroughly washed with normal saline. The appendix was thoroughly examined for the presence of perforation. Appendectomy was done, and further dissection was carried out depending upon the degree of gangrenous area. Drain was placed, and the abdomen was closed. Standard postoperative care was given to all patients, including adequate antibiotic care, analgesia, and fluids. Patients were evaluated for the next 15 days for postoperative outcomes. Data analysis was carried out using SPSS version 26.0. Continuous data were reported as means and standard deviations, and categorical data as frequencies and percentages. Outcome variables, including surgical site infection, wound dehiscence, and intestinal obstruction, were reported as frequencies and percentages, and hospital stay as means and standard deviations. Effect modifiers were controlled through stratification. Post-stratification chi-square test was applied, taking $p\text{-value}\leq 0.05$ as statistically significant.

## RESULTS

The mean age of the participants was 33.91 ± 11.834 years, the mean pain duration was 34.35 ± 4.897 hours, while the mean hospital stay was 7.12 ± 2.721 days, as reported in table 1.

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**Table 1:** Descriptive Statistics of Study Participants (n=149)

| Parameters | Mean ± SD |
|---|---|
| Age (Years) | 33.91 ± 11.83 |
| Pain Duration (Hours) | 34.35 ± 1.89 |
| BMI (kg/m$^2$) | 23.96 ± 2.60 |
| Hospital Stay (Days) | 7.12 ± 2.72 |

Participants aged less than 40 years were 107 (71.8%), while the majority of patients were male (n=101, 67.8%). Retrocecal position of the appendix was most frequently recorded in 98 patients (65.8%). 59 patients (39.6%) had abdominal collections of more than 150ml, and 101 patients (67.8%) underwent appendicectomy without any further dissection, as shown in table 2.

**Table 2:** Distribution of participants according to baseline characteristics (n=149)

| Parameters | Subgroups | n (%) |
|---|---|---|
| Age (Years) | 40 or below | 107 (71.8%) |
| | Above 40 | 42 (28.2%) |
| Gender | Male | 101 (67.8%) |
| | Female | 48 (32.2%) |
| BMI (kg/m$^2$) | 24.9 or below | 98 (65.8%) |
| | Above 24.9 | 51 (34.2%) |
| Education | Matric or below | 59 (39.6%) |
| | Above matric | 90 (60.4%) |
| Profession | Employed | 42 (28.2%) |
| | Unemployed | 107 (71.8%) |
| Appendix position | Retrocecal | 98 (65.8%) |
| | Pelvic | 39 (26.2%) |
| | Pre/post ileal | 12 (8.1%) |
| Collection (ml) | >150ml | 59 (39.6%) |
| | <150ml | 90 (60.4%) |
| Procedure | Appendicectomy | 101 (67.8%) |
| | Right Hemi | 36 (24.2%) |
| | Cecostomy | 12 (8.1%) |

Hospital stay more than seven days was observed in 57 patients (38.3%), followed by surgical site infection (n = 47, 31.5%). Wound dehiscence was the least frequently recorded in 21 patients (14.1%), as shown in table 3.

**Table 3:** Distribution of Postoperative Outcomes among Study Participants (n=149)

| Postoperative Outcomes | Subgroups | Frequency (%) |
|---|---|---|
| Surgical Site Infection | Yes | 47 (31.5%) |
| | No | 102 (68.5%) |
| Wound Dehiscence | Yes | 21 (14.1%) |
| | No | 128 (85.9%) |
| Hospital Stay (Days) | 7 or below | 92 (61.7%) |
| | Above 7 | 57 (38.3%) |
| Intestinal Obstruction | Yes | 30 (20.1%) |
| | No | 119 (79.9%) |

In patients aged 40 years or below, hospital stay more than 7 days was recorded in 27 patients (47.4%), compared to 30 patients (52.6%) aged more than 40 years, with chi-square p-value=<0.001. No other significant association was recorded between outcome variables and patient age. Surgical site infection was more frequent among male patients (n=25, 53.2%) compared to females (n=22, 46.8%), p-value=0.010. The difference in distribution of other outcome variables with respect to gender was statistically insignificant, as shown in table 4.

**Table 4:** Stratification of Postoperative Outcomes with Respect to Patient Age and Gender (n=149)

| Postoperative Outcomes | | Age (Years) | | Total | p-value |
|---|---|---|---|---|---|
| | | 40 or Below | Above 40 | | |
| Surgical Site Infection | Yes | 35 (74.5%) | 12 (25.5%) | 47 (100.0%) | 0.625 |
| | No | 72 (70.6%) | 30 (29.4%) | 102 (100.0%) | |
| Wound Dehiscence | Yes | 11 (52.4%) | 10 (47.6%) | 21 (100.0%) | 0.033 |
| | No | 96 (75.0%) | 32 (25.0%) | 128 (100.0%) | |
| Intestinal Obstruction | Yes | 19 (63.3%) | 11 (36.7%) | 30 (100.0%) | 0.248 |
| | No | 88 (73.9%) | 31 (26.1%) | 119 (100.0%) | |
| Hospital Stay (Days) | 7 or below | 80 (87.0%) | 12 (13.0%) | 92 (100.0%) | <0.001 |
| | Above 7 | 27 (47.4%) | 30 (52.6%) | 57 (100.0%) | |
| **Postoperative Outcomes** | | **Gender** | | **Total** | **p-value** |
| | | **Male** | **Female** | | |
| Surgical Site Infection | Yes | 25 (53.2%) | 22 (46.8%) | 47 (100.0%) | 0.010 |
| | No | 76 (74.5%) | 26 (25.5%) | 102 (100.0%) | |
| Wound Dehiscence | Yes | 14 (66.7%) | 7 (33.3%) | 21 (100.0%) | 0.906 |
| | No | 87 (68.0%) | 41 (32.0%) | 128 (100.0%) | |
| Intestinal Obstruction | Yes | 18 (60.0%) | 12 (40.0%) | 30 (100.0%) | 0.307 |
| | No | 83 (69.7%) | 36 (30.3) | 119 (100.0%) | |
| Hospital Stay (Days) | 7 or below | 59 (64.1%) | 33 (35.9%) | 92 (100.0%) | 0.225 |
| | Above 7 | 42 (73.7%) | 15 (26.3%) | 57 (100.0%) | |

The association between the amount of intra-abdominal collection and postoperative outcomes was statistically not significant (p-value>0.05) as shown in table 5.

**Table 5:** Stratification of Outcome Variable with Respect to Intra-Abdominal Collection (n=149)

| Postoperative Outcomes | | Collection | | Total | p-value |
|---|---|---|---|---|---|
| | | >150ml | <150ml | | |
| Surgical Site Infection | Yes | 19 (40.4%) | 28 (59.6%) | 47 (100.0%) | 0.888 |
| | No | 40 (39.2%) | 62 (60.8%) | 102 (100.0%) | |
| Wound Dehiscence | Yes | 10 (47.6%) | 11 (52.4%) | 21 (100.0%) | 0.417 |
| | No | 49 (38.3%) | 79 (61.7%) | 128 (100.0%) | |
| Intestinal Obstruction | Yes | 14 (46.7%) | 16 (53.3%) | 30 (100.0%) | 0.376 |
| | No | 45 (37.8%) | 74 (62.2%) | 119 (100.0%) | |
| Hospital Stay (Days) | 7 or below | 36 (39.1%) | 56 (60.9%) | 92 (100.0%) | 0.882 |
| | Above 7 | 23 (40.4%) | 34 (59.6%) | 57 (100.0%) | |

## DISCUSSIONS

In the circumstance of perforated appendicitis, late presentation with concurrent medical conditions is an important contributor to additional disability [11]. Acute appendicitis remains the most prevalent surgical emergency. Whenever acute appendicitis advances to

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perforation, its implications can be fatal or lead to a long and challenging recovery [12]. According to the results, patients under the age of forty years were the most likely to have presented with perforated appendicitis; the mean age of these patients was 33.91 ± 11.834 years. These results were consistent with other studies where patients in the third decade of life were the most prevalent age group [7, 8]. Moreover, the complication rate was higher among male patients in our study cohort. The male predominance is indicated by results with a male-to-female ratio of 2.1 to 1, which is consistent with other studies' results [5, 13]. Surgical site infection accounted for the most frequent postoperative complication, which was followed by wound dehiscence, intestinal obstruction, and prolonged hospital stay. Prolonged hospital stay was frequently recorded among patients aged more than 40 years [14]. According to the results, the average time between the onset of pain and hospital presentation was 34.35 ± 4.897 hours, showing a delayed presentation to hospital, i.e., after 24 hours of onset of pain. Patients who presented late had a higher morbidity rate than those who presented early. Patients with preexisting concurrent diseases who were presented late were the only ones who experienced more complications. These results are consistent with research [14, 15]. Therefore, one important factor affecting outcomes following surgery is the delay in undergoing surgery for appendicitis with perforation in patients who arrive at the emergency room late. According to study results, peritoneal collection of more than 150 ml was recorded in 59 (39.6%) patients. These findings were comparable to those of Afenigus AD and colleagues [7]. For patients with moderate to severe peritoneal collections, the corresponding rates of complications increase. Among patients with extensive peritoneal contamination, the death ratio was high; however, no mortality was recorded in our study. Severe intraperitoneal accumulation is therefore linked to a greater perioperative death and disability rate. Retrocaecal and pelvic were the most often reported positions for perforated appendicitis. This result is consistent with the observations of other studies [16, 17]. Another potential factor for increased complication rate was the position of the appendix. Retrocaecal location is most frequently linked to appendicular perforation and peritonitis because it frequently presents an identification challenge, both physically and on imaging, delaying diagnosis [18]. In the majority of instances, the surgical technique was an appendectomy followed by right hemicolectomy following appendix root perforation. No fecal fistula was recorded; hence, cecal resection with primary anastomosis or ileostomy was not performed. The procedure was reported on one patient who had undergone an appendicectomy originally but developed a fecal fistula in a study by Potey *et al.* [10]. The procedure was further complicated by a surgical site infection that was treated with antibiotics and daily dressings. Patients with an appendix base perforation had the greatest rates of morbidity and complications among all patients [19]. These results were consistent with those of Afenigus AD *et al.* [7]. The method used to treat perforated appendicitis is not mentioned in another research [20].

This study did not evaluate the impact of pre-hospital factors such as access to healthcare, referral delays, or prior antibiotic use on the timing of presentation and outcomes. Additionally, disease severity scoring and standardized intraoperative contamination grading were not applied, which may have limited risk stratification of postoperative complications. Prospective studies incorporating standardized severity scores and community-level delay analysis are needed to improve early detection and reduce complications of perforated appendicitis.

## CONCLUSIONS

A significant proportion of patients with perforated appendicitis suffered postoperative complications in the form of surgical site infection, prolonged hospital stays, and wound dehiscence. Postoperative complications were more common among male patients aged more than 40 years. Late hospital presentation was a contributing element to appendicular perforation and its unfavorable consequences.

## Authors' Contribution

Conceptualization: RK
Methodology: RK, SA[1], KN, MBUD, IA
Formal analysis: MBUD, IA, SA[2]
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# Carotid Artery Doppler Study in Patients Presenting with STEMI

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## ABSTRACT

Carotid Artery Disease (Carotid CAD) is a significant risk factor for cardiovascular events, particularly in patients with ST-Elevation Myocardial Infarction (STEMI). Carotid artery stenosis (CAS) has been related to poor outcomes in STEMI patients, but limited data exist on the prevalence and severity of CAS in this population, especially in Pakistan. **Objectives:** To evaluate the presence, severity, and characteristics of Carotid CAD through Doppler ultrasonography in STEMI patients, and to assess the relationship between CAS and clinical outcomes such as hospital stay duration. **Methods:** A cross-sectional observational study was conducted at Hayatabad Medical Complex, Peshawar, from May 2025 to August 2025. A total of 172 patients with STEMI were assessed using a Mindray® DC 70 Colour Doppler Ultrasound Scanner. The severity of CAS was classified as mild, moderate, or severe based on Peak Systolic Velocity (PSV). **Results:** The study found that 48 (27.9%) patients had mild CAS, 86 (50%) had moderate stenosis, and 38 (22.1%) had severe stenosis. The mean PSV values were 95.3 cm/s (mild), 123.4 cm/s (moderate), and 142.8 cm/s (severe). Patients with severe stenosis had significantly longer hospital stays (mean 9.2 days) compared to mild (6.3 days) and moderate stenosis (7.5 days); the p-values obtained were 0.025 and 0.035, respectively. Hypertension showed a significant association with severe stenosis ($p = 0.016$). **Conclusions:** This research work highlights the high prevalence of CAD in STEMI individuals.

## INTRODUCTION

Acute ST-Elevation Myocardial Infarction (STEMI) is a severe form of coronary artery disease (CAD) and a leading cause of mortality globally, including in Pakistan. The management of STEMI has significantly advanced with improvements in diagnostic imaging, particularly with the use of carotid artery Doppler ultrasonography. This technique gives helpful information about the atherosclerotic burden and cardiovascular risk in STEMI patients [1, 2]. Doppler ultrasound is an effective, non-invasive tool for detecting significant Carotid Artery Stenosis (CAS) in STEMI patients, allowing for the assessment of cardiovascular risks. Local studies conducted in Peshawar, Pakistan, have shown its effectiveness in screening for significant CAS, particularly in patients undergoing open-heart surgery, potentially helping to prevent strokes [3, 4]. Carotid Artery Disease (Carotid CAD) is a significant risk factor for cardiovascular events, especially in STEMI patients. Research indicates that the prevalence of clinically significant CAS increases with the extent of CAD, underscoring the importance of carotid screening in these patients [5]. The pathophysiology of STEMI often involves plaque rupture in the coronary arteries, which can also be reflected in the carotid arteries. Studies have shown a correlation between myocardial infarction and carotid atherosclerotic disease [6]. Doppler ultrasound also helps find carotid plaques, which are more common in people who have had heart disease in the past. This illustrates the importance of routine screening in high-risk individuals [7]. Recent studies have emphasised the prognostic value of

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haemodynamic parameters such as the pulsatility index and resistive index, which are associated with adverse outcomes in STEMI patients [8]. Birmpili et al. compared Doppler ultrasound with Computed Tomography Angiography (CTA) for grading carotid stenosis, finding that CTA has higher sensitivity for detecting significant CAS [9]. This study, conducted at a tertiary care centre in Peshawar, addresses the high prevalence of cardiovascular diseases in the region, compounded by risk factors such as diabetes, smoking, and hypertension [10]. Carotid Doppler ultrasonography is a non-invasive and accessible screening tool that could reduce the risk of future cardiovascular events through timely interventions [11]. It is hypothesized that STEMI patients have a high prevalence of CAS, and the severity of CAS is associated with longer hospital stays and a higher prevalence of hypertension. Doppler ultrasonography can be used effectively for early detection of Carotid CAD, which could help in improving patient outcomes by identifying those at greater risk for cardiovascular complications.

However, the clinical utility and outcome-related significance of Carotid Doppler ultrasonography remain underexplored in local populations. Evidence on the prevalence, severity, and characteristics of carotid artery disease in STEMI patients is limited in regional settings. This study aims to evaluate carotid artery disease using Doppler ultrasonography in STEMI patients. The findings may support early risk stratification and improved prevention of future cardiovascular events.

## METHODS

This was a cross-sectional observational study conducted to evaluate Carotid CAD in patients presenting with STEMI. The study was carried out at the Department of Cardiology, Hayatabad Medical Complex, Peshawar, between May and August 2025. The study focused on a cohort of patients diagnosed with STEMI and admitted to the Department of Cardiology, following synopsis approval (No: 2317). The sampling technique employed was non-probability sampling, specifically a convenience sampling approach. Patients who met the inclusion criteria and presented with STEMI during the study period were selected for participation. The sample size was calculated to be 172, based on a reported prevalence of 12.8% of patients with significant CAS (PSV > 125 cm/s) as reported by Steinvil et al. [5]. Sample size calculation was performed using the WHO formula, assuming a 95% confidence interval and a margin of error of 5%. Individuals aged between 18 and 80 years who were diagnosed with STEMI, confirmed based on clinical history, electrocardiographic findings of ST-segment elevation, and elevated cardiac biomarkers. Both male and female patients who met these criteria were included in the study. Individuals with a history of prior carotid artery surgery or intervention, those with chronic kidney disease requiring dialysis, patients who had experienced acute neurological events such as stroke within the past 30 days, and patients who were either unwilling or unable to undergo carotid Doppler ultrasound were excluded from the study. The data collection process began with identifying patients diagnosed with STEMI in the Emergency and Cardiology Wards. Once the diagnosis was confirmed, the patients were approached for participation, and informed consent was obtained from each participant. Following consent, each patient underwent a carotid artery Doppler ultrasound examination using the Mindray® DC 70 Colour Doppler Ultrasound Scanner. The severity of CAS was classified based on Peak Systolic Velocity (PSV) measurements: Mild stenosis: PSV < 125 cm/s, Moderate stenosis: PSV between 125 cm/s and 150 cm/s, and Severe stenosis: PSV > 150 cm/s. This classification was based on established guidelines for evaluating carotid artery stenosis using Doppler ultrasonography. A structured proforma was used for data collection, which included fields for patient demographics, medical history, characteristics of STEMI, and results from the carotid Doppler examination. The proforma was completed by the attending radiologist or trained medical staff, ensuring that all relevant information was accurately documented. Data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize the data. Means and standard deviations (SD) were employed to describe quantitative variables such as age, body mass index (BMI), and hospital stay duration. Frequencies and percentages were used to describe categorical variables such as gender, smoking status, hypertension, diabetes, and the degree of CAS. To assess the association between various factors and carotid artery disease, stratification was performed by age, gender, BMI, hospital stay, smoking status, hypertension, and diabetes. Post-stratification chi-square tests were used to assess the statistical significance of these factors on carotid artery disease and STEMI outcomes. A p-value of less than 0.05 was considered statistically significant, indicating a meaningful association between the studied variables.

## RESULTS

A total of 180 patients were initially screened for inclusion in the study. Out of these, 172 patients met the eligibility criteria and were included. Eight patients were excluded for the following reasons: five had a history of prior carotid artery surgery, two had acute neurological events within the last 30 days, and one patient declined the carotid Doppler ultrasound. The final sample consisted of 172 patients who all presented with STEMI and underwent carotid artery Doppler ultrasound. The mean age of the patients was 56.3 ± 12.4 years, with an age range of 18 to 80

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years. Out of the total 172 patients, 108 (62.8%) were male, and 64 (37.2%) were female. The majority of patients (n = 120, 69.8%) had a BMI ≥ 25, classifying them as overweight or obese. Hypertension was present in 93 patients (54.1%), diabetes in 62 (36.0%), and 45 patients (26.2%) were current smokers (Table 1).

**Table 1:** Baseline Characteristics of Study Participants

| Characteristics | Total (n= 172) | Male (n= 108) | Female (n= 64) | p-value |
|---|---|---|---|---|
| Age (Years) | 56.3 ± 12.4 | 55.2 ± 11.9 | 58.1 ± 13.0 | 0.118 |
| BMI (kg/m$^2$) | 27.4 ± 4.5 | 27.8 ± 4.6 | 26.8 ± 4.3 | 0.202 |
| Hypertension (%) | 93 (54.1%) | 62 (57.4%) | 31 (48.4%) | 0.178 |
| Diabetes (%) | 62 (36.0%) | 41 (38.0%) | 21 (32.8%) | 0.471 |
| Smoking (%) | 45 (26.2%) | 30 (27.8%) | 15 (23.4%) | 0.499 |

The severity of carotid artery stenosis (CAS) was determined based on Peak Systolic Velocity (PSV) measurements: Mild stenosis: PSV < 125 cm/s, Moderate stenosis: PSV between 125 cm/s and 150 cm/s, and Severe stenosis: PSV > 150 cm/s. Out of 172 patients, 48 (27.9%) had mild stenosis, 86 (50.0%) had moderate stenosis, and 38 (22.1%) had severe stenosis. The mean PSV for mild stenosis was 95.3 ± 13.2 cm/s, for moderate stenosis it was 123.4 ± 15.6 cm/s, and for severe stenosis it was 142.8 ± 18.3 cm/s. A significant positive correlation was found between increasing PSV values and the severity of stenosis ($p<0.001$). The hospital stay duration differed significantly between the severity groups. Patients with mild stenosis had an average stay of 6.3 ± 1.5 days, those with moderate stenosis had a mean stay of 7.5 ± 2.1 days, and patients with severe stenosis had the longest hospital stays at 9.2 ± 2.3 days. One-way ANOVA showed a statistically significant difference in hospital stay duration between the severity groups ($F = 7.13$, $p=0.024$). Post-hoc analysis indicated that patients with severe stenosis had significantly longer stays compared to those with mild ($p=0.025$) and moderate stenosis ($p=0.035$). Additionally, hypertension was significantly associated with the severity of carotid stenosis ($\chi^2 = 8.23$, $p=0.016$). A higher percentage of patients with severe stenosis had a history of hypertension (72.4%) compared to those with mild (51.2%) and moderate stenosis (58.1%) (Table 2).

**Table 2:** Hospital Stay Duration by Carotid Stenosis Severity

| Carotid Stenosis Severity | Mean Hospital Stay (Days) | Hypertension (%) | p-value |
|---|---|---|---|
| Mild | 6.3 ± 1.5 | 51.2% | 0.024 |
| Moderate | 7.5 ± 2.1 | 58.1% | |
| Severe | 9.2 ± 2.3 | 72.4% | |

Pearson's correlation coefficient revealed a weak positive correlation between age and PSV ($r = 0.28$, $p = 0.001$), suggesting that older patients tend to have higher PSV values, which are associated with more severe carotid stenosis. The correlation between age and PSV was investigated because older age is known to increase the likelihood of atherosclerotic changes in the arteries, including the carotid arteries (Figure 1).

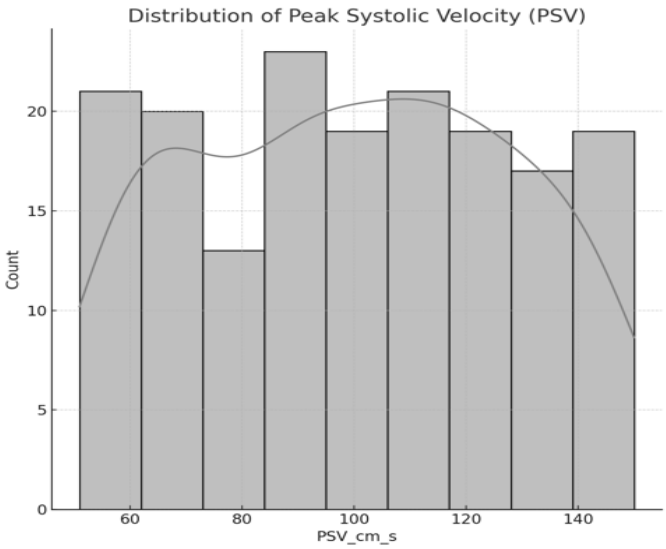


**Figure 1:** Histogram of PSV Distribution

Statistical analyses were conducted at a significance level of 0.05. Descriptive statistics were used for continuous variables, and chi-square tests for categorical variables. ANOVA assessed the relationship between hospital stay duration and stenosis severity, while Pearson's correlation coefficient evaluated the relationship between age and PSV. Additional analyses followed significant ANOVA results.

## DISCUSSION

This study highlights the significant prevalence of CAS in STEMI patients. Among the 172 patients, 50% had moderate stenosis, and 22.1% had severe stenosis. The mean PSV values increased with stenosis severity, confirming the expected relationship between PSV and CAS. Additionally, severe stenosis was associated with longer hospital stays, with patients exhibiting severe stenosis requiring more extended hospitalization. Hypertension was identified as a key risk factor for severe stenosis, consistent with existing literature on hypertension and vascular diseases [1]. These findings suggest that early carotid CAD screening could improve patient management and clinical outcomes in STEMI patients. This study is one of the first to examine carotid CAD in STEMI patients in Pakistan, contributing valuable insights to the limited local data on this association. While similar global studies exist, this research's focus on the Pakistani population using carotid Doppler ultrasound for diagnosis sets it apart. International studies have documented the relationship between carotid CAD and coronary artery disease (CAD). For instance, studies have demonstrated the predictive value of carotid intima-media

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thickness and carotid plaques in STEMI patients, emphasizing the role of non-invasive markers like CIMT and carotid plaques in predicting STEMI risk [12]. The current study's findings, linking severe carotid stenosis with worse clinical outcomes, align with these findings. Furthermore, studies from Europe and other regions highlight the connection between diabetes and carotid CAD, which is similar to our study's findings. Diabetes is recognized for contributing to the progression of carotid atherosclerosis [13]. In Asia, studies have reported the high prevalence of carotid CAD in patients with metabolic syndrome, reinforcing the need for carotid screening in high-risk populations. Our study found a similar pattern, with a high prevalence of carotid CAD in patients with hypertension and obesity [14]. In Bangladesh, a high rate of carotid CAD in elderly patients undergoing coronary artery bypass grafting (CABG) emphasizes the importance of carotid screening for those with concurrent CAD [15]. In Europe, prospective studies have highlighted the predictive role of carotid plaques in ischemic stroke and vascular dementia, further supporting the relevance of carotid screening in patients with cardiovascular diseases [16]. Additionally, studies in the U.S. have emphasized the importance of screening and early intervention in asymptomatic patients with carotid CAD, particularly for managing long-term risks [17]. Current findings support this, as patients with mild to moderate stenosis were still at risk for prolonged hospitalizations and adverse outcomes. Research on carotid CAD and STEMI in Pakistan remains limited, with studies focusing more on carotid CAD in stroke patients [6]. Current study addresses this gap, providing insights into the impact of carotid CAD on STEMI patient outcomes in Pakistan. While research by Yaqoob *et al.* explored Doppler ultrasound for screening cardiac surgery patients for CAS [18]. No studies have yet specifically targeted STEMI patients, indicating the need for further research in this area. Current findings underscore the clinical importance of identifying severe carotid stenosis as a comorbidity in STEMI patients. The association between severe stenosis and prolonged hospital stays highlights the need for early detection and management [19, 20]. The strong link between hypertension and severe stenosis further emphasizes the necessity of comprehensive cardiovascular risk management in STEMI patients.

The study's primary limitation is its cross-sectional design, which restricts the ability to assess long-term outcomes. Longitudinal studies with larger sample sizes are needed to better understand the long-term effects of carotid CAD on STEMI prognosis. Additionally, as the study was conducted at a single tertiary care center, its findings may not be generalizable to the broader Pakistani population. Future research should involve multiple centers to improve the generalizability of the findings and explore the benefits of early carotid CAD intervention in high-risk patients.

## CONCLUSIONS

This study highlights the high prevalence of moderate to severe CAS in STEMI patients, with severe stenosis associated with longer hospital stays and a higher prevalence of hypertension. Early detection of carotid CAD using Doppler ultrasonography may aid in identifying patients at risk, potentially improving clinical management of STEMI patients with carotid artery disease.

## Authors' Contribution

Conceptualization: OK
Methodology: OK, TIK, CH, YA
Formal analysis: OK, TIK, CH
Writing and Drafting: OK, TIK, CH, YA
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All authors approved the final manuscript and take responsibility for the integrity of the work

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**Original Article**

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# Knowledge, Attitude, and Practice of Parents of Children with Epilepsy

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## ABSTRACT

Epilepsy is considered to be present when 2 or more unprovoked seizures occur in a time frame of longer than 24 hours. **Objectives:** To determine the knowledge, attitude, and practice of parents of children with epilepsy. **Methods:** This descriptive cross-sectional study was conducted at the Outpatient Department of Pediatric Neurology, National Institute of Child Health, Karachi, Pakistan, from January to June 2025. A total of 262 parents of children aged 1–12 years with epilepsy for ≥6 months were enrolled through non-probability consecutive sampling. A structured 15-item KAP questionnaire (7 knowledge, 5 attitudes, 3 practice) was developed, validated by experts, pilot tested on 20 parents, and showed good reliability (Cronbach's alpha 0.81). Scores ≥12/15 were classified as good KAP. Analysis was performed using SPSS version 26.0, with chi-square applied post-stratification, taking $p<0.05$ as significant. **Results:** In 262 parents, the mean age was 34.6 ± 7.8 years; 117 (44.7%) were fathers, and 145 (55.3%) were mothers. Good knowledge was noted in 209 (79.8%), favorable attitude in 142 (54.2%), and good practice in 122 (46.6%). Overall, a good KAP was observed in 138 (52.7%). Good KAP was associated with urban residence ($p=0.006$), higher education ($p<0.001$), and healthcare professionals as information source ($p=0.002$), but not with gender, age, or income. **Conclusions:** Most parents had adequate knowledge about epilepsy, while attitudes and practices were comparatively less satisfactory. Better knowledge, attitude, and practice were observed among parents with higher education, those living in urban areas, and those who received information from healthcare professionals.

## INTRODUCTION

Epilepsy is among the most frequent neurological disorders seen in children [1]. According to the International League Against Epilepsy (ILAE), the condition is defined as the occurrence of two or more unprovoked seizures separated by at least 24 hours, a single unprovoked seizure with a recurrence risk exceeding 60%, or the presence of a recognized epilepsy syndrome [2]. Despite notable global progress in reducing idiopathic epilepsy-related deaths and disability-adjusted life years (DALYs), approximately 52 million individuals were living with active epilepsy in 2021, with more than 80% of the burden concentrated in low- and middle-income countries [3]. Early detection and consistent use of antiepileptic medications can achieve effective seizure control in roughly 70–80% of patients [4]. There has been increasing awareness regarding the effect of having a child with epilepsy has on parents and the reciprocal effect of parental knowledge and attitudes about epilepsy on the affected child [5, 6]. A parental attitude towards epilepsy is significantly related to child outcome, as are seizure history and epilepsy duration [7, 8]. The common misconceptions in epilepsy include the overprotection of epileptic children from their families by preventing them from going to school and participating in sports or social activities [9]. Misunderstandings and misinformation should be recognized and corrected for optimal care [10]. A study evaluating knowledge, attitude, and practice (KAP) of parents towards epilepsy reported poor KAP among 78.2% of parents and good KAP among 21.8% of parents [11]. Another study by Hassan et al reported that knowledge of

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most of the parents was adequate (68.2%), attitude was adequate among 76.4% of the parents, and practice was adequate among 72.5% of the parents [12]. Although global data have been pooled regarding KAP of parents with epileptic children, those data only depict assessments with respect to the local settings.

Parental knowledge, attitudes, and practices play a crucial role in seizure management, treatment adherence, and the child's social and developmental outcomes. Existing evidence on parental KAP shows wide variation and remains largely context-specific, with limited data available from local settings. This study aims to assess the knowledge, attitudes, and practices of parents of children with epilepsy. The findings may help identify gaps that can inform targeted educational and counseling interventions.

## METHODS

This descriptive cross-sectional study was conducted at the Outpatient Department of the Neurology Department, National Institute of Child Health (NICH), Karachi, Pakistan, from January 2025 to June 2025. Approval from the institutional ethical review committee was obtained before the study commencement (letter number: IERB-40/2024). A sample size of 262 was calculated using Good Calculators online sample size software [13], anticipated proportion of the parents with good KAP towards epilepsy as 21.8% (p) [11], setting the confidential level at 95% and z as 1.96, and the margin of error at 5% (e), using the formula: n=z2*p*(1-p)/e2. The inclusion criteria were parents of children of any gender aged 1-12 years who were diagnosed with epilepsy at least six months before the study. Only those parents who were visiting the Neurology Clinic for the usual follow-up of epilepsy were included in the study. The exclusion criteria were those epileptic children who were accompanied by caregivers and not by parents. Epilepsy was defined according to ILAE as the presence of ≥ 2 unprovoked seizures separated by at least 24 hours or previously diagnosed children taking antiepileptic drugs (AEDs) [2]. A non-probability consecutive sampling was used for sample selection. Parents were briefed about the objectives of the study and data secrecy to obtain informed and written consent from them. All of the eligible parents went through complete documentation of their demographics, including gender, age, and residential status (rural/urban). Socioeconomic details such as monthly income and level of education were also documented. Parents were interviewed about their knowledge, attitude, and practice regarding epilepsy by using a questionnaire. This study utilized a structured KAP questionnaire that was specifically developed for this research after reviewing the literature and adapting elements from previously validated tools. The questionnaire comprised a total of 15 items distributed across three domains as seven questions on knowledge, five questions on attitude, and three questions on practices regarding epilepsy. The questionnaire underwent content validation by three subject experts in pediatric neurology, public health, and epidemiology. A pilot study was conducted on 20 parents, not included in the final analysis, to pretest the questionnaire for clarity, comprehension, and cultural appropriateness, and minor modifications in wording were made accordingly. Internal consistency and reliability were assessed using Cronbach's alpha, which yielded a value of 0.81, indicating good reliability. Construct validity was established through factor analysis, confirming the three-domain structure of knowledge, attitude, and practice. The questionnaire was also reviewed and approved by the institutional ethics committee as part of the study protocol. The questionnaire was originally developed in English, translated into Urdu, and back-translated for validation. During data collection, questions were administered in Urdu through interviews to ensure understanding among participants with different educational backgrounds. Scoring was performed by assigning one point for each correct response in the knowledge section and for positive or appropriate responses in the attitude and practice sections, with incorrect or inappropriate responses scored as zero. The maximum possible score was 15. Parents achieving a score of 12 or higher (≥80%) were categorized as having good KAP, while those scoring below 12 (<80%) were categorized as having poor KAP [14]. Monthly family income was categorized as low with PKR<30,000, middle as PKR 30,000-70,000, or high as PKR>70,000 [15]. The statistical analysis was performed using "IBM-SPSS Statistics" version 26.0. The qualitative data were expressed as frequency and percentage. The normal distribution of the quantitative data was checked using the Shapiro-Wilk test. For the representation of numeric variables, means and standard deviations or medians and interquartile ranges (IQR) were calculated. The effect modifiers, like gender, age in groups, residential status, socioeconomic status, level of education, and source of knowledge, were controlled through stratification. A post-stratification chi-square test was applied to see the effect of effect modifiers on the outcome (KAP level), by taking p-value <0.05 as significant.

## RESULTS

In a total of 262 parents, the mean age was 34.6 ± 7.8 years, while 117 (44.7%) participants were fathers, and 145 (55.3%) were mothers. There were 160 (61.0%) patients who belonged to urban areas of residence. The main reported sources of knowledge about epilepsy were family or friends (95, 36.3%), media or internet (72, 27.5%), and healthcare professionals (68, 25.6%) (Table 1).

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**Table 1:** Characteristics of Study Participants (n=262)

| Characteristics | | Frequency (%) |
|---|---|---|
| Gender | Male | 117 (44.7%) |
| | Female | 145 (55.3%) |
| Age (Years) | <30 | 81 (30.9%) |
| | 30-40 | 110 (42.0%) |
| | >40 | 71 (27.1%) |
| Residence | Urban | 160 (61.0%) |
| | Rural | 102 (38.9%) |
| Education | Illiterate | 59 (22.5%) |
| | Primary to Middle | 50 (19.1%) |
| | Matriculation to Intermediate | 87 (33.2%) |
| | Graduate or above | 66 (25.2%) |
| Monthly Family Income (PKR) | Low (<30,000) | 125 (47.7%) |
| | Middle (30,000-70,000) | 102 (38.9%) |
| | High (>70,000) | 35 (13.4%) |
| Main Source of Knowledge About Epilepsy | Family / Friends | 95 (36.3%) |
| | Media / Internet | 72 (27.5%) |
| | Healthcare Professionals | 68 (25.6%) |

Overall, good knowledge was observed among 209 (79.8%) parents, while 53 (20.2%) had poor knowledge. There were 220 (84.0%) participants who had heard of epilepsy, and 193 (73.7%) knew that it is not contagious. Correct recognition that epilepsy can be treated with medications was seen in 180 (68.7%), although only 72 (27.5%) were aware that surgery is a treatment option. Misconceptions were common, with 154 (58.8%) acknowledging that epilepsy is not a mental illness and 152 (58.0%) recognizing a possible genetic contribution (Figure 1).

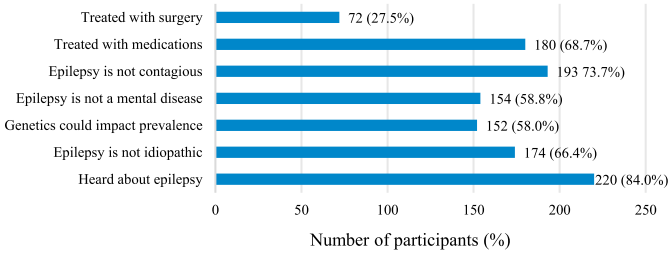


**Figure 1:** Correct Knowledge of Parents Regarding Epilepsy (n=262)

A favorable attitude towards epilepsy was noted in 142 (54.2%) parents, while 120 (45.8%) showed unfavorable responses. There were 161 (61.5%) participants who believed that persons with epilepsy can live equally in society, and 152 (58.0%) agreed they can perform daily activities (Figure 2).

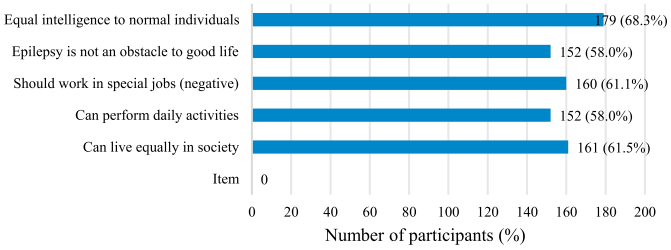


**Figure 2:** Favorable Attitude of Parents Regarding Epilepsy (n=262)

Good practices were reported by 122 (46.6%) parents, while 140 (53.4%) had poor practices. Appropriate responses to seizures (first aid or calling an ambulance) were reported by 117 (44.7%) parents, advising relatives or friends with epilepsy to follow medical care was reported by 150 (57.3%), whereas 166 (63.4%) stated they would act normally when interacting with individuals with epilepsy (Figure 3).

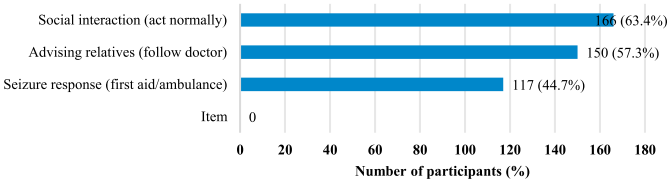


**Figure 3:** Good Practice of Parents Regarding Epilepsy (n=262)

When knowledge, attitude, and practice domains were combined, 138 (52.7%) parents demonstrated good overall KAP, while 124 (47.3%) had poor overall KAP. Good KAP was significantly more frequent among parents living in urban areas, compared with rural parents (68.8% vs. 31.2%, p=0.006). Increasing education showed a strong association with good KAP (p<0.001). Parents who identified healthcare professionals as their main source of information demonstrated significantly higher levels of good KAP compared with those relying on family or friends, or media/internet (p=0.002) (Table 2).

**Table 2:** Association of KAP with Demographic Characteristics of the Parents (n=262)

| Characteristics | | Good KAP, n (%) | Poor KAP, n (%) | p-value |
|---|---|---|---|---|
| Gender | Male | 58 (42.0%) | 59 (47.6%) | 0.367 |
| | Female | 80 (58.0%) | 65 (52.4%) | |
| Age (Years) | <30 | 37 (26.8%) | 44 (35.5%) | 0.290 |
| | 30-40 | 60 (43.5%) | 50 (40.3%) | |
| | >40 | 41 (29.7%) | 30 (24.2%) | |
| Residence | Urban | 95 (68.8%) | 65 (52.4%) | 0.006* |
| | Rural | 43 (31.2%) | 59 (47.6%) | |
| Education | Illiterate | 20 (14.5%) | 39 (31.5%) | <0.001* |
| | Primary to Middle | 23 (16.7%) | 27 (21.8%) | |
| | Matriculation to Intermediate | 48 (34.8%) | 39 (31.5%) | |
| | Graduate or above | 50 (36.2%) | 16 (12.9%) | |
| Monthly Family Income (PKR) | Low (<30,000) | 59 (42.8%) | 66 (53.2%) | 0.237 |
| | Middle (30,000-70,000) | 59 (42.8%) | 43 (34.7%) | |

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| | | | | |
|---|---|---|---|---|
| | High (>70,000) | 20 (14.4%) | 15 (12.1%) | |
| Main Source of Knowledge About Epilepsy | Family / Friends | 47 (34.1%) | 48 (38.7%) | 0.002* |
| | Media / Internet | 35 (25.4%) | 37 (29.8%) | |
| | Healthcare Professionals | 68 (49.3%) | 27 (21.8%) | |

*p<0.05 (significant)

## DISCUSSIONS

The finding that 79.8% parents demonstrated good knowledge about epilepsy, while 21.2% with poor knowledge, reflects an encouraging level of awareness, yet a considerable gap persists. A study from Faisalabad documented that 80% of parents had fair knowledge, which is very closely aligned with the proportion seen in this study, indicating that awareness levels in Pakistan may be broadly consistent across tertiary centers [16]. In contrast, an Egyptian study by Elsakka *et al.* revealed a poor knowledge score among 89.7% of parents of children with epilepsy, demonstrating substantial regional variation [17]. The discrepancy may relate to differences in health education campaigns and the level of integration of epilepsy services within primary health care. In Jordan, Masri *et al.* reported that 90.3% of parents knew epilepsy is not psychiatric, which again suggests that in countries with stronger healthcare communication structures, knowledge tends to be better [8]. These comparisons illustrate that while knowledge in parents appears relatively strong, there are still cultural and informational gaps that need targeted educational strategies. Within the domain of specific knowledge items, the proportion of parents who believed epilepsy is not contagious was 73.7%, while 26.3% still perceived contagion risk. This is comparable to local data, where a quarter of respondents linked epilepsy with transmissibility [16]. A Nigerian study by Frank-Briggs and Alikor found that a significant number of parents attributed epilepsy to demonic possession or contagion, underscoring the persistence of myths in low-resource settings [18]. In this study, 68.7% recognized that epilepsy can be controlled with medications, yet only 27.5% were aware of the surgical option. AlQaisi *et al.* from Iraq, reported that 57.0% of parents had good knowledge overall, but did not specify surgical awareness, while in Saudi Arabia, Zainy *et al.* found that 70% of parents felt informed about different treatment modalities [19, 20]. The lower awareness of surgery in this study could stem from the limited availability of pediatric epilepsy surgery in Pakistan and fewer references to this option by treating physicians. The clinical implication is that caregivers may be less likely to seek referral to specialized centers even when children are candidates, thereby prolonging exposure to uncontrolled seizures. Future public health education should include awareness about surgical options where appropriate. Attitudinal responses in this study indicated that 54.2% of parents expressed a favourable attitude, while 45.8% remained unfavorable. This mirrors the previously published local findings where 54.7% of parents held favourable attitudes, suggesting a consistent trend across Pakistani populations [16]. In Saudi Arabia, Zainy *et al.* observed that nearly half of parents considered epilepsy a mental disorder and over 40% linked it to evil, reflecting a more negative cultural perception [20]. In Ethiopia, Negussie *et al.* reported that 56.7% of caregivers doubted the cognitive abilities of epileptic children, and 39.1% felt they should not attend regular schools, demonstrating substantial unfavorable attitudes [21]. A striking finding in the attitude domain was that 61.1% of parents felt children with epilepsy should work in special jobs, and 58.0% considered epilepsy an obstacle to a good life. In North India, Sinha *et al.* observed that over 70% of parents believed epilepsy hindered family life and affected school performance, closely paralleling the perceptions reported in this study [22]. Parental practices in this study were the weakest domain, with only 46.6% demonstrating good practices. The most concerning was that less than half of the parents reported providing first aid or calling an ambulance during seizures. In contrast, an Iraqi study reported a higher proportion of parents demonstrating good practices at 84.1% [19]. The differences could be explained by methodological variations in defining good practice or by greater exposure to structured seizure management education. In Ethiopia, the researchers showed that 70% of caregivers sought alternative treatments alongside medical care, reflecting both poor practices and mistrust of formal health systems [21]. When domains were combined, 52.7% parents achieved good overall KAP, leaving a substantial 47.3% classified as poor. There is no previously published study on view that combined domains, but similar patterns for each domain have been reported previously [16]. In contrast, the Iraqi cohort displayed higher overall practice levels, while the Egyptian study showed overwhelmingly poor knowledge and attitudes [17, 19]. Sociodemographic analysis revealed that higher education was strongly associated with good KAP, with 76.0% of graduates or postgraduates demonstrating good levels compared with only 34.5% of illiterate parents. In Saudi Arabia, Zainy *et al.* found that misconceptions were significantly less common among college-educated parents [20]. In Jordan, Masri *et al.* reported that higher parental education correlated with positive attitudes and behaviours, while in North India, Sinha *et al.* observed that perception of epilepsy as a psychiatric illness was significantly higher among less educated parents [8, 22]. These parallels indicate that education is the single most powerful determinant of accurate knowledge and supportive attitudes. The clinical

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implication is that structured health education programs should be integrated into routine pediatric neurology clinics, with emphasis on reaching families with lower literacy levels [23, 24]. Residence also showed a clear association, with 59.4% of urban parents having good KAP compared with 42.2% in rural settings. Chidambar et al., in coastal Karnataka, also reported that urban parents had significantly better practices [25]. Public health campaigns must therefore extend into rural communities through schools, primary health workers, and local media. Parents who cited healthcare professionals as their main source achieved a good KAP in 71.2% compared with 49.0% for family or friends and 48.6% for the media. Similar trends have been reported in local and international data previously, where reliance on health professionals correlated with better knowledge [8, 16]. This underscores the clinical responsibility of physicians and nurses to actively provide structured counselling and educational material during follow-up visits.

A few limitations of this study should also be acknowledged. The cross-sectional design prevents assessment of causality between demographic factors and KAP. The nonprobability of consecutive sampling may limit generalizability beyond the study population. The study relied on self-reported responses that may be influenced by social desirability bias. The questionnaire, though validated with Cronbach alpha of 0.81 and factor analysis, was limited to 15 items, which may not capture all dimensions of parental perception. Future research should adopt longitudinal designs with probability sampling and more comprehensive instruments to better assess causal relationships and broader dimensions of parental knowledge, attitudes, and practices regarding epilepsy.

## CONCLUSIONS

The study found that most parents had adequate knowledge about epilepsy, while attitudes and practices were comparatively less satisfactory. Better knowledge, attitude, and practice were observed among parents with higher education, those living in urban areas, and those who received information from healthcare professionals.

## Authors' Contribution

Conceptualization: SK
Methodology: LK, SK, WH
Formal analysis: LK
Writing and Drafting: LK
Review and Editing: LK, SK, WH

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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# Knowledge of Seizures, Epilepsy, and Seizure First Aid among Teachers and Students at Various Educational Levels

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## ABSTRACT

Epilepsy remains poorly understood in low-resource settings, with critical gaps in seizure first aid knowledge. This study assessed awareness among Pakistani students and teachers. **Objectives:** To assess knowledge of epilepsy and seizure first aid among students and teachers of all educational levels in Pakistan. **Methods:** This cross-sectional survey using a non-validated Google questionnaire in English and Urdu was shared on various social media platforms by convenience sampling (N=330). Data was analyzed using SPSS version 26.0. **Results:** A total of 330 responses were included for final analysis. Of which, students were the most numerous (178, 53.9%). Higher proportion of females (219, 66.4%). The majority of both students (164, 49.7%) and teachers (114, 34.5%) had heard of epilepsy or seizures. 42.7% (141) of students and 32.1% (106) of teachers identified epilepsy as a brain disorder. A small percentage of both students (49, 14.8%) and teachers (28, 8.5%) knew how to respond to a seizure. **Conclusions:** Although limited by a non-validated tool and descriptive analysis, this study revealed major gaps in seizure first-aid knowledge among students and teachers. The findings support the need for structured seizure first-aid training programs for students and teachers, and emphasize the impact of this training upon students' well-being and mental health.

## INTRODUCTION

Epilepsy is a non-communicable disease of the brain and affects 50 million people worldwide, according to the WHO. The incidence and prevalence of epilepsy are higher in low and middle-income countries, and three-quarters of people living with epilepsy do not receive the appropriate treatment. The most recent study estimated the prevalence of epilepsy in Pakistan to be 9.99 per 1000. Epilepsy has historically been believed to be a demon or spiritual influence, or a psychological disorder, instead of a brain disorder. Stigma related to epilepsy hinders people living with epilepsy from seeking early treatment and compromises the quality of life in terms of both physical and cognitive well-being. This stigma can also lead to social isolation, rejection by peers, challenges in finding a partner, and reduced opportunities for education and employment [1, 2]. Frequent unrecognized seizures cause hippocampal or entorhinal neuronal loss, which is associated with declining cognitive processing skills and deterioration in memory [3]. Teachers and peers are often the first responders to seizures. Teachers must understand, recognize, and be knowledgeable about seizure responses, as their attitudes can significantly

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affect and impact children's physical and mental health. Knowledge about epilepsy has improved in recent years with the rise of health awareness campaigns, programs, and social media. However, knowledge about seizure first aid remains a significant challenge [4]. This study aimed to determine the level of expertise about seizures, epilepsy, and seizure first aid among students and teachers to identify the knowledge gaps. We plan to implement awareness campaigns, provide resources, and offer certification programs in seizure first aid to address these gaps. This study aims to assess knowledge of epilepsy and seizure first aid among students and teachers of all educational levels in Pakistan.

## METHODS

This cross-sectional study using a non-validated Google questionnaire in English and Urdu was conducted via various social media platforms by convenience sampling (N=330). The Institutional Review Board of King Edward Medical University approved the study (Ref. No. 119/RC/KEMU). The study duration was six months, covering January 2024 to June 2024. The study targeted high school, college, and university students, as well as teachers across all educational levels. The study excluded students and teachers from healthcare to avoid confounding bias and skewing of the results of the study. Consent was obtained in the predesigned Google questionnaire. Researchers designed a questionnaire, based on Adal *et al.* (2024), and modified it [5]. A Google questionnaire in English and Urdu was translated and approved by the institutional board. An invitation to participate in the survey was sent to participants on various social media platforms (Facebook, WhatsApp groups, and distributed in schools and colleges through peers). Currently, no questionnaire has been validated for assessing the knowledge of seizures and first aid among students and teachers; therefore, we developed one. The participants included students over the age of 15 years and teachers between the ages of 20 and 60, selected through a convenience sampling technique. Based on expected epilepsy awareness (50%) as the exact prevalence is unknown, margin of error (5%), and 95% CI, the target was 384 participants; 330 achieved (85.9% response rate). The questionnaire was divided into further sections; the first section consisted of six questions, including demographic data, such as age, gender, designation, education, teaching experience for teachers, and city. The age was calculated in age groups and divided into five groups (<20, 21-30, 30-40, 41-50, and 51-60). The second section included general questions regarding knowledge of epilepsy and seizures, such as if they are familiar with the term epilepsy or seizure, where they have heard it, have they ever witnessed a seizure if yes where, what they think what is epilepsy and seizure, are the seizures and epilepsy are synonymous, medical emergency, contagious or can cause death, if all seizures are the same or different, and the third section included questions related to seizure first-aid, such as do you know how to respond to a seizure, how will you respond, should teachers and students be taught seizure first-aid, and are they interested in learning seizure aid? Most of the questions were closed-ended with 'yes, 'No,' 'I don't know,' and 'Maybe 'responses, and multiple response questions for obtaining consistent and correct responses to avoid misinterpretation of the true awareness. All data were entered and analyzed using SPSS version 26.0. Categorical variables, including age groups, gender, teaching experience, and responses related to epilepsy, seizures, and seizure first-aid, were summarized as frequency and percentage. For key variables, prevalence estimates with 95% confidence intervals (CIs) were calculated using the exact/binomial method. Comparisons between students and teachers were performed using Chi-square tests, and Fisher's exact test was applied when expected cell counts were less than 5. A $p<0.05$ was considered statistically significant.

## RESULTS

Among 386 responses, a total of 330 responses were included for final data analysis. Among the respondents, the predominant group was students 178 (53.9%), and 152 (46.1%) were teachers (Figure 1).

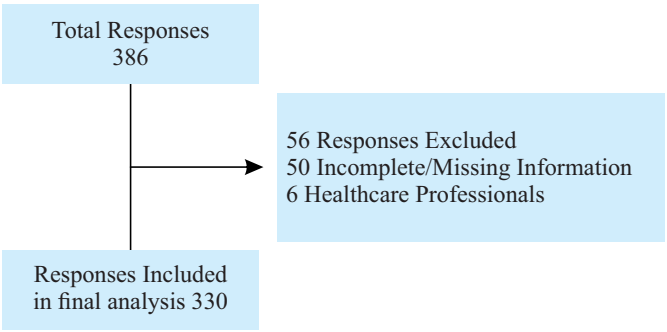


**Figure 1:** Distribution of Teaching Experience Among Participating Teachers (N=152)

The majority (142, 43%) of respondents were students aged less than 20, with one (0.3%) in the 31-40 age group. Teachers were more evenly distributed across various age ranges, with a notable concentration in the 31-40 age bracket (22.1%). Gender distribution showed a higher proportion of females (103, 31.2%) among students and teachers (116, 35.2%), contributing to 66.4% (219) of females across both groups. In terms of geographic distribution, the majority of students were from Lahore (144, 43.6%). Most were high school students (104, 31.5%) or bachelor's degree holders (66, 20%), while teachers predominantly held master's degrees (113, 34.2%) (Table 1).

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**Table 1:** Demographic Characteristics of Participants (N=330)

| Variables | Students (N= 178), n (%) | Teachers (N= 152), n (%) | Total (N= 330), n (%) |
|---|---|---|---|
| **Age (years)** | | | |
| <20 | 142 (43.0%) | 0 | 142 (43.0%) |
| 21–30 | 35 (10.6%) | 26 (7.9%) | 61 (18.5%) |
| 31–40 | 1 (0.3%) | 73 (22.1%) | 74 (22.4%) |
| 41–50 | 0 | 45 (13.6%) | 45 (13.6%) |
| 51–60 | 0 | 8 (2.4%) | 8 (2.4%) |
| **Gender** | | | |
| Female | 103 (31.2%) | 116 (35.2%) | 219 (66.4%) |
| Male | 71 (21.5%) | 36 (10.9%) | 107 (32.4%) |
| Not given / Prefer not to say | 4 (1.2%) | 0 | 4 (1.2%) |
| **City** | | | |
| Lahore | 144 (43.6%) | 28 (8.5%) | 172 (52.1%) |
| Islamabad | 14 (4.2%) | 0 | 14 (4.2%) |
| Sialkot | 0 | 50 (15.2%) | 50 (15.2%) |
| Okara | 0 | 48 (14.5%) | 48 (14.5%) |
| Multan | 2 (0.6%) | 9 (2.7%) | 11 (3.3%) |
| DG Khan | 4 (1.2%) | 1 (0.3%) | 5 (1.5%) |
| Faisalabad | 4 (1.2%) | 1 (0.3%) | 5 (1.5%) |
| Others | 10 (3.0%) | 15 (4.5%) | 25 (7.6%) |
| **Education** | | | |
| Middle School | 1 (0.3%) | 2 (0.6%) | 3 (0.9%) |
| High School | 104 (31.5%) | 6 (1.8%) | 110 (33.3%) |
| Bachelor's Degree | 66 (20.0%) | 25 (7.6%) | 91 (27.6%) |
| Master's Degree | 7 (2.1%) | 113 (34.2%) | 120 (36.4%) |
| Doctorate / PhD | 0 | 6 (1.8%) | 6 (1.8%) |

While teachers who had teaching experience between 5-10 years (39, 11.8%) and 11-20 years (30, 9.1 %) were aware of epilepsy, compared to teachers who had more than twenty years of teaching experience (15, 4.5%). Of the teachers with teaching experience of 5-10 years, the majority were in the age group between 31-40 years. Though statistical significance could not be assessed due to limited stratified data (Table 2).

**Table 2:** Teaching Experience of Participants (N=152 Teachers)

| Experience in Years | n (%) |
|---|---|
| <5 | 38 (11.5%) |
| 5-10 | 50 (15.2%) |
| 11-20 | 41 (12.4%) |
| <20 | 21 (6.4%) |
| Not given | 2 (0.6%) |

Among students, the most common sources of information about epilepsy were given from school/college/university (16.7%), whereas teachers most frequently cited other sources (16.4%), and school/college/university (11.8%). Students reported witnessing seizures in real life (17.6%), followed by TV/cinema (5.8%), while teachers predominantly observed seizures in real life (28.2%). The majority of students (42.7%) and teachers (32.1%) correctly identified epilepsy as a brain disorder, though smaller proportions attributed it to psychological or spiritual causes or considered it "not a disease," and 12.4% overall reported "I don't know." Regarding seizure characteristics, students commonly described seizures as whole-body shaking (29.1%), whereas teachers most frequently selected "all of the above" (50%), reflecting broader recognition of seizure manifestations. Awareness of seizure first-aid, the most commonly chosen correct action was staying with the patient (students 13.9%, teachers 16.1%) (Table 3).

**Table 3:** Source of Knowledge and Seizure Characteristics

| Items | Students (N= 178), n (%) | Teachers (N= 152), n (%) | Total (N= 330), n (%) |
|---|---|---|---|
| **Where have you heard about it?** | | | |
| Social media | 47 (14.2%) | 32 (9.7%) | 79 (23.9%) |
| Family/friends/relatives | 48 (14.5%) | 39 (11.8%) | 87 (26.4%) |
| School/college/university | 55 (16.7%) | 27 (8.2%) | 82 (24.8%) |
| Other | 28 (8.5%) | 54 (16.4%) | 82 (24.8%) |
| **Where have you witnessed a seizure?** | | | |
| Social media | 14 (4.2%) | 14 (4.2%) | 28 (8.5%) |
| TV/cinema | 19 (5.8%) | 5 (1.5%) | 24 (7.3%) |
| Real life | 58 (17.6%) | 39 (11.8%) | 97 (29.4%) |
| N/A | 87 (26.4%) | 93 (28.2%) | 180 (54.5%) |
| Others | 0 | 1 (0.3%) | 1 (0.3%) |
| **What do you think epilepsy is?** | | | |
| Brain disorder | 141 (42.7%) | 106 (32.1%) | 247 (74.8%) |
| Psychological disorder | 15 (4.5%) | 21 (6.4%) | 36 (10.9%) |
| Spiritual cause | 1 (0.3%) | 0 | 1 (0.3%) |
| Not a disease | 4 (1.2%) | 1 (0.3%) | 5 (1.5%) |
| I don't know | 17 (5.2%) | 24 (7.3%) | 41 (12.4%) |
| **What is a seizure?** | | | |
| Whole body shaking | 96 (29.1%) | 69 (20.9%) | 165 (50.0%) |
| Loss of consciousness | 5 (1.5%) | 10 (3.0%) | 15 (4.5%) |
| Loss of awareness | 1 (0.3%) | 4 (1.2%) | 5 (1.5%) |
| Loss of bladder control | 0 | 0 | 0 |
| Tongue bite | 1 (0.3%) | 6 (1.8%) | 7 (2.1%) |
| Fall | 1 (0.3%) | 3 (0.9%) | 4 (1.2%) |
| Pelvic thrusting | 0 | 1 (0.3%) | 1 (0.3%) |
| Body stiffening | 5 (1.5%) | 5 (1.5%) | 10 (3.0%) |
| Head shaking | 1 (0.3%) | 4 (1.2%) | 5 (1.5%) |
| All of the above | 51 (15.5%) | 24 (7.3%) | 75 (22.7%) |
| I don't know | 17 (5.2%) | 26 (7.9%) | 43 (13.0%) |

## Awareness of Epilepsy and Seizures

Among students, 92.1% (95% CI: 87.2–95.6) reported they have heard of epilepsy, compared with 75.0% (95% CI: 67.3–81.7) of teachers. (p-value = 0.0001). Overall, 50.6% of students (95% CI: 43.0–58.1) and 38.2% of teachers (95% CI: 30.4–46.4) reported ever witnessing a seizure (p = 0.031). Regarding whether seizures and epilepsy are synonyms, 35.4% of students (95% CI: 28.1–43.1) and 46.7% of teachers (95% CI: 38.9–54.6) answered "Yes." Regarding the contagiousness of seizures, 44.2% of students (95% CI: 37.0–51.6) and 38.8% of teachers (95% CI: 31.3–46.7)

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correctly responded "No". A total of 19.7% of students (95% CI: 14.0–26.7) and 25.7% of teachers (95% CI: 18.9–33.9) believed that seizures are not a medical emergency. When asked if seizures can cause death, 21.8% of students (95% CI: 16.0–28.6) and 27.6% of teachers (95% CI: 20.6–35.5) answered "Yes." Only 7.3% of students (95% CI: 4.3–11.4) and 10.6% of teachers (95% CI: 6.2–16.8) believed that all seizures present similarly (Table 4).

**Table 4:** Awareness and Misconceptions About Epilepsy and Seizures Among Students and Teachers

| Items | Students (N=178) | Teachers (N=152) | Chi-Square / Fisher's Exact |
|---|---|---|---|
| Have heard of epilepsy (Yes) | 92.1% (95% CI: 87.2–95.6) | 75.0% (95% CI: 67.3–81.7) | p=<0.01 |
| Ever witnessed a seizure (Yes) | 50.6% (95% CI: 43.0–58.1) | 38.2% (95% CI: 30.4–46.4) | p=0.03 |
| Seizures and epilepsy are synonyms (Yes) | 35.4% (95% CI: 28.1–43.1) | 46.7% (95% CI: 38.9–54.6) | p=0.05 |
| Are seizures contagious (Yes) | 9.7% (95% CI: 6.6–13.6) | 7.3% (95% CI: 4.8–11.0) | p=0.45 |
| Are seizures contagious (No) | 44.2% (95% CI: 37.0–51.6) | 38.8% (95% CI: 31.3–46.7) | – |
| Seizures are not a medical emergency (Yes) | 19.7% (95% CI: 14.0–26.7) | 25.7% (95% CI: 18.9–33.9) | p=0.24 |
| Is epilepsy contagious? (Yes) | 3.9% (95% CI: 2.1–7.0) | 4.5% (95% CI: 2.5–7.4) | Fisher's exact, p=0.81 |
| Can seizures cause death? (Yes) | 21.8% (95% CI: 16.0–28.6) | 27.6% (95% CI: 20.6–35.5) | Chi-square, p=0.26 |
| Can seizures cause death? (No) | 8.2% (95% CI: 5.0–13.0) | 15.5% (95% CI: 10.3–22.3) | p=0.04 |
| All seizures present similarly (Yes) | 7.3% (95% CI: 4.3–11.4) | 10.6% (95% CI: 6.2–16.8) | Fisher's exact, p=0.38 |

Knowledge of seizure first-aid was scarce among respondents. Among students, 27.5% (95% CI: 21.1–34.7) reported knowing how to respond correctly during a seizure, compared with 18.4% of teachers (95% CI: 12.6–25.5). Despite this, the majority supported educational training: 97.8% of students (95% CI: 94.3–99.4) and 94.1% of teachers (95% CI: 89.1–97.3) agreed that seizure first-aid should be taught in schools and colleges. Similarly, 81.5% of students (95% CI: 75.0–86.9) and 78.9% of teachers (95% CI: 71.6–85.1) expressed interest in learning seizure first-aid. The most common response chosen appropriately was to stay with the patients (students 46, 13.9%, teachers 53, 16.1%) (Table 5).

**Table 5:** Seizure First-aid Knowledge and Training

| Items | Students N=178, n (%) | Teachers N=152, n (%) | Chi-Square / Fisher's Exact p-value |
|---|---|---|---|
| Know how to respond to a seizure (Yes) | 49 (27.5%, 95% CI: 21.1–34.7) | 28 (18.4%, 95% CI: 12.6–25.5) | 0.08 |
| Support teaching First-aid (Yes) | 174 (97.8%, 95% CI: 94.3–99.4) | 143 (94.1%, 95% CI: 89.1–97.3) | 0.12 (Fisher's Exact) |
| Interested in learning First Aid (Yes) | 145 (81.5%, 95% CI: 75.0–86.9) | 120 (78.9%, 95% CI: 71.6–85.1) | 0.58 |
| **How will you respond?** | | | |
| Restrain the patient | 24 (13.5%) | 20 (13.2%) | – |
| Guide the patient away from danger | 46 (25.8%) | 53 (34.9%) | – |
| Stay with the patient | 61 (34.3%) | 45 (29.6%) | – |
| Give them food and water | 7 (3.9%) | 4 (2.6%) | – |
| Turn on the side and support the head | 25 (14.0%) | 21 (13.8%) | – |
| I don't know | 15 (8.4%) | 9 (5.9%) | – |

## DISCUSSIONS

It was also the first cross-sectional survey to establish the knowledge of epilepsy, seizures, and first aid among teachers at the different levels of education, high school, college, and university students. The majority of the students and teachers were aware of epilepsy (84.2%), and they knew it to be a disorder of the brain (74.8%). Nevertheless, the percentage of the respondents in the two groups who were aware of various forms of seizure (18%) and response to seizure (23.3%) was very low. Students with high school level were more conversant with epilepsy than the students with other levels of education, which aligns with other research works [4]. Regarding first aid response, only 16% of the students knew the proper responses, which was also true in Saudi Arabia (1.6%) [6]. In terms of the nature of seizure, 29.1% of them reported shaking the whole body as a symptom of a seizure, whereas 15.5% viewed all the listed symptoms as symptoms of a seizure. All in all, students were more aware of epilepsy compared to teachers, as seen in higher prevalence, no overlapping confidence interval, and a p-value below 0.0001. In the context of the awareness of the teachers, a number of studies have given more emphasis on training teachers on the acquisition of the recognition of the presence of seizures and the delivery of first aid [7]. Only 11.1% of teachers in Ethiopia were trained [7]; in Jeddah, Saudi Arabia, only one third were trained [8]; other studies reported training 9.2%, 8% and about a tenth of teachers trained [9-11]. In one study in Karachi, it was reported that 15.5 percent of the teachers had been trained on first aid [12]. Consistent with these results, we found that the

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majority of teachers were conversant with seizures and epilepsy, but there was still a large disparity in the knowledge of first aid for seizures (8.5%). Some teachers believed that epilepsy is contagious, similar to earlier research of 14.5% [12-14], although other researchers reported higher percentages (32.4-41.9) [15]. Awareness of epilepsy among teachers also depended on the years of teaching experience, whereby those with 5-20 years' experience were more aware, which could also be because of the epilepsy awareness provided by the media in recent years, in agreement with previous research [10,15-17]. Nonetheless, statistical significance was not provided as a result of scanty stratified data.

This research paper has some limitations. First, the questionnaire employed was non-validated, which may have been a source of measurement bias and a restrictive aspect of reliability. Even though the study was based on previous literature, validated instruments or formal validation should be used in future research. Second, respondents had poor knowledge of seizure first-aid response, and few studies regarding the same have been conducted recently [18-20]. Third, the analysis was descriptive, mainly frequencies and percentages, with no advanced statistical evaluation to explore the associations and predictors. Lastly, convenience sampling in a non-representative manner of the population restricts generalization. Future studies should use validated questionnaires, representative sampling, and advanced statistical analyses to identify predictors of seizure first-aid knowledge and inform targeted educational interventions.

## CONCLUSIONS

The study highlights critical gaps in seizure first-aid knowledge and provides an important foundation for larger, validated, and more analytically robust studies in the future. This study also stresses the importance of public education and training of teachers in recognizing the importance of seizure first aid response and how unrecognized seizures can significantly impact the physical and cognitive health of children. The prompt recognition and prompt initiation of treatment can reduce the morbidity and mortality associated with epilepsy.

## Authors' Contribution

Conceptualization: ZS
Methodology: ZS, NK, JS, AH, SL, SB
Formal analysis: JS, SL, SB, HM
Writing and Drafting: ZS, NK, JS, AH, SL, SB, HM
Review and Editing: ZS, NK, JS, AH, SL, SB, HM

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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# Clinical Characteristics of HIV Patients Presenting with Weight Loss: A Cross-Sectional Study

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## ABSTRACT

Recognizing the epidemiology of human immunodeficiency virus (HIV) infection is essential for managing HIV infection. Research on the nutritional health of patients infected with HIV has revealed significant weight loss during the course of the infection, and this occurrence is frequently viewed as a negative indicator of survival prognosis. Over 26 million individuals with HIV are currently undergoing antiretroviral therapy (ART), which has greatly lessened the impact of HIV disease. **Objectives:** To determine the frequency of human immunodeficiency virus in patients presenting with weight loss at Lady Reading Hospital, Peshawar. **Methods:** This observational cross-sectional study was conducted at the Department of General Medicine, Lady Reading Hospital, Peshawar, from 1st July 2022 to 1st January 2023. 117 patients of both genders with weight loss were included in this study. Every patient was tested for HIV through an initial screening test. Patients with positive status on initial screening tests were referred to the special testing clinic for further confirmation. Human immunodeficiency virus was noted. **Results:** The mean age was 41.5±7.8 years and the age range in this study was from 25 to 60 years. Males were 69.2% and females were 30.8%. Human immunodeficiency virus (HIV) was positive in 7.7% of patients. HIV had a significant association with family socioeconomic status, with a p-value of 0.00. **Conclusion:** In conclusion this study demonstrates that HIV is associated with weight loss and wasting remains a highly prevalent complication in the modern antiretroviral era.

## INTRODUCTION

According to the Joint United Nations Programme on HIV/AIDS, 2019 saw 1.7 million new infections of human immunodeficiency virus (HIV) and approximately 700,000 deaths related to AIDS, representing a 37% and 50% decline since 2000. Over 26 million individuals living with HIV were receiving antiretroviral therapy (ART), which has notably alleviated the impact of the disease [1]. The foundation of the global strategy for AIDS control is presently a universal test-and-treat (UTT) approach aimed at identifying all person with HIV (PWH), starting ART without delay, and achieving long-term viral load suppression to enhance health outcomes and stop further HIV transmission; however, it is estimated that one in five PWH globally do not know their HIV status [2]. Starvation is a common but varied occurrence with HIV infection and remains one of the leading causes of mortality in this setting. Dietary decrease, healthy malabsorption, metabolic abnormalities, and endocrine dysfunction are all etiological aspects that are still poorly understood [3]. Prior studies have identified variations in the ways men and women living with HIV recognize and encounter stigma associated with the virus [4]. Studies on the dietary state of HIV-infected individuals have revealed significant weight loss during infection, which has typically been seen as a negative predictor for survival [5]. However, some research has been undertaken on the association between

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malnutrition and illness progression, and the majority of them focused on specific communities [6]. While scientific markers are currently employed in clinical practice, the effectiveness of clinical markers for nutritional status to forecast the progression of HIV disease warrants additional investigation since they are more often and cheaply available [7]. An increase in hospitalizations among people living with HIV due to weight loss remains a relevant issue [8]. This is primarily due to various factors, including medication side effects, gastrointestinal complications, metabolic changes, and nutritional deficiencies [9,10]. The clinical characteristics and effects of HIV infection seen in studies from developed nations cannot be uniformly applied to the various virus subtypes found in Asia, especially in Pakistan. This research was carried out to assess how often human immunodeficiency virus occurs in patients showing weight loss at Lady Reading Hospital, Peshawar, ensuring that all clinicians recognize these indicators and that appropriate and prompt screening for HIV infection is conducted. By investigating this relationship, we aim to fill gaps in the existing research and provide valuable insights into the management and care of people living with HIV.

Nutritional and clinical indicators of HIV are often underrecognized, particularly in resource-limited settings where advanced laboratory testing may not be readily available. Evidence linking unexplained weight loss with HIV infection is limited in local populations, especially in Pakistan, where disease patterns and subtypes differ from developed countries. This study aims to determine the frequency of HIV among patients presenting with weight loss at Lady Reading Hospital, Peshawar. Early identification through clinical presentation may support timely diagnosis and improved patient management.

## METHODS

This observational cross-sectional study was conducted at the Department of General Medicine, Lady Reading Hospital, Peshawar, from July 2022 to January 2023. Ethical approval was obtained from the Institutional Review Board of Lady Reading Hospital Medical teaching institution (Ref. No. 382/LRH/MTI) and the College of Physicians and Surgeons Research evaluation unit (Ref. No. CPSP/REU/MED-2020-022-17115). All patients underwent an initial screening test for HIV. Those who tested positive in this initial screening were directed to the special testing clinic for further confirmation. Sample size for this study was calculated using G*Power version 3.1.9.7, based on a two-tailed t-test for comparing means between two independent groups, HIV patients presenting with weight loss versus those without. The primary outcome variable selected for sample size estimation was Body Mass Index (BMI), a clinically relevant indicator of nutritional status and disease progression in HIV-positive individuals. An effect size of 0.4 (medium effect) was used, with a significance level ($\alpha$) of 0.05 and statistical power of 0.95. Parameters yielded a required sample size of 105, which was increased to 117 after accounting for a 10% non-response rate [11]. All the patients between the ages of 25 to 60 years of both genders were included, and pregnant women and those patients who had a previous history of Anemia, any malignancy, or tuberculosis were excluded from this study. We took three measurements for weight using a digital scale and height using a stadiometer (Seca, Germany), and used their median values to calculate body mass index (BMI) as weight (kg)/(height(m))2. All the data was collected with the help of a well-designed questionnaire, which included the personal information of patients, age, gender, drug addiction, weight loss, and family socioeconomic status. Eligible patients filled out the consent form, and patients underwent a standard baseline evaluation with laboratory tests and chest X-ray. The initial screening test was done for HIV, along with antibodies to P24 antigen. When these two came back positive, then these patients were sent for PCR for further confirmation. All the data was confidential, and the benefits of the study were communicated to the patients. The data were entered and analyzed in the SPSS version 25.0. The quantitative variables were described as Mean ±SD. The categorical variables were described as Frequency and percentages, like gender, drug addiction, and family socioeconomic status. To check the association between the variables, the chi-square test was used. The level of significance was 5%.

## RESULTS

The mean age was 41.5±7.8 years. Out of 117, 81(69.2%) were male and 36(30.8%) were female. According to sociodemographic status, most of the patients were poor 66, 56.4%), 42(35.9%) belonged to middle-class families, and 9(7.7%) were rich. According to our results, 91(77.8%) patients had no drug addiction while 26(22.2%) had drug addiction. Similarly, when checking the HIV status of these patients, out of 117 patients, 9(7.7%) were HIV positive while 108(92.3%) were HIV negative (Table 1).

**Table 1:** Demographic Parameters of Patients

| Parameters | n (%) |
|---|---|
| Age (years) (mean ± S.D) | 41.50±7.80 |
| **Gender** | |
| Male | 81 (69.2%) |
| Female | 36 (30.8%) |
| **Socioeconomic Status** | |
| Poor | 66 (56.4%) |
| Middle | 42 (35.9%) |
| Rich | 9 (7.7%) |

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| | |
|---|---|
| **Drug Addiction** | |
| Yes | 26 (22.2%) |
| No | 91 (77.8%) |
| **Weight Loss** | |
| Yes | 21 (17.7%) |
| No | 97 (82.3%) |
| **HIV** | |
| Yes | 9 (7.7%) |
| No | 108 (92.3%) |

Age was categorized into two categories: 25-40 years and 41-60 years. 5(11.1%) patients belonged to the 1st category, and 4(5.66%) belonged to the 2nd category, who were HIV positive. Out of 9 patients, 8(9.9%) were male who were suffered from HIV. 7(10.6%) patients were poor, 2(4.8%) were belonged to middle class family who had HIV. Most HIV patients were drug-addicted. There was no significant association observed among Human immunodeficiency virus for age, gender, or drug addiction. While HIV had a significant association with family socioeconomic status, with a p-value of 0.00 (Table 2).

**Table 2:** Characteristics of Demographic Parameters for Human Immunodeficiency Virus (HIV)

| Parameters | Human Immunodeficiency Virus (HIV) | | p-Value |
|---|---|---|---|
| | Yes | No | |
| **Age (Years)** | | | |
| 25-40 | 5 (11.1) | 40 (88.9) | 0.273 |
| 41-60 | 4 (5.6) | 68 (94.4) | |
| **Gender** | | | |
| Male | 8 (9.9) | 73 (90.1) | 0.184 |
| Female | 1 (2.8) | 35 (97.2) | |
| **Socioeconomic Status** | | | |
| Poor | 7 (10.6) | 59 (89.4) | <0.001* |
| Middle | 2 (4.8) | 40 (95.2) | |
| Rich | – | 9 (100) | |
| **Drug Addiction** | | | |
| Yes | 7 (26.9) | 19 (73.1) | 0.359 |
| No | 2 (2.2) | 89 (97.8) | |
| **Weight Loss** | | | |
| Yes | 14 (66.7) | 7 (33.3) | 0.02* |
| No | 38 (39.2) | 59 (60.8) | |

*Statistically significant

## DISCUSSION

The mean age of patients was 41.5±7.8 years. Male patients were 69.2% and females were 30.8%. According to sociodemographic status, most of the patients were poor, 56.4%. Human immunodeficiency virus was observed in 7.7% of patients. Stratification of human immunodeficiency virus for age, gender, drug addiction, and family socioeconomic status was studied in our research. Research determined that individuals with lower socioeconomic status experience higher stress levels due to factors like food scarcity. This heightened stress has been associated with a greater tendency to partake in risky sexual behaviors, which, over time, increases the risk of contracting HIV. [12] In our study, 7(10.6%) patients had a lower socioeconomic status, with a significant p=0.000. Additionally, a study by Funke B found that any type of drug dependency may lead to engaging in risky behaviors, further increasing the chances of acquiring or transmitting HIV. Such actions can have detrimental effects on the health of those living with HIV. Specifically, the use of substances like drugs and alcohol can weaken the immune system and cause significant liver damage. Moreover, the interactions between recreational drugs and HIV medications can heighten the risk of severe side effects [13]. According to our study, HIV and drug addiction were statistically insignificant. According to our study, patients who were newly diagnosed with HIV, only 17.7 % experienced significant weight loss. HIV infection is linked to weight loss and wasting, even with significant progress in antiretroviral therapies and improved survival rates for those infected. In a study involving HIV-positive adults, weight loss and wasting were prevalent issues, with an overall occurrence rate of 38% when broader definitions beyond the original AIDS-defining criteria were considered.[14] Weight loss associated with HIV is a complex issue influenced by two primary factors: reduced nutrient intake and changed metabolism [15]. Decreased intake may stem from HIV-related anorexia, oral health issues, difficulties in swallowing, diarrhea, and socioeconomic factors impacting food access. Malabsorption may also contribute, as nearly 90% of patients exhibit some level of gastrointestinal dysfunction [16]. Weight loss primarily involved fat reduction when CD4 counts were sufficient, whereas both fat and lean mass were lost as immunosuppression worsened. Greater weight loss was linked to lower CD4 counts, more advanced stages of HIV disease, and increased mortality. [17] Even a 5% reduction in weight over six months was indicative of higher mortality risks, while higher lean body mass was associated with better physical functioning and quality of life in men. Therefore, weight loss and wasting have notable negative effects on clinical outcomes and remain critical complications in the management of HIV [18]. The study depended on self-reported dietary intake, which can be subject to recall bias. More objective assessments, like measuring resting energy expenditure, were not conducted for all participants. finally, the interventions were limited pilot trials with brief follow-up periods. Larger clinical trials are necessary to more accurately assess treatments for HIV-related wasting. [19] Regarding our study, most of the patients belonged to the lower middle class who were suffering from HIV, and did not have enough resources for proper dietary intake. Weight loss and

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muscle wasting still impact a significant number of individuals living with HIV, even with current treatment options. The reasons for this are complex and include both insufficient nutritional intake and metabolic issues. Even small amounts of weight loss can lead to worse clinical results and a decline in quality of life.[20] Further research is warranted to enhance strategies for recognizing and managing wasting in HIV patients on antiretroviral therapy. Some limitations should be considered when interpreting the findings. As this was an observational study, causal relationships could not be determined between variables. The patients were predominantly from one geographic area, which may limit generalizability.

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## CONCLUSIONS

These findings highlight the significance of identifying and managing weight issues in HIV patients despite advances in therapy. Effective strategies are available to improve weight, but they need to be customized for each person. Further investigation is needed to refine nutritional approaches, address disparities, and improve results for HIV patients in the context of managing chronic illnesses.

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## Authors' Contribution

Conceptualization: AA, SB
Methodology: SB
Formal analysis: SU, O
Writing and Drafting: SB, QI, NU
Review and Editing: AA, SB, QI, NU, SU, O

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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# Comparative Impact of Olanzapine and Aripiprazole on the Development of Metabolic Syndrome in Patients with Psychiatric Disorders

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## ABSTRACT

Antipsychotic medications are associated with metabolic side effects, which vary across different drugs. **Objectives:** To compare the development of metabolic syndrome in patients treated with olanzapine versus aripiprazole. **Methods:** This prospective observational study was conducted at Shahida Islam Medical College and Hospital over six months (June–November 2024). Patients with psychiatric disorders who had received either olanzapine or aripiprazole for ≥6 months were included. Metabolic syndrome was assessed using the International Diabetes Federation (IDF) criteria. Patients were divided into two treatment groups: olanzapine (n=104) and aripiprazole (n=104). Data were analyzed using SPSS version 23.0. Chi-square, Fisher's exact, independent t, and Mann-Whitney U tests were applied where appropriate, with $p<0.05$ considered significant. **Results:** A total of 208 patients were analyzed (mean age: olanzapine 46.42 ± 9.21 years; aripiprazole 47.44 ± 8.78 years). Metabolic syndrome prevalence was significantly higher in the olanzapine group (45.2%) compared to the aripiprazole group (30.8%) ($p<0.05$). Patients on olanzapine had higher waist circumference, BMI, and blood pressure. Metabolic abnormalities were also more frequent with olanzapine: diabetes (34.0% vs. 15.6%), hyperlipidemia (25.5% vs. 9.4%), and microalbuminuria (25.5% vs. 6.3%). **Conclusions:** Aripiprazole demonstrated a significantly lower risk of metabolic syndrome and better metabolic outcomes than olanzapine, highlighting the need for careful monitoring and the consideration of safer alternatives in clinical practice.

## INTRODUCTION

Atypical antipsychotics are the cornerstone of treatment for psychotic disorders; however, accumulating evidence indicates that they are associated with significant metabolic side effects, including weight gain, hyperglycemia, obesity, dyslipidemia, and type 2 diabetes [1]. These metabolic disturbances substantially increase the risk of cardiovascular disease and premature mortality [2]. The extent of metabolic syndrome varies among different atypical antipsychotics. Studies consistently report the highest risk with olanzapine and clozapine, whereas amisulpride, risperidone, and quetiapine are associated with intermediate risks [3, 4]. In contrast, aripiprazole has been shown to exert fewer metabolic adverse effects compared to most other atypical antipsychotics [5]. Some researchers have advocated switching patients from high-risk antipsychotics to aripiprazole to improve metabolic profiles. However, treatment switching has often been associated with poor adherence and treatment discontinuation, raising concerns about the feasibility of this approach [6].

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Alternatively, aripiprazole has been studied as an adjunct to high-risk antipsychotics, such as olanzapine, demonstrating improvements in fasting glucose, body mass index (BMI), serum triglycerides, and lipid profile [7, 8]. Despite these findings, the exact mechanisms by which aripiprazole influences metabolic regulation remain unclear, and evidence regarding its comparative benefits in routine clinical practice is limited. Olanzapine, in particular, has been strongly associated with increases in body weight, triglycerides, and reductions in HDL cholesterol, making it one of the most metabolically adverse antipsychotics [9, 10]. According to the International Diabetes Federation (IDF), metabolic syndrome was defined by central obesity, reduced HDL cholesterol, elevated blood pressure, fasting glucose, and triglyceride abnormalities [11]. Prevalence of metabolic syndrome among patients on long-term antipsychotic therapy ranges from 19% to 50% [12, 13].

Given the high burden of metabolic syndrome in patients receiving antipsychotics, it is critical to evaluate the comparative metabolic effects of individual drugs. While existing literature highlights the risks of olanzapine and the relatively safer profile of aripiprazole, there remains a need for direct comparative studies in local populations to guide safer prescribing practices [14]. This study aims to compare the development of metabolic syndrome in patients receiving olanzapine versus aripiprazole for the treatment of psychiatric disorders. It evaluates differences in metabolic outcomes associated with these two antipsychotic medications.

## METHODS

This prospective observational study was carried out at the Shahida Islam Medical College and Hospital, Lodhran, Pakistan, for a period of six months from June 2024 to November 2024 after taking approval from the Institutional Review Board committee of Shahida Islam Medical Complex, IRB certificate no SIMC/ET.C/00029/24. Using a non-probability convenience sampling technique, patients diagnosed with a psychiatric disorder and on treatment with either olanzapine or aripiprazole for at least six months or more were included in the study after obtaining informed consent. In addition, patients using hypnotics or benzodiazepines were allowed to continue them in therapeutic doses, as abrupt withdrawal could influence sleep and anxiety levels, potentially confounding metabolic assessments. However, no other antipsychotic medication was permitted during the study to maintain pharmacological consistency between comparison groups. Patients who were on antipsychotics other than olanzapine or aripiprazole were excluded to avoid overlapping metabolic effects of multiple psychotropics. Use of stable somatic medications (e.g., antihypertensives, thyroid supplements, or antidiabetic agents) was permitted, provided the doses remained unchanged throughout the study period. This approach aligns with previous observational protocols that allowed continuation of essential somatic medications to ensure patient safety and clinical stability without significantly affecting metabolic outcome measures [6]. The criterion used for assessing the absence or presence of metabolic syndrome was through the International Diabetes Federation (IDF). Patients were first randomly divided into two groups, one group taking olanzapine and the other aripiprazole. On the basis of IDF classification, patients were further classified into two sub-groups: cases diagnosed with metabolic syndrome and those without metabolic syndrome. The IDF classification for metabolic syndrome used was as follows: HDL <40 mg/dl for males and <50 mg/dl for females. Waist circumference >102 cm for male and >88 cm for female. Systolic blood pressure >130 mmHg or diastolic blood pressure >85 mmHg. Fasting plasma glucose >110 mg/dl and fasting triglycerides >150 mg/dl [11]. The sample size was calculated using the Open EPI online software. The parameters included a population size of 1,000,000, an expected outcome frequency of 16% ± 5, a 95% confidence level, a 5% margin of error, and a design effect of 1. The calculated minimum sample size was 207 participants. To meet this requirement, 208 patients were enrolled and equally divided into two groups: olanzapine (n=104) and aripiprazole (n=104). The demographics of the patients were recorded on a pre-designed pro forma. It included the patient's age, gender, duration of disease, treatment medication and duration, co-morbidities, and family history of diabetes or hyperlipidemia. For laboratory tests, patients were fasting for about 12 hours overnight for the collection of a blood sample for fasting lipid profile and fasting blood glucose. Other laboratory tests included C-reactive protein (CRP), which is an inflammatory marker used in diagnosing metabolic syndrome. For the collection of blood samples, venous puncture was done for all patients in-between 8 am and 9 am after a 12-hour overnight fast. Fasting lipid profile and fasting glucose levels were tested using commercial kits and enzyme methods (Olympus Diagnostic, GmbH, Hamburg, Germany) using an Olympus AU 600 automated analyzer, immediately after collection of the blood sample [9]. For CRP, the cut-off level was 5 mg/L. The detection of micro-albuminuria was carried out through a specimen of standard spot urine albumin (reference range between 30-300 mg/L). Waist circumference was measured as a marker of central obesity (midpoint distance in-between the iliac crest and the costal arc in the standing position and at the point of mid-expiration. BMI was calculated through weight and height (weight in kg/height in m2). The average dose of

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olanzapine in patients was 10 to 20 mg/day, and aripiprazole was 15 to 30 mg/day, depending upon the severity of illness. Patients showing symptoms of acute or chronic infection, allergy, or any other condition affecting their immune systems for a minimum of 2 weeks were excluded from the study. Patients on any drug affecting the immune system were also excluded. Data were analyzed using SPSS version 23.0. Continuous variables were summarized as mean ± standard deviation, while categorical variables were reported as frequencies and percentages. For group comparisons, independent t-tests (or Mann–Whitney U test where applicable) were applied to continuous variables. Fisher's exact test or Chi-square test was used for categorical variables. To evaluate the association between type of antipsychotic (olanzapine vs. aripiprazole) and the presence of metabolic syndrome (binary outcome), binary logistic regression was performed, adjusting for potential confounders (age, sex, BMI, and duration of treatment). Effect sizes were presented as odds ratios (OR) with 95% confidence intervals (CI). A p-value<0.05 was considered statistically significant.

## RESULTS

The study included 208 patients, equally divided between the olanzapine (n=104) and aripiprazole (n=104) treatment groups. The mean age of patients receiving olanzapine was 46.42 ± 9.21 years, while for those on aripiprazole, it was 47.44 ± 8.78 years. The mean duration of antipsychotic treatment was 4.97 ± 2.58 years for olanzapine and 5.7 ± 3.31 years for aripiprazole. The treatment duration in months was 9.2 ± 2.28 for olanzapine and 11.85 ± 2.83 for aripiprazole. The prescribed medication dose was 14.2 ± 5.3 mg for olanzapine and 21.45 ± 5.82 mg for aripiprazole. The mean duration of illness was 10.77 ± 4.2 years in the olanzapine group and 12.65 ± 7.41 years in the aripiprazole group. Smoking status was positive in 82 (78.84%) patients from the olanzapine group and 87 (83.65%) from the aripiprazole group. Metabolic syndrome was observed in 47 (45.2%) patients on olanzapine compared to 32 (30.77%) in the aripiprazole group (Table 1).

**Table 1:** Baseline Demographics of Patients Included in the Study (n=208)

| Variables | Olanzapine (n=104) | Aripriprazole (n=104) |
|---|---|---|
| Age (Years) | 46.42 ± 9.21 | 47.44 ± 8.78 |
| Antipsychotic Treatment (Years) | 4.97 ± 2.58 | 5.7 ± 3.31 |
| Treatment (Months) | 9.2 ± 2.28 | 11.85 ± 2.83 |
| Medication Dose (Mg) | 14.2 ± 5.3 | 21.45 ± 5.82 |
| Duration of Illness (Years) | 10.77 ± 4.2 | 12.65 ± 7.41 |
| Smoking Status (Yes) | 82 (78.84 %) | 87 (83.65 %) |
| Metabolic Syndrome | 47 (45.2 %) | 32 (30.77 %) |

Metabolic syndrome was analyzed based on demographics, anthropometric parameters, and laboratory investigations. Among patients without metabolic syndrome (n=129), the mean age was 47.21 ± 8.91 years, while it was 46.88 ± 8.98 years in those with metabolic syndrome on olanzapine (n=47) and 47.1 ± 8.11 years in those on aripiprazole (n=32), with a non-significant p-value of 0.09. Waist circumference was significantly higher in patients with metabolic syndrome, measuring 97.57 ± 11.19 cm in the olanzapine group and 95.48 ± 10.91 cm in the aripiprazole group, compared to 82.74 ± 10.3 cm in patients without metabolic syndrome (p<0.001). The mean BMI was also significantly elevated in patients with metabolic syndrome, at 27.88 ± 4.48 kg/m$^2$ in the olanzapine group and 27.2 ± 4.12 kg/m$^2$ in the aripiprazole group, compared to 23.29 ± 3.58 kg/m$^2$ in patients without metabolic syndrome (p=0.04). Blood pressure values were significantly different among the groups. Patients on olanzapine with metabolic syndrome had a mean systolic blood pressure of 133.78 ± 15.88 mmHg, while those on aripiprazole had 129.52 ± 14.7 mmHg, both significantly higher than the 117.3 ± 18.7 mmHg observed in those without metabolic syndrome (p<0.001). Similarly, diastolic blood pressure was 84.55 ± 8.72 mmHg in the olanzapine group and 83.4 ± 8.25 mmHg in the aripiprazole group, compared to 76.52 ± 7.24 mmHg in those without metabolic syndrome (p=0.03). The prevalence of type II diabetes mellitus was significantly higher in the olanzapine group, with 16 (34%) patients affected, compared to 5 (15.63%) in the aripiprazole group and 18 (14%) in patients without metabolic syndrome (p<0.001). Hyperlipidemia was present in 12 (25.5%) of the olanzapine group and 3 (9.4%) of the aripiprazole group, compared to 16 (12.4%) in those without metabolic syndrome (p<0.001). Microalbuminuria (>300 mg/L) was found in 12 (25.5%) of the olanzapine group and 2 (6.25%) of the aripiprazole group, whereas it was absent in those without metabolic syndrome (p<0.001) (Table 2).

**Table 2:** Presence of Metabolic Syndrome Related to Demographics, Anthropometrics, and Laboratory Investigations (n=208)

| Variables | Without MetS (n= 129) | MetS (Olanzapine) (n=47) | MetS (Aripiprazole) (n=32) | p-value |
|---|---|---|---|---|
| Age (Years) | 47.21 ± 8.91 | 46.88 ± 8.98 | 47.1 ± 8.11 | 0.090 |
| Waist Circumference (cm) | 82.74 ± 10.3 | 97.57 ± 11.19 | 95.48 ± 10.91 | <0.001 |
| BMI (kg/m$^2$) | 23.29 ± 3.58 | 27.88 ± 4.48 | 27.2 ± 4.12 | 0.040* |
| Systolic Blood Pressure (mmHg) | 117.3 ± 18.7 | 133.78 ± 15.88 | 129.52 ± 14.7 | <0.001* |
| Diastolic Blood Pressure (mmHg) | 76.52 ± 7.24 | 84.55 ± 8.72 | 83.4 ± 8.25 | 0.030* |
| Type II Diabetes Mellitus | 18 (14 %) | 16 (34 %) | 05 (15.63 %) | <0.001* |
| Hyperlipidemia | 16 (12.4 %) | 12 (25.5 %) | 03 (9.4 %) | <0.001* |
| Microalbuminemia (>300 mg/L) | 0 | 12 (25.5 %) | 02 (6.25 %) | <0.001* |

The study represents the graphical representation of

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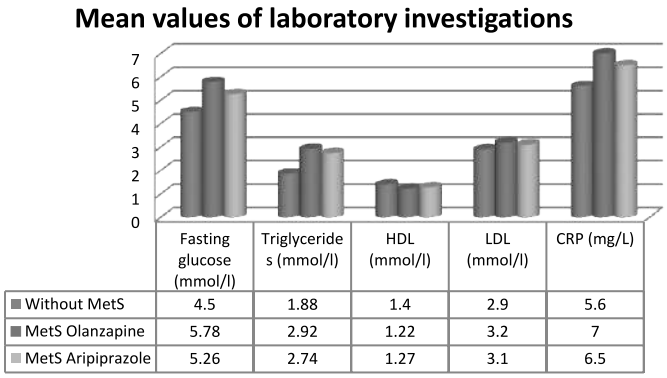
metabolic syndrome in relation to laboratory findings, demonstrating the increased prevalence of metabolic disturbances among patients on olanzapine compared to aripiprazole. Significant differences between the three groups were observed in terms of fasting glucose levels, triglycerides, HDL, and CRP levels ($p<0.05$).




| | Fasting glucose (mmol/l) | Triglycerides (mmol/l) | HDL (mmol/l) | LDL (mmol/l) | CRP (mg/L) |
|---|---|---|---|---|---|
| Without MetS | 4.5 | 1.88 | 1.4 | 2.9 | 5.6 |
| MetS Olanzapine | 5.78 | 2.92 | 1.22 | 3.2 | 7 |
| MetS Aripiprazole | 5.26 | 2.74 | 1.27 | 3.1 | 6.5 |

**Figure 1:** Graphical Representation of Metabolic Syndrome in Relation to Laboratory Findings (n=208)

## DISCUSSION

This study demonstrated that patients receiving aripiprazole had significantly better anthropometric and laboratory outcomes compared with those on olanzapine. The prevalence of metabolic syndrome was higher in the olanzapine group (45.2%) than in the aripiprazole group (30.8%). These findings are consistent with earlier reports, where olanzapine use was strongly associated with increased risk of metabolic syndrome [15], while aripiprazole was linked with comparatively lower rates [16]. Our results also highlight that, except for age, all parameters were significantly better in the aripiprazole group compared to the olanzapine group. This aligns with placebo-controlled studies that found improvements in triglycerides, HDL, and weight in aripiprazole-treated patients [17]. Olanzapine-controlled trials have similarly demonstrated significant differences between the two drugs in terms of lipid and weight profiles [18]. The metabolic syndrome rate in our olanzapine group (45.2%) closely matches other studies reporting rates around 47% [19]. By contrast, the aripiprazole group's lower rate (30.8%) supports the notion that aripiprazole carries a safer metabolic profile. Beyond pharmacological differences, lifestyle factors, including duration of illness and smoking, have been shown to influence metabolic syndrome development, particularly with olanzapine [20]. Our findings also demonstrated that waist circumference, BMI, and blood pressure were significantly higher in olanzapine patients compared with aripiprazole, reinforcing previous observations. Mechanistically, these differences may be attributed to receptor activity. Aripiprazole acts as a partial agonist at dopamine D2 and serotonin 5-HT receptors, mechanisms associated with reduced appetite and improved metabolic regulation. Conversely, olanzapine acts as a serotonin 5-HT antagonist, a pathway linked with weight gain and obesity [21]. The beneficial effects of aripiprazole on lipid metabolism are further supported by both our results and published data [22]. Given that dyslipidemia is a strong independent risk factor for cardiovascular morbidity [23], the better lipid profile observed with aripiprazole suggests potential cardioprotective benefits compared with olanzapine. Overall, this study strengthens existing evidence that aripiprazole is metabolically safer than olanzapine, but it also underscores the necessity for ongoing metabolic monitoring in all patients prescribed antipsychotics.

This single-center, observational study had a small sample size, limiting generalizability and causal inference. Potential selection and recall bias, lack of randomization, short follow-up, and unmeasured confounders (e.g., lifestyle, diet, concomitant medications) may have influenced metabolic outcomes; thus, findings should be interpreted cautiously. Future studies should use larger, multi-center cohorts with longer follow-up. Randomized or interventional designs, including lifestyle modifications or adjunctive aripiprazole strategies, are recommended to better assess and mitigate metabolic risks.

## CONCLUSIONS

Aripiprazole was associated with significantly better anthropometric and metabolic outcomes than olanzapine, with a lower prevalence of metabolic syndrome (30.8% vs. 45.2%). Olanzapine-treated patients exhibited higher rates of obesity, dyslipidemia, hypertension, and diabetes, underscoring its higher metabolic risk. Clinically, these findings recommend careful baseline and follow-up metabolic screening in patients receiving olanzapine, with consideration of safer alternatives such as aripiprazole when appropriate.

### Authors' Contribution

Conceptualization: SM
Methodology: NK
Formal analysis: MM, SLA
Writing and Drafting: NK, SLA, KA, AI
Review and Editing: SM, NK, MM, SLA, KA, AI

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**

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# Effectiveness and Safety of Carbamazepine versus Gabapentin in the Pharmacological Management of Trigeminal Neuralgia

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## ABSTRACT

Carbamazepine is considered the first-line pharmacological therapy for trigeminal neuralgia (TN). Gabapentin, another antiepileptic drug, is increasingly used, but its role as a substitute for carbamazepine remains uncertain. **Objectives:** To compare the effectiveness and safety of gabapentin and carbamazepine in the management of trigeminal neuralgia. **Methods:** This prospective comparative study included 80 patients presenting to the Department of Oral and Maxillofacial Surgery at Sharif Medical and Dental Hospital from February 2023 to January 2024. Patients were divided into two groups of 40 each: Group A received gabapentin 300 mg twice daily, and Group B received carbamazepine 200 mg twice daily. Pain intensity was assessed using the Visual Analogue Scale (VAS), and frequency of attacks was recorded on the 3rd, 7th, and 15th days of follow-up. Side effects were also documented. Mann-Whitney U and Chi-square tests were used for statistical analysis, with $p \leq 0.05$ considered significant. **Results:** Group A exhibited lower median VAS scores compared to Group B at all follow-up intervals, with statistically significant differences on the 2nd and 3rd follow-ups. Although gabapentin demonstrated fewer adverse effects, carbamazepine showed the highest percentage of good therapeutic response based on reduced frequency of attacks. **Conclusions:** Both drugs are effective in managing trigeminal neuralgia. Carbamazepine provides superior pain relief and reduction in attack frequency, whereas gabapentin is associated with fewer side effects.

## INTRODUCTION

Trigeminal neuralgia (TN) is a prevalent form of neuropathic pain. It is abrupt, typically unilateral, intense, short, acute, and persistent, with attacks lasting some few seconds to around two minutes within in region over one or even more trigeminal nerve divisions [1]. The condition typically contains trigger zones and is frequently brought on by regular activities. The pain always seems to be ipsilateral to the trigger point. Frequent extra-oral trigger zones are found laterally to the ala nasi, just over the mental foramen, as well as over the supraorbital foramen. Touching, specific neck gestures, speaking, eating, swallowing, shaving, tooth brushing, and even brisk airflow can all be triggers [2]. An estimated 5.9 per 100,000 females and 3.4 per 100,000 males are affected each year. With increasing age, the prevalence rises notably, with females showing a slightly higher susceptibility [3]. The American Academy for Neurology, as well as the European Federation of Neurological Societies, both suggested carbamazepine (CBZ) for a first medical treatment for TN, since this has been shown to reduce episodes in up to 88% of cases. Pharmacotherapy is presently the most popular method for treating TN [4]. The curative efficacy of CBZ is indeed somewhat limited. Poor tolerance of major side reactions, including dizziness, nausea, and especially white blood cell depletion, compromises the medication's effectiveness [5]. In addition, several studies indicate that CBZ is ineffective for partial cases [6]. When evaluating the degree of pain associated with trigeminal neuralgia, the

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Visual Analogue Scale (VAS) is a sensitive and dependable instrument. It uses a 0–10 scale, with 0 denoting no discomfort and 10 denoting the worst conceivable suffering. Its usage in TN is still validated by recent research. For instance, Al Habil et al. employed VAS scores to measure pain reduction in patients with trigeminal neuralgia receiving non-pharmacological therapy, demonstrating its sensitivity and applicability for tracking changes in TN-related pain [7]. Meanwhile, more contemporary Antiseizure medications called gabapentin (GBP) are now frequently utilized in the therapeutic practice of TN. Investigations have shown that GBP has many potential applications in severe pain disorders, particularly neuropathic pain [8]. Moreover, in numerous international pain management clinics, GBP has become the medicine of first preference for treating all varieties of severe neuropathic pain. Its side effects include a minimal incidence of negative responses, no interactions with certain other medicines that affect the neurological systems, as well as a clear feeling of its effectiveness [9]. Additionally, GBP can be utilized as a substitute for CBZ if TN cannot be controlled to lessen its severity [10]. Yet compared to CBZ, its effectiveness and safety are still debatable [11].

Gabapentin (GBP) has emerged as an alternative with fewer adverse effects and promising analgesic potential, but evidence directly comparing its effectiveness and safety to CBZ in TN is limited. Few studies have systematically evaluated patient-reported pain reduction using validated tools like the Visual Analogue Scale (VAS) in this context, especially in local populations. This study aims to compare CBZ and GBP in terms of pain control and safety profiles among patients with TN, providing insight into optimal pharmacological management strategies.

## METHODS

This observational study was conducted on 80 patients; the sample size was calculated with the WHO sample size determination software, taking the effectiveness of carbamazepine in the treatment of trigeminal neuralgia as 94.1% with a 95 % confidence level at 0.06 precision [12]. The study was conducted on 80 patients visiting the oral and maxillofacial OPD, Sharif Medical and Dental Hospital Lahore, during 1 1-year period from February 2023 to January 2024. The study was approved by the institutional ethics review committee of Sharif Medical Research Center (Ref. No: SMRC/279-23). All participants provided written informed consent before enrollment, in accordance with the Declaration of Helsinki (2013 revision) [13]. Participant confidentiality was ensured through complete de-identification of personal data and secure, restricted-access storage. Data handling and management followed the FAIR (Findable, Accessible, Interoperable, and Reusable) data principles [14], ensuring that data were organized systematically, stored securely, and made accessible only in accordance with ethical and institutional requirements. Patients with diagnosed trigeminal neuralgia were included in this study irrespective of their age. Patients taking any anti-epileptic or Anticonvulsant, patients with a history of any surgical treatment for trigeminal neuralgia, or patients not willing to undergo follow-up were excluded from the study. After informed consent, using a non-probability convenience sampling technique, patients were allocated into two groups of 40 patients each: group A and group B. The patients with trigeminal neuralgia type 1 (A spontaneously occurring facial pain consisting of transient electric shock-like aches, acute in onset as well as termination," meaning that the discomfort signs are only present for as long as the pain incident lasts (temporary pain) were included in group A. The patients having trigeminal neuralgia type 2 (A sudden commencement of facial discomfort that is marked by short, electric shock-like aches, quick onset, and a persistent, dull, diffuse background discomfort. This ongoing discomfort could last anywhere between a few minutes to several hours, and was included in group B [15]. Group A was treated with gabapentin 300mg BD daily. Group B was treated with carbamazepine daily at 200mg twice a day. Another physician who was blind about the patients as well as the drugs reviewed the response of the drug and handed it over to the first physician who diagnosed and numbered the patients. Pain relief was observed at the 3rd, 7th, and 15th day intervals during follow-up. All information was collected on a specially designed form. A visual analogue scale was used to score the pain. The response of VAS was recorded as 1 (no pain) - 10 (worst pain). The response of the patients to the therapeutic effectiveness of the drug was decided based on the frequency of attacks, i.e., good response: no attacks of pain; average response: two to three attacks of pain per day; and nonresponsive with no decrease in frequency of attacks of pain [11]. All participants were actively monitored for adverse drug reactions (ADRs) throughout the study. At each follow-up visit (Day 3, Day 7, and Day 15), ADRs were assessed using a structured WHO-UMC–based checklist covering common reactions to carbamazepine and gabapentin, including dizziness, fatigue, headache, constipation, nausea, and dry mouth. Any new symptoms after treatment initiation were documented and graded for severity (mild, moderate, severe) and temporal association with the drug. Participants were also advised to report symptoms occurring between follow-ups. All ADRs were recorded in the proforma, and their frequencies were compared between the two treatment groups. Because of their non-normal distribution, continuous variables have

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been presented as median (IQR) and evaluated using the Shapiro-Wilk test. VAS scores were compared between treatment groups using the Mann-Whitney U test. The Chi-square test was used to assess categorical variables, such as attack incidence and adverse outcomes. The Bonferroni correction was used to take into consideration multiple comparisons between visits to follow up. A statistically significant p-value was defined as<0.05. SPSS version 23.0 was used for the analyses.

## RESULTS

A total of 80 participants were included in the study, with a mean age of 43±9.5 years, with 46% males and 34% females. The study showed that the VAS scores on the 1st follow-up of group A (Gabapentin) (md=5.00, n=40) were lower than group B (Carbamazepine) (md=6.00, n=40). The same was the case regarding VAS scores at the 2nd and 3rd follow-ups as well. It was reported that a significant difference in the VAS scores on the 2nd follow-up was seen between both groups, with group A (md=6.50, n=40) having a lower score as compared to group B (md=7.00, n=40). Similarly, Group A (md=7.00, n-40) had a lower VAS score on the third follow-up as compared to Group B (md=8.00, n=40), and this difference was statistically significant (Table 1).

**Table 1:** Therapeutic Effectiveness of Gabapentin and Carbamazepine in Trigeminal Neuralgia Patients as Assessed by VAS Score on Follow-Up Visits

| Follow-up | Gabapentin Median (IQR) | Carbamazepine Median (IQR) | p-value |
|---|---|---|---|
| 1st | 5.0 (4–6) | 6.0 (5–7) | 0.001* |
| 2nd | 6.5 (5–7) | 7.0 (6–8) | 0.025* |
| 3rd | 7.0 (6–8) | 8.0 (7–9) | 0.001* |

Study results showed a statistically significant association between the therapeutic efficacy of Gabapentin and Carbamazepine and the patient response based on frequency of attacks on follow-up visits. It was seen that the highest percentage of good response was reported by patients who were treated using Carbamazepine (Table 2).

**Table 2:** Therapeutic Efficacy of Gabapentin and Carbamazepine as Assessed by Frequency of Attacks on Follow-Up Visits

| Follow-up | Response | Gabapentin n (%) | Carbamazepine n (%) | p-value |
|---|---|---|---|---|
| 1st | Good | 5 (21%) | 19 (79%) | 0.001* |
| | Average/Not responsive | 35 (87.5%) | 21 (52.5%) | |
| 2nd | Good | 15 (37%) | 26 (63%) | 0.025* |
| | Average/Not responsive | 25 (62.5%) | 14 (37%) | |
| 3rd | Good | 14 (27%) | 38 (73%) | 0.001* |
| | Average/Not responsive | 26 (73%) | 2 (27%) | |

Results showed a statistically significant association between the side effects of dizziness, fatigue, headache, and constipation with the drugs administered (Gabapentin and Carbamazepine). It was seen that dizziness and headache were reported more by the group administered Carbamazepine, while fatigue and constipation were experienced more by patients who were given Gabapentin (Table 3).

**Table 3:** Side Effects Associated with Gabapentin and Carbamazepine as Reported by Trigeminal Neuralgia Patients

| Side Effect | Gabapentin n (%) | Carbamazepine n (%) | p-value |
|---|---|---|---|
| Dizziness | 9 (27.3%) | 24 (72.7%) | 0.001* |
| Fatigue | 17 (100%) | 0 (0%) | 0.001* |
| Headache | 0 (0%) | 6 (100%) | 0.026* |
| Constipation | 11 (100%) | 0 (0%) | 0.001* |
| Nausea | 18 (41.9%) | 25 (58.1%) | 0.116 |
| Dry mouth | 11 (52.4%) | 10 (47.6%) | 0.799 |

## DISCUSSION

In our study, it was found that both gabapentin and carbamazepine reduce the intensity of the pains in trigeminal neuralgia, although their side-effects are also different: the former (gabapentin) has more side-effects (constipation, exhaustion), whereas the latter (carbamazepine) has more side-effects (headaches, dizziness). Such results are in line with the previous studies [7], although other data indicate that carbamazepine is a little more efficient with certain subtypes of TN. These differences could be due to differences in the patient groups, dosage schedule, and study designs. Carbamazepine has been viewed as the most effective treatment for TN [8]. It acts by inhibiting voltage-gated sodium channels and hence making neurons less excitable [9]. As the meta-analysis reveals, the effect of carbamazepine was 1.600 (95% CI 1.1852161, p=0.002), which is much more effective than placebo in pain treatment [15]. Systematic review too proved that carbamazepine was able to significantly decrease the frequency and intensity of pain among the TN patients [16]. Gabapentin is an antiseizure drug that is a calcium channel modulator, which can regulate the release of neurotransmitters and has been researched as an alternative to carbamazepine. A 2023 meta-analysis and review indicated that both gabapentin and carbamazepine had identical efficacy (OR=2.02, 95% CI 1.562.62, p=0.00001), whereas the rate of adverse events was significantly lower with gabapentin (OR=0.28, 95% CI 0.2137, p=0.00001) [17]. These findings are consistent with ours, in which carbamazepine-medicated patients had a higher number of headaches and dizziness, and gabapentin-medicated patients had a higher number of fatigue and constipation. It has also been reported that the side-effect profile of gabapentin is usually not as strong as that of carbamazepine, which is an important determinant of medication adherence and general quality of life [18]. One clinical study found that the difference in treatment

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response was significant ($p<0.05$): with 15 days of treatment, Group I demonstrated good therapeutic efficacy, 56.2, and Group II demonstrated good therapeutic efficacy, 58.4 average good therapeutic efficacy was 43.8 and 41.6, respectively [11]. In line with this, our research established that the highest proportion of excellent responders was the carbamazepine group. There was another study that reported that after 72 hours, 52.38% of patients who were treated with 400 mg carbamazepine showed excellent response, 28.57% showed average response, and 19% did not show any significant pain reduction. Comparatively, a good response occurred in 52.38 percent of the gabapentin group and an average response in 42.8 percent of the same group at 600 mg [19]. Several other studies also verify the fact that pharmacological therapy has never been tried before any intervention undertaken in the management of TN pain [7, 10]. Carbamazepine remains a good first-line therapy with mixed results in the benefits and relapse rates reported [17, 20]. There is also evidence of Pregabalin and gabapentin concerning efficacy in neuralgic pain [16]. There are some significant limitations to this study. Initially, non-probability convenience sampling was used to recruit patients, and TN subtype rather than randomization was used to assign patients to therapy groups. Selection bias and confounding could be introduced by this method, which could restrict the capacity to draw conclusive causal inferences and impact the groups' comparability. this study was conducted just for educational purposes. It was an observational study on a group of patients. So, the findings cannot be used for treatment strategies and outcomes. As a result, the findings should be regarded cautiously and mainly as representative of actual clinical practice. Future research should include large-scale, randomized controlled trials with longer follow-up periods to validate these preliminary findings, minimize bias, and provide stronger evidence for establishing treatment guidelines. Additionally, standardized diagnostic criteria, validated outcome tools, and stratified randomization should be incorporated to improve methodological rigor.

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## CONCLUSIONS

The results of this study show that carbamazepine and gabapentin are both useful medications for treating trigeminal neuralgia, but they have different clinical advantages. Over the course of follow-up visits, carbamazepine had superior treatment efficacy, as seen by larger reductions in pain intensity and attack frequency. Gabapentin, on the other hand, was linked to a more favorable side-effect profile, suggesting improved tolerance. Consequently, gabapentin may be a good substitute for people who cannot handle carbamazepine or have negative side effects, but carbamazepine is still the more efficient first-line medication for quick pain relief. It is advised to conduct more extensive, long-term research to validate these results and direct the choice of customized treatments.

## Authors' Contribution

Conceptualization: MJ
Methodology: MJ, UBA, KA, MK
Formal analysis: KA
Writing and Drafting: MJ, UBA, MAK, MK
Review and Editing: MJ, UBA, KA, MAK, MK

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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# Clinical and Echocardiographic Profile of Pediatric Patients with Ventricular Septal Defect

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## ABSTRACT

Ventricular septal defect (VSD) is the most common congenital heart disease in children, contributing significantly to pediatric morbidity and mortality globally. In resource-limited settings like Pakistan, delayed diagnosis and limited access to pediatric cardiology services can exacerbate disease outcomes. **Objectives:** To evaluate the clinical presentation and echocardiographic profile of pediatric patients diagnosed with VSD at a tertiary care center in Pakistan. **Methods:** This retrospective, cross-sectional descriptive study was conducted at the Department of Pediatric Cardiology of the Peshawar Institute of Cardiology from July 1, 2025, to September 31, 2025. A total of 200 children under 18 years of age with echocardiographically confirmed VSD were included. Data on demographics, clinical symptoms, and physical examination findings were collected. Echocardiographic assessment was used to determine the size, type, and location of VSD, along with associated cardiac anomalies. **Results:** The median age at diagnosis was 9.4 months, with 78% diagnosed within the first year of life. The most common presenting feature was cardiac murmur (60%), followed by recurrent respiratory infections (49%), feeding problems (42.5%), and failure to thrive (38%). Perimembranous VSD was the most prevalent type (62%), followed by muscular (19%), inlet (10%), and outlet (9%) defects. Associated cardiac lesions included patent ductus arteriosus (18%), atrial septal defect (14%), aortic valve prolapse (11%), and pulmonary hypertension (24%). **Conclusions:** Early recognition and echocardiographic screening, especially in high-risk groups like children with Down syndrome, are essential to improving outcomes. These findings support the need for enhanced screening and resource allocation in pediatric cardiology services in Pakistan.

## INTRODUCTION

Ventricular septal defect (VSD) is the most prevalent of the congenital heart diseases (CHDs), which continue to be a major cause of morbidity and mortality in infants and children around the world. The hallmark of VSD is aberrant communication between the left and right ventricles, which permits oxygen-poor blood in the right ventricle to mingle with oxygen-rich blood from the left. Increased pulmonary blood flow from this left-to-right shunting may cause congestive heart failure, pulmonary hypertension, and failure to thrive if treatment is delayed. With an estimated prevalence of 2.5 to 3.5 per 1,000 live births, VSD makes up approximately 20–30% of all congenital heart abnormalities worldwide [1, 2]. In order to avoid long-term consequences, moderate to large-sized defects frequently require medical or surgical intervention, even though many minor VSDs close on their own [3, 4]. Due to delayed diagnosis, restricted access to specialized pediatric cardiology care, and a lack of national screening methods, congenital heart disease presents a significant health burden in Pakistan. According to a recent multicenter study conducted in Pakistan, the majority of confirmed instances of congenital heart defects (CHDs) are VSD, with an incidence of 9–12 cases per 1,000 live births [5]. The need for early detection and therapy of congenital heart

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diseases, especially VSDs, has become more pressing due to the rapidly expanding pediatric population in Pakistan, where over 35% of the population is under the age of 15. The danger of consequences such as pulmonary vascular disease or irreversible pulmonary hypertension is raised since many cases in rural or resource-constrained areas go undiagnosed until symptoms worsen [6, 7]. The primary method for diagnosing and categorizing VSDs is still echocardiography. It evaluates shunt direction, chamber dilatation, and related anomalies in addition to assisting in determining the defect's existence, size, and location. Perimembranous, muscular, inlet, and outlet VSDs are among the morphological subtypes that have different risks of spontaneous closure, comorbidities such as aortic valve prolapse, and surgical techniques [8, 9]. Clinical decision-making requires prompt and precise echocardiographic examination, particularly in healthcare systems with limited resources, when postponed therapies may increase morbidity. Comprehensive national-level data examining the clinical and echocardiographic characteristics of children with VSD is lacking in Pakistan. The majority of published research is retrospective, small-scale, and frequently restricted to urban tertiary care facilities, which may not accurately reflect the pediatric community as a whole. Furthermore, many families put off seeking care until symptoms are more severe because of social stigma, ignorance, and financial limitations. This fact emphasizes the necessity of doing epidemiological research relevant to a certain region in order to inform the development of policies, the distribution of resources, and community-based screening initiatives [10].

By examining the clinical presentation, echocardiographic characteristics, and related cardiac abnormalities of a cohort of pediatric patients with VSD in a tertiary care facility in Pakistan, the current study seeks to close this knowledge gap. The study aims to enhance early detection and direct focused interventions by offering a thorough description of these cases. Clinicians can better predict difficulties, plan surgical procedures, and provide families with appropriate counselling by having a thorough understanding of the typical presenting signs, distribution of VSD types, and prevalence of concomitant lesions, including PDA and pulmonary hypertension.This study aimed to evaluate the clinical presentation and echocardiographic profile of pediatric patients diagnosed with VSD at a tertiary care center in Pakistan.

## METHODS

This was a retrospective, cross-sectional descriptive study conducted at the Department of Pediatric Cardiology of the Peshawar Institute of Cardiology, a specialized tertiary care facility, from July 1, 2025, to September 31, 2025, with data were collected from July 2023 to May 2024. The study comprised children under 18 years of age with echocardiographically validated VSD. The ethical approval was taken from the Institutional Review Board with ref no. IRC/25/203. Patients with a history of surgical or device closure of VSD or with intricate congenital heart conditions (e.g., tetralogy of Fallot, atrioventricular septal defect, transposition of the great arteries) were excluded to facilitate a concentrated analysis of isolated or predominantly VSD lesions. Based on the expected prevalence of pulmonary hypertension in children with VSD (approximately 24%, as reported by Hopper et al. [11]), a confidence level of 95%, and a margin of error of 6%, the minimum required sample size was calculated to be 200 using standard sample size formulas for proportions in descriptive studies. The calculation was performed using the formula: $n = Z^2 \times p \times (1 - p) / d^2$. where Z = 1.96 (for 95% confidence), p = 0.24, and d = 0.06. Informed consent was taken from each participant. This ensured adequate power to estimate the prevalence of key echocardiographic findings, including pulmonary hypertension, among children with VSD. A standardized proforma was used to collect data on patients' demographics (age, gender, and anthropometric measurements), clinical history (e.g., syndromic features, recurrent respiratory infections, hospitalizations), and specific physical examination findings. The study got the information from the hospital's electronic medical records and patient charts. Transthoracic echocardiography was conducted utilizing pediatric transducers. Defects were categorized based on dimensions (small: <3 mm, moderate: 3–6 mm, large: >6 mm) and anatomical location (perimembranous, muscular, inlet, outlet). Atrial septal defect (ASD), patent ductus arteriosus (PDA), aortic valve prolapses, and pulmonary hypertension (PH) were among the associated findings recorded. The study used SPSS version 25.0 to do the statistical analysis. Qualitative variables (e.g., gender, defect type, presence of pulmonary hypertension, and associated cardiac lesions) were summarized using frequencies and percentages. Quantitative variables (e.g., age and weight) were reported as mean ± standard deviation (SD) for normally distributed data, or as median and interquartile range (IQR) for non-normally distributed data. The Chi-square test or Fisher's exact test was utilized for categorical data when comparisons were pertinent. We used independent samples t-tests for continuous variables that were normally distributed, and Mann–Whitney U tests for continuous variables that were not normally distributed. A p-value of less than 0.05 was deemed statistically significant.

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## RESULTS

A total of 200 children diagnosed with ventricular septal defect (VSD) were included in the study. The mean age was 11.6 ± 9.4 months (range 1 month to 17 years), with a male-to-female ratio of 1.27:1. Most patients (78%) were diagnosed during the first year of life. Approximately 38% of the children were underweight or exhibited growth parameters below the 5th percentile for their age. Clinical history revealed that 49% of patients experienced recurrent respiratory tract infections, 42.5% had feeding difficulties, and 38% presented with features of failure to thrive. Syndromic characteristics, primarily Down syndrome, were observed in 13% of cases. Hospitalizations due to cardiac or respiratory issues occurred in 37% of the cohort (Table 1).

**Table 1:** Clinical Presentation of Patients

| Variables | Frequency (%) |
|---|---|
| **Gender** | |
| Male | 112 (56%) |
| Female | 88 (44%) |
| **Age Distribution** | |
| ≤1Year | 156 (78%) |
| >1Year | 44 (22%) |
| **Anthropometric Status** | |
| Normal Growth | 124 (62%) |
| Failure to Thrive / Underweight | 76 (38%) |
| **Clinical Presentation** | |
| Cardiac Murmur | 120 (60%) |
| Recurrent Respiratory Infections | 98 (49%) |
| Feeding Difficulties | 85 (42.5%) |
| Cyanosis | 12 (6%) |
| **Syndromic Features** | |
| Down syndrome | 26 (13%) |
| **Hospitalizations** | |
| Due to Cardiac or Respiratory Issues | 74 (37%) |

Comparative analysis showed that pulmonary hypertension was significantly more frequent in patients with large VSDs compared to those with small or moderate defects ($p<0.001$). It was also more common among patients with associated PDA ($p=0.02$). No statistically significant difference was found between male and female ($p=0.48$) or between syndromic and non-syndromic children ($p=0.31$). Perimembranous VSDs were the most common subtype (62%), followed by muscular (19%), inlet (10%), and outlet (9%) types, aligning with global patterns of VSD morphology in children. Among children with Down syndrome (n=26), inlet-type VSDs were common (53.8%), reflecting the known link between trisomy 21 and AVSD, and highlighting the need for targeted screening. Small VSDs were the most commonly observed, comprising 44% of the cases (n=88), followed by moderate-sized defects in 34% (n=68), and large VSDs in 22% (n=44) (Table 2).

**Table 2:** Echocardiographic Findings of Patients (VSD Type and Size) (n=200)

| Variables | Frequency (%) |
|---|---|
| **VSD Type** | |
| Perimembranous | 124 (62%) |
| Muscular | 38 (19%) |
| Inlet | 20 (10%) |
| Outlet | 18 (9%) |
| **VSD Size** | |
| Small | 88 (44%) |
| Moderate | 68 (34%) |
| Large | 44 (22%) |

No significant association was observed between the type of VSD and the presence of pulmonary hypertension ($p=0.27$).

Most patients (93%, n=186) had a left-to-right shunt, while 5% (n=10) had bidirectional flow and 2% (n=4) showed right-to-left shunting (Table 3).

**Table 3:** Echocardiographic Findings of Patients (Shunt Direction) (n=200)

| Shunt Direction | Frequency (%) |
|---|---|
| Left-to-right | 186 (93%) |
| Bidirectional | 10 (5%) |
| Right-to-left | 4 (2%) |

PDA was present in 18% of cases, ASD in 14%, and aortic valve prolapse in 11%, mainly linked to perimembranous VSDs. Pulmonary hypertension was found in 24% of patients, highlighting the need for early detection to prevent long-term complications (Table 4).

**Table 4:** Echocardiographic Findings of Patients (Associated Lesions) (n=200)

| Associated lesions | Frequency (%) |
|---|---|
| PDA | 36 (18%) |
| ASD | 28 (14%) |
| Aortic Valve Prolapse | 22 (11%) |
| Pulmonary Hypertension | 48 (24%) |

Bivariate analysis of associated cardiac lesions revealed that pulmonary hypertension (PH) was present in 48 (24%) of the 200 children. PH was significantly more frequent among patients with patent ductus arteriosus (PDA), with 18 of 36 children with PDA (50%) exhibiting PH ($p = 0.02$). Atrial septal defect (ASD) and aortic valve prolapse were present in 28 and 22 children, respectively, with PH observed in 12 (6%) and 10 (5%) cases; however, these associations were not statistically significant ($p > 0.05$). Among children without additional lesions, 8 (4%) had PH. The total number of children with PH aligns with the overall prevalence of 24%, reinforcing the importance of early detection and management of high-risk lesions such as PDA. The distribution of PH in relation to cardiac lesions is summarized (Table 5).

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**Table 5:** Association of Pulmonary Hypertension (PH) with Common Cardiac Lesions in Children with VSD (n=200)

| Cardiac Lesion | PH Present, n (%) | PH Absent, n (%) | Total, n (%) | Statistical Test | p-value |
|---|---|---|---|---|---|
| Patent Ductus Arteriosus | 18 (9%) | 18 (9%) | 36 (18%) | Chi-square | 0.02 |
| Atrial Septal Defect | 12 (6%) | 16 (8%) | 28 (14%) | Chi-square | 0.18 |
| Aortic Valve Prolapse | 10 (5%) | 12 (6%) | 22 (11%) | Chi-square | 0.11 |
| No Associated Lesion | 8 (4%) | 106 (53%) | 114 (57%) | – | – |
| Total | 48 (24%) | 152 (76%) | 200 (100%) | – | – |

## DISCUSSION

The most common congenital cardiac abnormality in children, ventricular septal defect (VSD), is evaluated clinically and echocardiographically in 200 pediatric patients. According to the demographic data, there is a small male predominance (56%), which is in line with findings from another study [1], which found that males had a slightly greater incidence of VSD. In line with findings of a study [11], where early detection within the first year was critical due to the severity of symptoms in hemodynamically significant abnormalities, the median age of diagnosis was 9.4 months, with 78% of cases being discovered in infancy. In 60% of patients, cardiac murmur was the most common initial presentation, highlighting its crucial function as the first clinical hint in the screening for congenital heart disease. Similar results were noted in a study, which found that 64% of patients with VSD had an audible murmur at presentation, which prompted an echocardiogram [12]. In VSDs, murmurs are usually pansystolic, produced by high-velocity turbulent flow through the septal defect, and are best audible near the left lower sternal border [13]. In 49% of our cohort, recurrent lower respiratory tract infections were documented. Pulmonary overcirculation due to a left-to-right shunt is a known consequence. There may be a connection between VSDs and pediatric respiratory morbidity, as seen in studies [14, 15], which both showed a high rate of respiratory infections. Poor weight gain and frequent hospital stays are also caused by the load of these illnesses. 42.5% of our patients have feeding issues, which is a common yet sometimes underappreciated symptom. Tachypnea and perspiration during feedings cause infants with VSD to consume more energy, which is reflected in these problems. This aligned with the previous research [16], which highlighted feeding issues as a precursor to congestive heart failure in newborns with large shunts. Out of the youngsters in this study, 38% were found to have failed to flourish. This finding is consistent with research [17], which discovered that growth retardation is common in children with large or moderate VSDs because of increased metabolic demands, recurrent infections, and chronic undernutrition. After a defect is closed or the shunt flow naturally decreases, these growth issues frequently go away. Cyanosis was detected in only 6% of instances, mostly in individuals with bidirectional or right-to-left shunts or severe VSDs worsened by pulmonary hypertension. Although cyanosis is uncommon in isolated VSD, it can indicate severe illness, Eisenmenger physiology, or other cardiac abnormalities. This is consistent with research [18], which found that patients with higher pulmonary vascular resistance were more likely to have cyanosis. Among our cohort, 13% had Down syndrome. Crucially, inlet-type VSDs were seen in over half (53.8%) of children with Down syndrome, supporting the established link between trisomy 21 and atrioventricular septal defects (AVSDs). Nearly 40–50% of children with Down syndrome have congenital heart disease, with AVSD being the most common kind that frequently affects the inlet septum [11, 19]. 62% of patients in our study had the peri-membranous type, which was the most common anatomical subtype. Muscular (19%), inlet (10%), and outlet (9%) types were next in line. This distribution reflects developments in epidemiology worldwide. Over 70% of all VSDs are caused by peri-membranous abnormalities [20]. Both the membrane septum's embryological vulnerability and its frequent inclusion in diagnostic echocardiographic planes are reflected in the high frequency of peri-membranous VSDs. The second most frequent type of VSD was muscular (19%). Despite being smaller and more prone to closure on their own, these abnormalities are occasionally underdiagnosed because of their faint Doppler signals, especially in newborns. According to research, up to 80% of muscle VSDs spontaneously close during the first two years of life [21]. On the other hand, our cohort's children with Down syndrome had a disproportionately high number of inlet-type VSDs, indicating the necessity for closer echocardiographic monitoring in these groups. Small VSDs accounted for the biggest percentage of defects (44%), followed by moderate (34%) and large (22%). This is consistent with research [22], which found that the greater usage of neonatal echocardiographic screening led to a higher frequency of tiny VSDs. The hemodynamic cost imposed by a defect's size has clinical implications; larger flaws are more likely to cause heart failure, pulmonary hypertension, and volume overload. As would be predicted in the absence of pulmonary vascular disease or elevated right-sided pressures, left-to-right shunting was the predominant flow pattern (93%). Only a small percentage of individuals showed right-to-left (2%) or bidirectional (5%) shunting. These examples probably indicate more severe pulmonary vascular alterations that could lead to Eisenmenger syndrome. Shunt reversal is a serious prognostic indicator that frequently necessitates early surgical or palliative

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intervention [23]. With 18% of patients having it, patent ductus arteriosus (PDA) was the most common related lesion. PDA and VSD together have the potential to greatly increase pulmonary over-circulation and worsen symptoms. Similar prevalence was reported in a study [24], which also underlined the importance of co-management of both disorders in order to avoid pulmonary hypertension. A trend towards multiple septal defects in certain children is suggested by the 14% of patients who had an atrial septal defect (ASD). Such combinations may result from common embryologic abnormalities in the atrioventricular septation and call for a customized interventional strategy [25]. Eleven percent of patients, primarily those with peri-membranous VSDs, had aortic valve prolapse. The fact that this issue is linked to aortic regurgitation makes it noteworthy. Up to 10–15% of children with peri-membranous VSDs experience aortic valve prolapse over time [26], highlighting the significance of serial echocardiographic surveillance. Twenty-four percent of patients had pulmonary hypertension, which is indicative of a significant burden of chronic volume overload and delayed diagnosis. Long-term results are greatly impacted by pulmonary hypertension since it can result in Eisenmenger physiology and inoperability. This prevalence is consistent with a study [27], which emphasized early intervention to mitigate pulmonary vascular remodeling in children with congenital left-to-right shunts.

This study has a few limitations that should be acknowledged. Its cross-sectional and single-center design may limit the generalizability of the findings to wider pediatric populations in Pakistan or similar low-resource settings. The retrospective nature of data collection could have introduced information bias due to incomplete or inconsistently recorded clinical data. The absence of long-term follow-up restricted assessment of outcomes such as spontaneous closure of the defect, progression of pulmonary hypertension, or the need for surgical intervention. Additionally, potentially influential factors such as socioeconomic status and nutritional assessments were not included, which might have affected the observed growth parameters and clinical presentation. Future research should include prospective, multicenter studies with larger sample sizes and long-term follow-up to better evaluate clinical outcomes and disease progression in children with VSD. Incorporating socioeconomic and nutritional indicators would also provide a more comprehensive understanding of growth and health disparities in this population.

## CONCLUSIONS

This study provides an extensive analysis of the clinical and echocardiographic characteristics of pediatric patients with ventricular septal defect (VSD) at a tertiary care facility in Pakistan. Most patients were diagnosed within the first year of life, and the most common signs were a heart murmur, repeated respiratory infections, trouble eating, and not growing. Peri-membranous VSD was the most common subtype, followed by muscular, inlet, and outlet types. A significant number of patients had heart problems that were linked to their condition, such as patent ductus arteriosus, atrial septal defect, aortic valve prolapse, and pulmonary hypertension. Notably, pulmonary hypertension was present in nearly one-fourth of the cohort, underscoring the consequences of delayed diagnosis.

## Authors' Contribution

Conceptualization: RM
Methodology: AA, HDW
Formal analysis: AZ
Writing and Drafting: HDW
Review and Editing: RM, AA, AZ, HDW

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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# Impact of Tobacco Cessation Curriculum on Professional Competency of Dental Students: A Survey

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## ABSTRACT

Tobacco cessation counseling (TCC) has become a crucial component in comprehensive patient care. Dentists are in a unique position to identify tobacco users due to regular patient contact and are pivotal in delivering TCC as part of comprehensive oral healthcare. **Objectives:** To assess the impact of the tobacco cessation curriculum on the professional competency and intention of dental students to provide TCC. **Methods:** An analytical cross-sectional study was conducted from January 2025 to March 2025. It involved students from clinical years, dental interns, and postgraduate students from all Public and Private Dental Colleges in Karachi who had a tobacco cessation curriculum in formal dental teaching. A structured, self-administered questionnaire was used to assess intentions and perceived barriers in TCC using constructs of the Theory of Planned Behaviour. Data were entered and analyzed using SPSS version 22.0. Frequencies and percentages were obtained for variables. The chi-square test was applied to evaluate associations. **Results:** The majority of participants, 239 (79.7%), demonstrated a high intention to deliver tobacco cessation counseling. No significant difference was observed in the intention of dental students and dentists to provide effective TCC (p-value>0.05). Statistically significant differences were observed between the barriers faced by dental students and dentists in that the students were more concerned that they lacked skills of TCC in comparison to dentists (p-value=0.04). **Conclusions:** The tobacco cessation curriculum effectively boosts dental students' intention to provide counseling, although skill deficits and concern over patient relationships remain notable barriers.

## INTRODUCTION

In the past few years, there has been massive research on the impact of tobacco use on general and oral health [1]. Reports by the World Health Organization have revealed nearly six million tobacco-related deaths every year [2]. Literature has demonstrated that tobacco has an integral role in the etiology of oral conditions like halitosis, periodontal diseases, oral cancer, and changes in salivary glands [3]. The oral cavity of active smokers shows a higher prevalence of Streptococcus mutants, increasing the risk of dental caries [4]. Clinical practice guidelines have recommended that brief tobacco cessation counseling is the responsibility of dental professionals [5]. Dental students or dentists are incredibly positioned to contribute to cessation activities [6, 7]. Many countries have focused on the addition of tobacco cessation curriculum in the course [8, 9]. Therefore, dental surgeons can take the lead in helping patients quit smoking [7, 10]. Intention to provide effective TCC is explained by the Theory of Planned

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Behavior (TPB). It states that a specific behavior is predicted by the intention to engage in this behavior, which is based on attitude and perceived control [11, 12]. Limited studies have been done to investigate the intention of dentists to provide TCC. The rationale of this study is grounded in the critical public health challenge posed by tobacco use, which significantly impacts both general and oral health. Tobacco use is a leading cause of severe oral diseases such as periodontal disease, oral cancer, halitosis, and dental caries, as well as systemic health problems, leading to millions of deaths annually worldwide. Given this, dental professionals are uniquely positioned and have an ethical responsibility to provide tobacco cessation counseling (TCC) due to their frequent contact with patients' oral health and tobacco-related oral conditions.

However, despite the recognized need, tobacco cessation curricula are not universally integrated into dental education, and limited research has focused on the intention and competency of dental students to provide TCC, particularly through the lens of behavioral theories like the Theory of Planned Behavior (TPB). This study has addressed this research gap; the present study aims to assess the impact of the tobacco cessation curriculum on the professional competency of dental students towards TCC. This study aimed to assess the impact of a tobacco cessation curriculum on the professional competency and intention of dental students in providing effective TCC and whether this intention can be explained by TPB. Also, identify barriers in providing effective TCC.

## METHODS

An analytical cross-sectional study was carried out from January 2025 to March 2025 for 3 months in all Public and Private Dental Colleges in Karachi. The study sample included dental students in clinical years, house officers, and postgraduate trainees who had a tobacco cessation curriculum as a part of their dental teaching. Exclusion criteria included participants who were not in clinical years, house officers, or postgraduate trainees. Additionally, those unwilling to participate or who provided incomplete or missing data in the survey were excluded to maintain the integrity of the analysis. Sample size was calculated as 323, considering the population size as 2000, at 5% margin of error, at a 95% Confidence Interval using Raosoft calculator. The consecutive sampling technique was used for the selection of study participants. Approximately 750 participants were approached, out of which 376 consented to take part, 76 were excluded due to missing data, so the final sample achieved was 300. Ethical approval was taken from the Institutional Review Board of Hamdard University Dental Hospital, approval no: 13152-01-25, and ref no: KCM&D/HUDH/13152-25. Before participation, informed consent was obtained from all participants. They were provided with detailed information about the study's purpose, procedures, risks, and benefits, and assured that participation was voluntary with the option to withdraw at any time without penalty. All participants signed a consent form indicating their voluntary agreement to take part in the study, ensuring ethical compliance with research standards. A self-administered structured questionnaire designed on Google Forms was used. It was divided into three sections: Attributes of study participants, intention of dental students to provide TCC, and perceived barriers. Attributes of participants were recorded in terms of gender, program level, whereas intention was assessed in terms of attitude, perceived confidence, and support to provide TCC. These items corresponded to the constructs of the Theory of Planned Behavior: attitude towards particular behavior, perceived control, and subjective norms. Participants were instructed to respond with either 'yes' or 'no'. The questionnaire was developed based on a thorough review of existing literature, validated instruments in tobacco cessation research, and guidelines from recognized health organizations to ensure relevance and comprehensiveness for assessing dental students' competency and intention regarding tobacco cessation counseling. The questionnaire was pre-tested on a small group of participants to ensure clarity, validity, and reliability before the main study, allowing for necessary revisions based on feedback. Data were entered and analyzed using SPSS version 22.0. Frequencies and percentages were obtained for all categorical variables, like gender, program level, tobacco consumption status, variables related to TCC counseling intention, and perceived barriers. The chi-square test was applied to examine associations. Results were considered statistically significant when the p-value was less than 0.05

## RESULTS

Amongst all participants, there were 67 (22.3%) male and 233 (77.7%) female with the age range of 19-34 years, mean age 23 ± 2.6 (Table 1).

**Table 1:** Attributes of Study Participants

| Variables | Frequency (%) |
|---|---|
| **Gender** | |
| Male | 67 (22.3%) |
| Female | 233 (77.7%) |
| **Program Level** | |
| 3rd Year BDS | 103 (34.3%) |
| 4th Year BDS | 82 (27.3%) |
| Dental Interns | 80 (26.7%) |
| Postgraduate Students | 35 (11.7%) |

Over 239 (79.7%) participants believed that giving tobacco cessation advice is the role of dental students/dentists (Figure 1).

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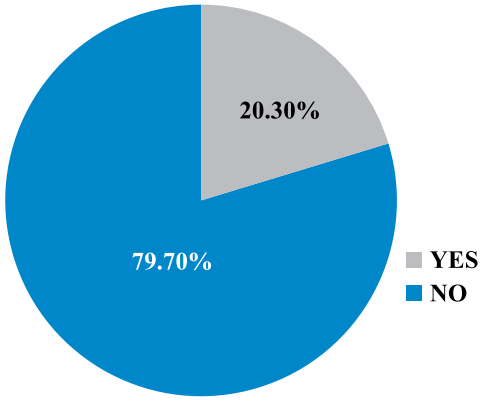


**Figure 1:** I Believe TCC Is Part of My Role as A Dental Student

Willingness towards tobacco cessation counseling was seen in 283 (94%). Whereas, 291 (97.0%) confidently provided verbal information to encourage quitting. From clinical practices, almost all 282 (94%) were interested in enquiring about the history of tobacco, and 201(67%)kept a proper record of tobacco consumption. Surprisingly, 240 (80%) persuaded patients to quit tobacco, out of which 164 (54.7%) were successful in motivating patients towards cessation. The result of the Chi-square test showed statistically insignificant differences in the intention of dental students and dentists to provide effective TCC (p-value>0.05). Hence, we can say that both have equal intentions of providing counseling. The p-values of variables like giving TCC were our responsibility, and willingness to pursue TCC was statistically insignificant, suggesting no difference in opinion between groups (p-value 0.65 and 0.98, respectively), but overall responses were highly positive between groups. However, a significant difference was found in preferred methods for tobacco cessation counseling; it was seen that almost all of them were more into verbal counseling (97%), but 3rd-year and 4th-year students preferred demonstrations by leaflets and pamphlets(58%)(Table 2).

**Table 2:** Intention of Dental Students/Dentists to Provide TCC

| Variables | Frequency (%) | p-value |
|---|---|---|
| Giving TCC is Our Responsibility | 239 (79.7%) | 0.65 |
| 3rd Year BDS | 75 (72.8%) | |
| 4-Year BDS | 66 (80.5%) | |
| Dental Interns/H.OS | 71 (88.8%) | |
| Postgraduate Students | 27 (77.1%) | |
| Willingness to Pursue TCC | 283 (94.3%) | 0.98 |
| 3rd Year BDS | 97 (94.2%) | |
| 4-Year BDS | 75 (93.8%) | |
| Dental Interns/H.OS | 33 (94.3%) | |
| Postgraduate Students | 29 (90%) | |
| Tobacco Cessation Advice Could Help to Quit Tobacco | 284 (94.7%) | 0.14 |
| 3rd Year BDS | 98 (95.1%) | |
| 4-Year BDS | 81 (98.8%) | |
| Dental Interns/H.OS | 73 (91%) | |
| Postgraduate Students | 32 (71.4%) | |
| NRTs Is Helpful in Tobacco Cessation | 271 (90.3%) | 0.66 |
| 3rd Year BDS | 100 (97.1%) | |
| 4-Year BDS | 76 (87 .7%) | |
| Dental Interns/H.OS | 73 (91.2%) | |
| Postgraduate Students | 30 (85.7%) | |

Dental students and dentists are generally confident and intend to provide verbal tobacco cessation counseling, with clinical practice improving skills(Figure 2).

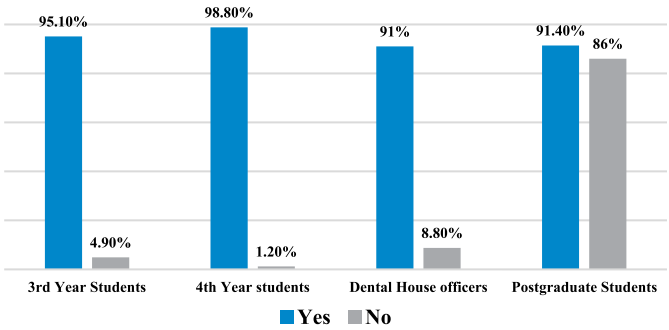


**Figure 2:** TCC by Dentists Could Assist Patients to Quit Smoking

Among participants, verbal counseling emerged as the overwhelmingly preferred method, selected by 291 (97.0%) respondents across all educational levels with no significant differences observed (p-value=0.97). Leaflets or pamphlets were favored by 78 (54%) participants, showing statistically significant variation between groups (p-value<0.05). Dental students, particularly those studying in 3rd year of BDS, were actively involved in TCC as compared to others through making brochures. While nicotine replacement therapy preference differed notably across 3rd year BDS, 4th year BDS, house officers, and postgraduates (p-value=0.02). These findings highlight verbal methods' universal appeal in dental settings due to their direct, patient-centered approach, whereas adjuncts like printed materials and pharmacotherapy exhibit group-specific preferences influenced by training stage and experience. Statistically significant differences were observed between the barriers faced by dental students and dentists in that the students were more concerned that they lacked skills of TCC in comparison to dentists (p-value=0.04); they were also hesitant in involved in TCC as they thought it might impact the dentist-patient relationship (p-value=0.01). Whereas, dentists faced time issues in dental practice to provide TCC (p-value=0.04) (Table 3).

**Table 3:** Perceived Barriers

| Variables | Dental Students | Dentists | Total |
|---|---|---|---|
| Lack of Motivation | 150 (57%) | 113 (43%) | 263 (87.7%) |
| Lack of Skills | 130 (67.4%) | 63 (32.6%) | 193 (64.3%) |

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| | | | |
|---|---|---|---|
| Impact on the Dentist-Patient Relationship | 140 (66.7%) | 70 (33.3%) | 210 (70.0%) |
| Time Restriction | 80 (34.8%) | 150 (65.2) | 230 (76.7%) |
| Insufficient Information | 100 (52.15) | 92 (47.9%) | 192 (64.0%) |
| Lack of Awareness of Referral Pathways | 104 (51.5%) | 98 (48.5%) | 202 (67.3%) |

## DISCUSSION

Throughout the world use of tobacco has profound health consequences [13]. Considering the magnitude of the problem, dental organizations have devised certain policies, like the implementation of tobacco cessation curriculum into dental institutes in Pakistan [14, 15]. In the present study, it was hypothesized that tobacco cessation as a part of Community Dentistry in dental education has an encouraging role in tobacco cessation counseling; this study accepts this hypothesis. The findings of the present study revealed that a significant proportion of participants, nearly 79.7% showed a strong inclination to offer TCC. The Majority had the true intention; these findings are in agreement with another study in which nearly 69.2% have incorporated TCC in their regular practice [16]. In contrast, some studies have identified disparities in the intention of dental professionals to provide TCC and in real practice [17, 18]. The high intention for TCC among participants, that is 79.7% aligns with findings from Pakistani dental students, where 97.9% recognized dentists' role in cessation, but only 11% actively counseled due to inadequate training. Moreover, during clinical practice, 67% reported that they documented the amount of tobacco consumption, which highlights an interesting aspect of TCC in the studied group [19]. Confidence of students has been positively correlated with TCC delivery [20]. In the current study greater proportion of participants, nearly 89.3% believed that they are confident enough in their capability. Conversely, limited health literacy among patients was identified as the primary hurdle in performing TCC [21]. Barriers like lack of skills were prevalent in 64.3% participants, and fear of impacting dentist-patient relationships was seen in 70%. This mirrors Saudi dental professionals, whereas 51.7% cited time/literacy issues, and global reviews noted patient resistance [21]. Lack of time was the second most common barrier identified, i.e, 76.7%. These findings are congruent with another study, which revealed that 51.7% dentists tend to neglect TCC as they are more in favor of addressing immediate dental issues [16]. Approximately 70.0% of participants were afraid of the fact that taking part in TCC might affect the doctor-patient relationship. Numerous researchers have provided insight on this topic and have concluded that involving patients in planning their quitting strategies cements the doctor-patient relationship [22, 15].

The low response rate in this study may have introduced potential nonresponse bias, which could affect the generalizability of the findings. Factors such lack of perceived importance of the survey among participants may have contributed to the lower participation. Despite this limitation, the responses obtained still provide valuable insights, but results should be interpreted with caution. Future studies could consider strategies such as follow-up reminders or incentives to improve response rates and enhance representativeness.

## CONCLUSIONS

In conclusion, the majority of participants show willingness to engage in TCC. Students in their 3rd year were just as prepared and aware as postgraduates. This finding may indeed be intriguing and suggests that foundational TCC education in early dental curriculum aids efficient counseling.

### Authors' Contribution

Conceptualization: WA
Methodology: WA, SHA, TBT
Formal analysis: TBT
Writing and Drafting: MBB, SA, SJAZ
Review and Editing: WA, SHA, TBT, MBB, SA, SJAZ

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

### Conflicts of Interest

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# Functional Outcome of Arthroscopic Anterior Cruciate Ligament Reconstruction Using Hamstring Tendon Autograft

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## ABSTRACT

Anterior cruciate ligament (ACL) injuries are among the most common knee injuries, particularly in active individuals and athletes. Untreated ACL tears can lead to joint instability, meniscal damage, and early osteoarthritis. **Objectives:** To assess the efficacy of hamstring tendon autografts in arthroscopic ACL reconstruction. **Methods:** A longitudinal descriptive study was undertaken from July 2023 to January 2024, including 70 patients with ACL rupture with an arthroscopic ACL reconstruction using hamstring autografts. Patients were assessed through Lysholm knee scoring and International Knee Documentation Committee (IKDC) scores at 6 weeks, 3 months, and 6 months postoperatively. Demographic data, clinical characteristics, and outcomes were analyzed using statistical methods, using a p-value≤0.05 as significant. **Results:** Participants were predominantly male (80%), with a mean age of 35.6 years (SD 5.76). Causes of ACL injury included road traffic accidents (40%), sports activities (31.4%), and falls (28.6%). Preoperative IKDC scores improved significantly from 52.6 (95% CI: 50.9–54.3) to 89.6 (95% CI: 88.8–90.4) postoperatively (p<0.001, Cohen's d = 5.2). Lysholm scores indicated excellent outcomes (90–100) in 44.3% (SD 4.1), good (80–89) in 38.6% (SD 3.8), fair (65–79) in 12.9% (SD 2.5), and poor (<65) in 4.3% (SD 1.2). Right-sided injuries showed better outcomes (p<0.001). Sports-related injuries had superior outcomes (p<0.001). **Conclusions:** The study contributes valuable insights into demographic factors influencing results, emphasizing the importance of graft choice in achieving favorable postoperative knee function.

## INTRODUCTION

The anterior cruciate ligament (ACL) is one of the four primary knee joint ligaments. It is crucial for preserving joint stability when performing daily tasks [1, 2]. A frequent injury among soccer and basketball players, it is the most often injured ligament in the knee [3]. Female athletes have a three to ten times higher risk of this ligament disruption than male athletes [4]. One in 3,500 people in the general population is thought to get ACL damage each year [3]. Untreated cases have a markedly increased incidence of osteoarthritis in the knee, meniscus tears, and functional instability [5]. Treating ACL injuries is essential. ACL repair is the standard course of therapy for those with ACL injuries who wish to return to sports [6]. Following an ACL injury, operative and non-operative treatment modalities are employed. Management is influenced by objectives, goals, concurrent injuries, risk factors, and patient activity

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levels [7]. The primary treatment options for ACL injury as first-line are ACL reconstruction and post-operative rehabilitation, followed by ACL reconstruction and post-operative rehabilitation, and rehabilitation (followed by ACL reconstruction in patients who develop functional instability) [8]. ACL reconstruction surgery is performed under arthroscopic guidance, and the torn ACL can be replaced either with an autograft, which is a tissue from the patient's own body, such as a hamstring tendon or an allograft, which can be a cadaveric ligament, or a well-managed tendon. However, synthetic grafts have recently been used [9, 10]. The ideal option for ACL restoration is a graft that is comparable biomechanically to the original torn ligament, easy to harvest, has lower morbidity at the harvest site, can be secured reliably, and has good integration with bone [10]. The most often employed graft for ACL restoration surgery was the bone-patellar tendon-bone (BPTB) graft for a very long period. That said, issues including the knee joint's ineffective extensor mechanism, decreased motion, subsequent patellar fractures, and anterior knee discomfort compelled surgeons to develop alternative graft retrieval sources for ACL restoration. The hamstring graft is an excellent substitute as it does not endanger the extensor apparatus, as the BPTB transplant did. It has shown outstanding outcomes when patients with ACL tears undergo reconstruction using hamstring tendon transplants and proper patient selection. The cells of a quadrupled hamstring graft likely live longer and produce better effects than those of a BPTB transplant because the surrounding synovial fluid feeds the hamstring tendon graft. A meta-analysis undertaken by Biau et al. in 2007 to gather subjective data on whether hamstring graft or BPTB results in a more functioning knee as determined by the overall IKDC rating, and the return to daily and athletic activity to pre-injury status. Comparing the outcomes in terms of functionality of the hamstring and BPTB grafts revealed no discernible variations [11]. Despite the growing use of hamstring tendon autografts, there is a need for further investigation into their functional outcomes and factors influencing success.

Understanding the functional outcomes associated with hamstring tendon autografts is essential for orthopedic surgeons, as it guides clinical decision-making and improves patient counseling. By conducting this study, we aim to provide evidence-based data that can enhance the understanding of factors influencing the success of ACL reconstruction using hamstring autografts, ultimately contributing to improved patient care and outcomes in orthopedic surgery.This study aimed to contribute a valuable understanding of the efficacy of ACL reconstruction using hamstring autografts, shedding light on demographic variables such as gender, side of injury, and the cause of injury that may impact postoperative functional outcomes.

## METHODS

This longitudinal descriptive study, approved by the Ethical Committee of Ghurki Trust Teaching Hospital, Lahore (Ref. No 2023/06/R-22). The study included isolated anterior cruciate ligament (ACL) ruptures that underwent arthroscopic reconstruction with hamstring tendon autografts. By using the WHO sample size estimation formula, $n=Z^2.P.(1-P) / E^2$. A sample size of 70 was calculated by using the following values: expected proportion (p=0.85), confidence interval (z=95%), and precision (d=0.09) [12]. From July 2023 to January 2024, the study ensured relevance to both American and international orthopedic settings. A convenient sampling technique was used to collect the data from patients, so easily available participanst were added according to the convenience of the researchers. Eligible patients were over 18 years with a normal contralateral knee, excluding those with fractures, multiple ligament injuries, knee osteoarthritis, or intra-articular pathologies requiring revision surgery. Written informed consent was taken. Demographic and clinical data, including age, gender, injury side, and cause (road traffic accidents, sports activities like soccer or basketball, or falls such as from height or tripping), were extracted from electronic patient records at the hospital. Preoperative assessments included standard tests, complete blood count, erythrocyte sedimentation rate, C-reactive protein, blood glucose, and renal function tests, to confirm surgical eligibility, alongside Lachman and pivot-shift tests to evaluate knee instability. A single experienced orthopedic surgeon performed all procedures using a single-bundle technique, harvesting ipsilateral semitendinosus and gracilis tendons with a tendon stripper, quadrupling the graft, and fixing it with an EndoButton (Smith and Nephew) on the femoral side and a bioabsorbable interference screw on the tibial side, with anatomic tunnel placement achieved via an anteromedial portal under arthroscopic visualization. Patients followed a standardized postoperative rehabilitation program, starting with immediate weight-bearing as tolerated, quadriceps strengthening, and range-of-motion exercises on day 1, with pre-operative rehabilitation recommended only for significant swelling or stiffness, and progressive return to sports allowed at 6–9 months based on functional milestones. Functional outcomes were assessed at 6 weeks, 3 months, and 6 months postoperatively using the Lysholm knee scoring scale (0–100, excellent: 90–100, good: 80–89, fair: 65–79, poor: <65), which evaluates eight patient-reported items like pain and instability (ICC = 0.88, high validity for ACL outcomes) [13], and the IKDC subjective knee form (0–100), assessing symptoms, sports activities, and function (ICC = 0.94, validated for ACL

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reconstruction) [14], with higher scores indicating better function and a minimum score of 0 (severe disability) to a maximum of 100 (normal function). Data were analyzed using IBM SPSS Statistics version 27.0, with descriptive statistics (means, standard deviations, frequencies) for quantitative variables (e.g., age, IKDC scores) and qualitative variables (e.g., gender, injury cause). Normality of data was tested using Kolmogorov-Smirnov's test, after which parametric tests were applied. paired t-tests for pre- and postoperative IKDC score comparisons, chi-square tests for Lysholm score stratification by demographics, and 95% confidence intervals, using a 95% confidence level and p≤0.05 as the significance threshold.

## RESULTS

The study presents a detailed overview of the demographic and clinical characteristics of the 70 patients included in the study. Most participants were male (80%), with a mean age of 35.6 years, reflecting a diverse adult population undergoing arthroscopic anterior cruciate ligament (ACL) reconstruction. The distribution of ACL injuries on either side, with 55.7% on the right and 44.3% on the left, sheds light on the lateralization of these injuries. Causes of ACL injury varied, with road traffic accidents (RTAs) accounting for 40%, sports activities for 31.4%, and falls for 28.6% (Table 1).

**Table 1:** Descriptive Statistics of Qualitative Variables (n=70)

| Parameters | n (%) |
|---|---|
| **Gender** | |
| Male | 56 (80%) |
| Female | 14 (20%) |
| **Side** | |
| Right | 39 (55.7%) |
| Left | 31 (44.35%) |
| **Cause** | |
| RTA | 28 (40%) |
| Sports activity | 22 (31.4%) |
| Fall | 20 (28.6%) |

** statistically significant at 0.05, 0.01

The preoperative International Knee Documentation Committee (IKDC) score indicated a baseline functional status (52.6 ±7.2), significantly improving postoperatively to 89.6 ± 3.75. The postoperative Lysholm scores were categorized into Excellent (44.3%), Good (38.6%), Fair (12.9%), and Poor (4.3%), providing a detailed breakdown of functional outcomes (Table 2).

**Table 2:** Descriptive Statistics of Quantitative Variables (n=70)

| Parameters | n (%) | Mean ± SD (Range) | p-value |
|---|---|---|---|
| Age (Years) | – | 35.6 ± 5.76 (20–60) | – |
| IKDC Score | – | – | – |
| Pre | – | 52.6 ± 7.2 (95% CI: 50.9–54.3) | **<0.001 |
| Post | – | 89.6 ± 3.75 (95% CI: 88.8–90.4) | – |
| **Lysholm Score** | | | |
| Excellent (90–100) | 31 (44.3%) | 94.2 ± 4.1 | **<0.050 |
| Good (80–89) | 27 (38.6%) | 84.5 ± 3.8 | |
| Fair (65–79) | 9 (12.9%) | 70.3 ± 2.5 | |
| Poor (<65) | 3 (4.3%) | 60.1 ± 1.2 | |

** statistically significant at 0.05, 0.01

Results offer a nuanced analysis by stratifying Lysholm scores based on demographic factors. While male patients tended to have more Excellent and Good outcomes than female, the difference was not statistically significant (p-value=0.152). However, the side of injury significantly influenced outcomes, with right-sided injuries demonstrating better results than left-sided injuries (p-value=<0.001). Moreover, the cause of injury played a significant role, with sports-related injuries showing the most favorable outcomes compared to RTAs and falls (p-value<0.001). These tables provide a comprehensive understanding of the study population, highlighting the diverse factors contributing to functional outcomes following arthroscopic ACL reconstruction with hamstring grafts (Table 3).

**Table 3:** Stratification of Lyshlom Score According to Demographic Profile

| Variables | Excellent | Good | Fair | Poor | p-value |
|---|---|---|---|---|---|
| **Gender** | | | | | |
| Male | 29 | 22 | 7 | 1 | 0.152 |
| Female | 5 | 5 | 3 | 2 | |
| **Side** | | | | | |
| Right | 20 | 19 | 0 | 0 | **<0.001 |
| Left | 11 | 8 | 9 | 3 | |
| **Cause** | | | | | |
| RTA | 22 | 4 | 2 | 0 | **<0.001 |
| Sports activity | 6 | 15 | 1 | 0 | |
| Fall | 3 | 8 | 6 | 3 | |

** statistically significant at 0.05, 0.01

## DISCUSSION

Patients who suffer from knee impairment due to an ACL injury that is neglected and not treated promptly may experience joint complications if the damage worsens. Patients' goals to regain their pre-injury levels have increased significantly due to developments in surgical techniques and better results. A significant factor in meeting and exceeding these objectives is graft choice, with hamstring grafts becoming increasingly popular, particularly the quadrupled hamstring graft. Compared to patellar tendon grafting, the four-string or quadruple hamstring graft has demonstrated superior strength and tension. During the research period, hamstring autograft was used for ACL restoration in all 70 patients. Among these, 56 were male, while 14 were female. The research

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included 12 male and three female, most of whom had right knee injuries. According to research by Brown *et al.* although women are more likely to get hurt, men are more likely to get hurt because of restricted exposure to conditions related to the manner and cause of injury. Additionally, it was concluded that the affected limb's side had no bearing on the functional result [15]. The anatomic placement of the tunnel during the single-bundle technique likely enhanced graft stability, thus preventing tunnel widening as well as fixation failures. The usual time frame for graft maturation spans 6–12 months, but the results we obtained at 6 months support this timeline. Additional research is necessary to understand biomechanical factors that affect long-term stability, including how tunnel widening and graft healing processes affect results [4]. The study results showed improved outcomes in sports-related injuries, possibly because patients involved in sports are often younger with better pre-injury health; however, the results lack adjustment for these variables. Future trials need to consider these confounding variables for their analyses. Our study results are consistent with a previous study: 44.3% of patients had excellent outcomes, 38.6% had good, 12.9% had fair, while 4.3% of cases were found with poor outcomes using the knee scoring scale by Lysholm. 94% of participants in a comparable investigation by Bourke *et al.* which comprised 143 patients, had an outstanding Lysholm score at the end of the study's 1-year follow-up [16]. According to the same research conducted by Jeyaraman, 27% of cases had great outcomes, 53% had good results, 13% had fair results, and 7% had bad results [17]. In our study, the mean operative IKDC score was 52.6 ± 7.2, and the postoperative score was 89.6±3.75. A study was conducted by Lind *et al.* The IKDC scores at baseline, 6 months, and 1 year following ACL reconstruction surgery were found to have mean values of 50.6 (19%), 70.8 (1.6)%, and 73.7 (1.9%), respectively, according to their research [18]. The findings of another study showed that the IKDC scores were 51.4 (3.00%) at baseline and 92.1 (2.36) at six months [3]. The results of another study indicate that the mean IKDC score pre-operatively of 38.95 ± 5 increased to 67.92 ± 2 in the 6th month and to 90.73 ± 7 at 12 months. The mean Tegner-Lysholm score pre-operatively was 51 (poor), which increased to 87 (good) in the 6th month and 97 (excellent) in the 12th month [19, 20]. Recent Cochrane reviews emphasize the need for standardized rehabilitation and surgeon expertise, which our single-surgeon design addressed [8].

There are several limitations to this study. First, additional prospective research, such as randomized controlled trials, should be carried out to strengthen the data presented in this retrospective analysis. Secondly, the study's sample size could be a lot bigger. However, subsequent data collected in a real-world environment for this study adds significance. The IKDC and Lysholm scores show that a substantial association with the body of current research supports the study's results. Future studies should involve large-scale, prospective randomized trials with standardized rehabilitation protocols to improve generalizability and evidence strength. Long-term follow-up and evaluation of patient- and graft-related factors are also recommended to optimize ACL reconstruction outcomes.

## CONCLUSIONS

Arthroscopic ACL reconstruction with hamstring tendon autografts yielded patients achieving excellent or good Lysholm scores (44.3% excellent, 38.6% good), indicating successful knee function restoration. Sports-related and right-sided injuries showed superior results, though further studies are needed to address potential biases.

## Authors' Contribution

Conceptualization: FUH, HA, HK
Methodology: FUH, FAK, HA, RK, WA, ZN, LK HUH
Formal analysis: FUH
Writing and Drafting: FUH
Review and Editing: FUH, FAK, HA, RK, WA, ZN, LK, HUH

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

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# Comparison of Ureteral Stents-Related Symptoms among Patients with Ureteral Stents of 4.7Fr and 6Fr Diameter

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## ABSTRACT

Ureteric stents are essential in urology, but factors like diameter, position, and design can significantly impact patients' quality of life. **Objectives:** To compare the mean IPSS scores among patients with ureteral stents of 4.7Fr and 6Fr diameter. **Methods:** The quasi-experimental study was conducted at the Department of Urology and Renal Transplant, Mayo Hospital, Lahore, from March to September 2024. 124 patients were selected for this study who required DJ Stenting after open or endourological surgery. Patients were categorized into two groups. Each group contains 62 patients. All patients underwent open or endourological surgery followed by DJ Stenting as indicated. 4.7 Fr DJ Stents were placed in Group A and 6 Fr DJ Stents in Group B. **Results:** A Total of 124 patients, the mean age of the 4.7 Fr DJ stent group was 47.88 ± 6.56 years, and 49.48 ± 6.57 years in the 6 Fr DJ stent group. The p-value = 0.178, duration of operation 50.85 ± 0.64 minutes in group A and 55.25 ± 0.76 minutes in group B. The p-value = 0.000). There were 43 (55.1%) male and 19 (41.3%) female in group A, and 35 (44.9%) male and 27 (58.7%) female in group B. A (p=0.193) IPSS score was 2.21 ± 0.11 in group A and 6.33 ± 0.19 in group B (p=0.000). **Conclusions:** It was concluded that ureteral stents with larger diameters result in notably more severe urinary symptoms. It is advisable to use ureteral stents with smaller diameters to alleviate symptoms related to stent use.

## INTRODUCTION

DJ stenting is a common urological procedure performed under a variety of circumstances. DJ Stents are flexible tubes placed in the ureter with their coiled upper and lower ends placed in the Kidney and Urinary bladder, respectively. They prevent stricture formation after endoscopic or open surgeries by keeping the ureters open during the healing process [1]. They are also used in the identification of ureters during retroperitoneal or pelvic surgeries and to keep ureters patent during conditions like retroperitoneal fibrosis [2]. DJ Stents are associated with significantly lower UT signs, pain, sexual dysfunction, and reduced labor capacity in 80% of patients. These indications are due to bladder mucosa irritation by the distal coil, leading to detrusor contraction [3]. Some research indicates that stents can shift up to 2.5 cm during regular daytime activities. This shifting is believed to increase the pain and lower UTIs due to the direct discomfort of the bladder [4]. Much work has been done in the past studying the etiology of DJ Stent-related LUTS and ways to improve these symptoms, with authors advocating for improvements in stent material, stent placement technique, stent positioning, and pharmacological therapy [5]. The

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mainstays of pharmacologic therapy have been alpha-blockers and anticholinergic agents. However, to date, an optimal strategy to improve stent-related symptoms still doesn't exist [6]. The effect of stent diameter on DJ stent-related LUTS found an insignificant association in pain or irritative symptoms among patients. However, smaller diameter stents had a propensity to migrate downward and become dislodged [7]. Ureteral stents with narrower diameters are suggested for alleviating stent-related symptoms when associated with larger diameter stents, as evaluated using the International Prostate Symptom Score (IPSS) [8]. Patients with larger diameter stents had worse IPSS, intermittency, urgency, voiding symptoms, and storage symptoms sub-scores on IPSS, and total OABSS [9]. The Urinary Symptom Index Score and patients reporting discomfort were notably more favorable for PSS compared to DJ. Urinary stents come with various side effects that impact patients both physically and mentally. The design and models of ideal or nearly ideal stents should focus on minimizing these side effects while maintaining a high level of tolerability, safety, and effectiveness [10]. Urinary stents can lead to a variety of side effects that impact patients both physically and mentally. The optimal or nearly optimal stent designs and models should focus on reducing these side effects, while being as comfortable, safe, and effective as possible.

Stent-related discomfort has been linked to factors such as bladder irritation, stent migration, and design characteristics, yet consensus on an optimal stent diameter to minimize symptoms remains lacking. Existing evidence on the relationship between stent diameter and LUTS is inconsistent, with limited comparative data using standardized symptom scores. This study aims to compare the mean International Prostate Symptom Score (IPSS) among patients with 4.7Fr and 6Fr ureteral stents to evaluate the impact of stent diameter on symptom severity.

## METHODS

A quasi-experimental study was conducted in the Department of Urology and Renal Transplant, Mayo Hospital, Lahore, from March 2024 to September 2024 using a non-probability consecutive sampling technique. Patients aged 16-60 years with unilateral DJ Stents without externalized strings, placed after Open or Endo-urological procedures in Urology Unit II, were included. Patients with positive preoperative Urine Culture, diagnosed with bladder outlet obstruction or neurogenic bladder, experiencing treatment with alpha-blockers, anti-cholinergic mediators, or painkillers, performing clean intermittent catheterization, patients with indwelling urethral catheters, suprapubic catheters, or nephrostomy tubes, and pregnant female were not included. This study was approved by the ethical committee of Mayo Hospital, Lahore, with the reference number: CPSP/REU/URO-2021-066-1396. Informed consent about the study was taken from each patient. Demographic data/information (age, gender, and duration of symptoms) were recorded. Investigations including CBC, Urine Culture, Ultrasound of Abdomen and Pelvis, and Kidney-Ureter-Bladder radiography were performed. 124 Patients were classified into 2 categories: group A (n=62) and group B (n=62) according to stent diameters. All patients undergo open or endourological surgery followed by DJ Stenting as indicated. 4.7 Fr DJ Stents and 6Fr DJ Stents were placed in patients. Sample size was calculated by using G-power software, using effect size 9.8%, power 80% and 5% as margin of error [9]. Broad-spectrum antibiotics and non-steroidal analgesics were prescribed to patients postoperatively as indicated. Patients were followed up 7 days after undergoing DJ Stenting and filled validated International Prostate Symptom Score (IPSS) Questionnaire. The IPSS is a standardized tool used to evaluate urinary symptoms, consisting of seven questions, each scored from 0 to 5, with a total score ranging from 0 to 35. The severity of symptoms is classified as mild (0–7), moderate (8–19), and severe (20–35). In this study, the IPSS was used to assess stent-related urinary symptoms, quantifying symptom severity and tracking changes over time. The IPSS scores from both groups were compared to determine whether ureteral stent diameter influenced the frequency and severity of DJ Stent-related lower urinary tract symptoms. Follow-up was limited to seven days due to challenges related to patient availability and significant data loss beyond this period. Moreover, investigations, including Urinalysis and Ultrasound of Abdomen and Pelvis, were performed. Patients who reported severe symptoms or complications during follow-up were evaluated further and provided appropriate management, including medication adjustments, additional diagnostic tests, or early stent removal if necessary. Cases of significant pain, infection, or obstruction were managed following standard urological guidelines, ensuring individualized patient care and intervention as required. Data were arranged and analyzed by SPSS version 22.0. The continuous variables, like age, duration of operation, and IPSS Score, were presented as means. Qualitative variables like gender were presented as frequencies and percentages. T-test was applied for the difference between the two groups of IPSS Score (Group A with 4.7 Fr DJ Stents and Group B with 6 Fr DJ Stents), and chi-square test was used for the comparison of IPSS with age, gender, and duration of symptoms. The level of significance was 5%.

## RESULTS

Out of 62 patients, 43 (55.1%) were male and 19 (41.3%) were female in Group A, and 35 (44.9%) were male and 27 (58.7%) were female in Group B. The p-value = 0.178. The mean age

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was 47.88 ± 6.56 years and 49.48+6.57 years, in Groups A and B, respectively (p-value = 0.178), and the mean duration of procedure was 50.85 ± 0.64 and 55.2 ± 50.76, in both Groups, respectively. Regarding to IPSS score, the mean and standard deviation were 2.21 ± 0.11 in Group A and 6.33 ± 0.19 in Group B. Duration of operation and IPSS were significantly associated in both groups, with the p-values of 0.000 (Table 1).

**Table 1:** Demographic Characteristics of Patients

| Variables | Group A (4.7 Fr DJ Stent) | Group B (6 Fr DJ Stent) | p-Value |
|---|---|---|---|
| Age (Years) | 47.88 ± 6.56 | 49.48 ± 6.57 | 0.178 |
| Male | 43 (55.1%) | 35 (44.9%) | 0.193 |
| Female | 19 (41.3%) | 27 (58.7%) | |
| Duration of Operation (Minutes) | 50.85 ± 0.64 | 55.25 ± 0.76 | <0.001 |
| IPSS score | 2.21 ± 0.11 | 6.33 ± 0.19 | <0.001 |

Chi-square test was used for the p-values, α<0.05 considered as statistically significant

The mean and standard deviation of patients who were 16-40 years of age in group A, according to IPSS, were 2.24 ± 0.09, and in Group B mean with the age group 41-60 years was 6.38 ± 0.17 (p-value= <0.001. Similarly, the mean ± SD of patients who were 41-60 years of age in group A according to IPSS was 2.21± 0.11, and in Group B mean with age group 41-60 years was 6.33 ± 0.19 (p-value=<0.001 ). The mean and standard deviation of male in Group A were 2.21 ± 0.10, and in Group B were 6.34 ± 0.21 (p-value=<0.001 ). The mean ± SD of female in Group A was 2.20 ± 0.12 and in Group B mean was 6.33 ± 0.15 (p-value=<0.001 ). The mean ± SD of 1-7 days of symptoms in Group A was 2.19 ± 0.12 and in Group B was 6.36 ± 0.11 (p-value=<0.001 ). The mean ± SD of the above 7 days in Group A was 2.21 ± 0.11 and in Group B was 6.33 ± 0.21 (p-value=<0.001 ) (Table 2).

**Table 2:** Comparison of IPSS Score in Both Groups to Age, Gender, and Duration of Symptoms

| Parameters | Group A | Group B | p-value |
|---|---|---|---|
| **Age (Years)** | | | |
| 16-40 | 2.24 ± 0.09 | 6.38 ± 0.17 | <0.001 |
| 41-60 | 2.21 ± 0.11 | 6.33 ± 0.19 | <0.001 |
| **Gender** | | | |
| Male | 2.21 ± 0.10 | 6.34 ± 0.21 | <0.001 |
| Female | 2.20 ± 0.12 | 6.33 ± 0.15 | <0.001 |
| **Duration of Symptoms** | | | |
| 1-7 Days | 2.19 ± 0.12 | 6.36 ± 0.11 | <0.001 |
| >7 Days | 2.21 ± 0.11 | 6.33 ± 0.21 | <0.001 |

The t-test was used for the p-values, and α<0.05 was considered statistically significant

A comparison of the two groups' IPSS changes from baseline was displayed. Changes between before and after insertion were evident in the values. The IPSS sub-scores of urgencies (p= <0.001) and intermittency (p= <0.001), as well as the overall IPSS (p=<0.001), worsened more in Group 2 patients than in Group 1 (Table 3).

**Table 3:** Comparison Between Baseline in the IPSS and After Using the DJ Stent in Both Groups

| IPSS | Baseline | | | After Using the DJ Stent | | |
|---|---|---|---|---|---|---|
| | Group A | Group B | p-value | Group A | Group B | p-value |
| Q1: Incomplete Emptying | 0.4 ± 1.2 | 0.3 ± 0.8 | 0.500 | 0.68 ± 1.3 | 1.3 ± 0.4 | 0.200 |
| Q2: Frequency | 1.2 ± 1.0 | 0.7 ± 1.2 | 0.700 | 0.4 ± 0.1 | 1.0 ± 0.9 | 0.100 |
| Q3: Intermittency | 0.7 ± 1.2 | 0.5 ± 1.3 | 0.500 | 0.3 ± 0.5 | 0.5 ± 1.2 | <0.001 |
| Q4: Urgency | 0.8 ± 1.4 | 0.6 ± 1.2 | 0.600 | 0.2 ± 0.7 | 1.1 ± 0.9 | <0.001 |
| Q5: Weak stream | 0.6 ± 1.7 | 0.4 ± 1.5 | 0.700 | 0.3 ± 1.1 | 1.0 ± 1.2 | 0.200 |
| Q6: Straining | 0.6 ± 1.1 | 0.4 ± 1.0 | 0.190 | 0.1 ± 0.9 | 0.6 ± 0.8 | 0.020 |
| Q7: Nocturia | 0.8 ± 0.7 | 1.2 ± 0.5 | 0.180 | 03 ± 0.8 | 0.8 ± 0.2 | 0.020 |
| Voiding Symptoms | 2.3 ± 5.2 | 1.6 ± 4.6 | 0.300 | 1.6 ± 2.8 | 3.4 ± 3.5 | 0.040 |
| Storage Symptoms | 2.8 ± 3.1 | 2.5 ± 2.9 | 0.800 | 0.9 ± 1.6 | 2.9 ± 2.0 | 0.010 |
| Total Score | 5.1 ± 8.3 | 4.1 ± 7.5 | 0.610 | 2.2 ± 5.4 | 6.33 ± 5.5 | <0.001 |

Voiding symptom scores were calculated by adding questions 1,3,5, and 6, and Storage symptom scores were calculated by adding questions 2, 4, and 7.

## DISCUSSION

Research indicates that 80% patients after the ureteral stenting experience adverse impacts on quality of life (QoL) [11]. Several reasons, including the length, diameter, softness, positioning, and design of the stent, as well as the patient's age and gender, have been examined in the symptoms that affect the ureteral stents [12]. The placement of a DJ stent is a key element linked with symptoms related to the stent; it has been noted that a stent positioned across the bladder's midline correlates with increased urinary issues [13]. The relationship between symptoms associated with the stent and stent diameter remains ambiguous. Harper *et al.* found that while the diameter of the stent was linked to the work competence component, it didn't have a relationship with the Urinary Symptoms component of the USSQ, with stent positioning demonstrating the strongest relationship with most areas of the USSQ [14]. Given these insights, it is essential to account for stent positioning when exploring the relationship between stent diameter and stent-related signs. The current study compared the mean IPSS scores among patients with ureteral stents of 4.7 Fr and 6 Fr diameters. Study found that out of 124 (62 in each group), the mean age of the 4.7 Fr DJ stent group was 47.88 ± 6.56 years, and 49.48 ± 6.57 years in the 6 Fr DJ stent group. (p=0.178), duration of operation 50.85 ± 0.64 minutes in the 4.7 Fr DJ stent group and 55.25 ± 0.76 minutes in the 6 Fr DJ stent group. (p=<0.001 ) IPSS score was 2.21 ± 0.11 in the 4.7 Fr DJ stent group and 6.33 ± 0.19 in the 6 Fr DJ stent group. (p=<0.001 ) There were 43 (55.1%) male and 19 (41.3%) female in the 4.7 Fr DJ stent group and 35 (44.9%) male and 27

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(58.7%) female in the 6 Fr DJ stent group. p=0.193. Stents with a reduced diameter exhibited less curvature both proximally and distally, resulting in minimal contact with the bladder mucosa and subsequently leading to a decreased reduction of lower urinary tract symptoms [15]. Additionally, smaller-sized stents demonstrated lower scores on the USSQ concerning the areas of work performance, pain, and sexual function [16].https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9612741/ Although earlier studies conducted before the establishment of the USSQ reported negligible differences in urinary symptoms related to ureteral stent size, more recent studies utilizing the USSQ indicate that ureteral stent size does influence urinary symptoms. A retrospective study found that urinary symptoms were significantly milder with smaller ureteral stents, according to the International Prostate Symptom Score (IPSS) and OABSS outcomes [17]. Nestler et al., noted that there was no notable variation between ureteral stents measuring F4.7 and F6 in diameter. Previous studies have reported similar results, suggesting better outcomes with smaller diameter stents (4.7F), although these findings lacked statistical significance [18]. One study highlighted certain advantages of using smaller diameter stents but didn't distinguish among the various subdomains [18]. The incidence of stent migration was noted to be higher with F4.7 stents, with occurrences at 23.5% and 32%, compared to 10% for F6 stents. In that research, stents of two distinct sizes (4.7 and 7 Fr) were utilized, and comparisons were made regarding irritative voiding symptoms and pain. Various studies have found no significant correlations between the diameter of the stent and stent-related issues [13]. It is believed that physical activity with the stent contributes to stent-related symptoms, and the flexibility of stents can also influence these symptoms. Smaller stents can bend more easily than larger ones, making them softer, and this reduced physical stimulation from smaller stents may lead to weaker symptom manifestation [19]. The diameter and material of stents were analyzed alongside patient symptoms such as hematuria, dysuria, incontinence, discomfort, and frequent urination, which showed an insignificant association within the diameters of the stents [20]. Ehsanullah *et al.* studied whether ureteral stents lead to adverse signs and problems and discovered no link between stent size (6 vs 7 Fr) and the occurrence of symptoms [13]. Allam *et al.* conducted a prospective evaluation of the effect of ureteral stents in the management of renal stones [21]. Although the USSQ is deemed valuable for assessing symptoms related to ureteral stents and quality of life post-stenting, our research utilized the IPSS to evaluate urinary symptoms. The OABSS was developed and validated within Japanese populations in 2006. Earlier research has indicated a fairly strong correlation between the OABSS and patients' perceptions of their bladder health [22].

This study had several limitations, including its retrospective, non-randomized design and short follow-up period of only seven days, which may not capture the full spectrum of stent-related symptoms. Moreover, the single-center setting and use of only the IPSS questionnaire may limit the generalizability of the findings. Future studies should employ prospective, randomized multicenter designs with longer follow-up and multiple validated assessment tools to better evaluate stent-related symptoms and improve generalizability.

## CONCLUSIONS

It was concluded that stents that have larger diameters greatly worsen urinary issues, and it is recommended to utilize ureteral stents with smaller diameters to improve symptoms associated with the stents.

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## Authors' Contribution

Conceptualization: MZA
Methodology: RNA
Formal analysis: MA, SS
Writing and Drafting: AR, MA, ABZ
Review and Editing: MZA, AR, MA, ABN, RNA, SS

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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# An Assessment of Functional Status of Stroke Patients Using the Functional Independence Measure on the Hospitalization, Discharge, and Three Months Post-Stroke: Analytical Cross-Sectional Study

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## ABSTRACT

Stroke is one of the leading causes of impairment in the world, with effects on the motor functions, cognitive and mental processes, and the general quality of life of the patients. **Objectives:** To determine the full functional condition of stroke patients through the change in the Functional Independence Measure (FIM) scores at the time of admission, discharge, and three months post-stroke. **Methods:** This was an analytical cross-sectional study conducted on 108 patients with ischemic stroke in the age group of 18-75 years, at the Department of Neurology, Services Hospital, Lahore. Functional independence was assessed with the FIM scale thrice, on admission, at discharge from the hospital, and three months post-stroke. Repeated ANOVA and paired t-tests were used to compare the changes in FIM scores over time. **Results:** The average age of the participants was 58.4 years with a standard deviation of 10.2, and men made up 61.1% of the sample. The mean FIM scores did increase significantly between 86.33 +/-14.5 at the time of admission and 102.7 ± 16.5 at discharge, and 118.9 ± 15.8 at three months after stroke ($p<0.001$). The younger patients (18-50 years) had more functional improvement than the older patients (>=50 years) ($p=0.002$). A high negative correlation was found between age and functional recovery ($r = -0.42$, $p=0.004$). **Conclusions:** Patients with ischemic stroke recover much of their functional abilities with time, with age at younger years, fewer days in the hospital, and higher baseline FIM scores serving as independent predictors of improved outcomes.

## INTRODUCTION

Recent data on stroke and stroke mortality present the picture of a high burden of the disease in the whole world, even though stroke is one of the conditions that can be prevented [1]. In addition, post-stroke disability also contributes to such indicators as Disability Adjusted Life Years (DALYs) [2]. The impairments that may be experienced by a stroke patient include those affecting cognitive functioning, both gross and fine motor skills, the sensory system, activities of daily living (ADLs), and consciousness [3]. These post-stroke outcomes are not temporary because they may persist even more than a year in patients, affecting their quality of life, and this is why a patient-centered program of rehabilitation should be introduced to enhance these post-stroke sequelae [4]. Besides healthcare management of stroke, the patient-centered rehabilitation should involve an extensive examination of the impairments or deficits due to a stroke in a multidisciplinary approach strategy that integrates psychological support, physical therapy, and occupational therapy [5]. This rehab program can also be changed or modified according to various phases of the stroke, in order to enhance the overall quality of life and recovery of self-

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sustenance in day-to-day activities. Rehabilitation efficacy is also multi-factorial and highly relies on the time of intervention, intensity of the intervention, and some patient-specific factors, including underlying health conditions, motivation, and social support [6]. The need to quantify the consequences of stroke and rehabilitation over time is enhanced by a standard measurement known as the Functional Independence Measurement, which assesses a comprehensive functional recovery among the affected patients. The Functional Independence Measure (FIM) is a measure of dependence, which gathers information about functional recovery and subsequently compares the findings of therapy, which aids in monitoring the progress of patients and their treatment plan [7]. The FIM documents recovery or degradation through the scrutiny of activities of daily living (ADLs) such as eating, cleaning, washing, dressing, using the toilet, swallowing, control of the sphincter, moving, transferring, and moving [8]. The FIM questionnaire is employed to survey regularly on subjects regularly at the time when they are admitted, when they are discharged, and on regular follow-ups. The questionnaire is simple to complete, and it takes approximately 30 minutes.

The research can play a significant role in terms of the recovery of stroke patients and possibly offer shorter stays and less dependency with stroke patients in several ways. The study will be able to determine the trends and patterns in functional recovery by evaluating the overall and all-encompassing functional status of stroke patients at different stages in the rehabilitation process using the FIM scale. It is then possible to use this information to design rehabilitation programs that are more customized. This study aimed to determine the mean FIM score at the time of admission, discharge, and 3 months follow-up in patients with ischemic stroke presenting in the Department of Neurology in Services Hospital, Lahore.

## METHODS

This analytical cross-sectional study was carried out at the Department of Neurology, Services Hospital, Lahore, in the span of 4 months from January 2025 to April 2025. Ethical approval was obtained from the College of Physicians and Surgeons (Ref # CPSP/REU/NEU-2021-068-695) as well as from IRB Services Hospital (Ref # IRB/2025/1518/SIMS). All eligible patients were asked for their written consent during the initial appointment after being informed about the study's methodology. A non-probability consecutive sampling technique was used to recruit patients based on predefined criteria of inclusion and exclusion. The study was done on 108 ischemic stroke patients of both genders, aged 18 to 75 years, who had experienced their very first stroke event leading to functional loss or impairment. Only patients with medical and hemodynamic stability and a stroke duration of at least one day were enrolled. Patients who had a history of recurrent stroke events, transient ischemic attack, or hemorrhagic stroke were excluded from the investigation. Candidates having orthopedic surgeries, cancers, or chronic neurological diseases like dementia were also not featured in the study. Individuals who had other conditions that made them disabled or unable to function, and those who didn't agree to take part, were also eliminated. The same doctor did all the examinations and visits. After enrolling in the study, participants' medical information was recorded, including gender, age, stroke type (ischemic or hemorrhagic), length of hospital stays, and FIM scores. The FIM scale, the most widely used instrument in rehabilitation medicine, has eighteen categories divided into two primary domains: motor function (13 items) and cognitive function (5 items). Tasks in the motor function area include self-care (e.g., eating, grooming, bathing), mobility (e.g., transferring, walking), and sphincter control. The cognitive function domain evaluates both communication (e.g., understanding, expression) and social cognition (e.g., problem-solving, memory). Each item on the FIM scale will be rated on a 1–7 scale, with 1 representing total dependency and 7 indicating complete independence [9]. The FIM scale has shown significantly strong evidence of validity and reliability (Cronbach's alpha of 0.94), be it inter-observer or intra-observer, in multiple studies [10-12]. Using the FIM questionnaire, the functional status of the subjects was evaluated during admission, upon discharge, and at three months following the occurrence of stroke. An expert in physical medicine and rehabilitation conducted the examinations. An assigned physician monitored the patient during task completion during the admission and discharge visits to gauge their level of independence. Patients were questioned about their condition at a three-month follow-up appointment, and data were gathered based on their verbal responses. The services of a rehabilitation expert were provided to patients admitted to the neurology department. During their stay, all patients received physical therapy. In the time after discharge, they also got a home plan and follow-up in the physiotherapy department, depending on their disability. SPSS software (version 18, SPSS Inc., Chicago, IL, USA) was employed for the purpose of data analysis. Descriptive statistics were employed to characterize the research population's demographic as well as the Functional Independence Measure (FIM) scores at several time points (hospitalization, discharge, and three months post-stroke). Continuous variables that include age and FIM scores were reported as means with standard deviations (SD). Categorical factors like gender were characterized in terms of frequencies and percentages. The Shapiro-Wilk test and Kolmogorov–Smirnov test were employed to

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assess the normality of data after descriptive analysis. A Repeated Measures ANOVA was used to evaluate changes in FIM scores across three repeated time points (admission, discharge, and three months after the stroke) within the same patients. This test is used for comparing means when measurements are taken repeatedly on the same subjects and takes into account within-subject correlations. Paired sample t-tests were applied to make pairwise comparisons (admission versus discharge, discharge versus three months, and admission versus three months) to identify specific intervals that can be used as indicators of a significant functional improvement. In order to examine the relationship between continuous data, we applied the Pearson correlation test, which measures the strength and direction of a linear relationship. They were also able to establish correlations between age and FIM improvement, length of hospital stay, and FIM improvement as they were interested in analyzing the importance of these variables concerning recovery. The level of significance of p was taken to be p<0.05.

## RESULTS

A total of 108 patients were included in the investigation, and the mean age of the study patients was 58.4 ± 10.2. The total of the male participants was 61.1%. Conversely, 38.9% of the participants were female (Table 1).

**Table 1:** Demographic and Clinical Characteristics of Study Participants

| Characteristics | Mean ± SD / n (%) |
|---|---|
| Sample Size | 108 |
| Mean Age (Years) | 58.4 ± 10.2 |
| Male | 66 (61.1%) |
| Female | 42 (38.9%) |
| Mean Length of Hospital Stay (days) | 7.6 ± 3.2 |

After running the descriptive statistics, both normality tests (K–S and S–W) were found significant with p>0.05.

The mean Functional Independence Measure (FIM) scores recorded at admission, discharge, and three months post-stroke were 86.3 ± 14.5, 102.7 ± 16.2, and 118.9 ± 15.8, respectively. A repeated measures ANOVA test was conducted to analyze the differences in FIM scores across the three time points, showing a statistically significant improvement over time (p<0.001) (Table 2).

**Table 2:** Functional Independence Measure (FIM) Scores at Different Time Points

| Time Point | FIM Score (Mean ± SD) | p-value (Repeated Measures ANOVA) |
|---|---|---|
| At Admission | 86.3 ± 14.5 | <0.001* |
| At Discharge | 102.7 ± 16.2 | |
| 3 Months Post-Stroke | 118.9 ± 15.8 | |

*A Repeated Measures ANOVA test was employed to see the statistical comparison between the three-time intervals.

Paired t-tests showed that there is a significant difference in the FIM scores, admission and discharge (p<0.001), and discharge to the three-month follow-up (p<0.001). The paired sample t-test was used to test the differences between FIM scores across various time points (Admission vs. Discharge, Discharge vs. 3 Months Post-Stroke, and Admission vs. 3 Months Post-Stroke). The test was used to identify whether the differences in the functional status between the two-time intervals were statistically significant (Table 3).

**Table 3:** Results of Paired Sample t-Test for Functional Independence Measure (FIM) Scores

| Comparisons | Mean ± SD | p-value |
|---|---|---|
| Admission vs. Discharge | 16.4 ± 8.5 | <0.001** |
| Discharge vs. 3 Months Post-Stroke | 16.2 ± 7.9 | <0.001** |
| Admission vs. 3 Months Post-Stroke | 32.6 ± 10.2 | <0.001** |

**Paired t-test was employed to see the statistical differences between two different time intervals.

Age-specific stratified analysis revealed that younger patients (1850 years) had a greater improvement in functional independence than older patients (50 years and above) (p=0.002) (Table 4).

**Table 4:** Comparison of Functional Independence Measure (FIM) Improvement Across Age Groups

| Age Group (Years) | n | Mean FIM Score at Admission (Mean ± SD) | Mean FIM Scoreat Discharge (Mean ± SD) | Mean FIM Score at 3 Months (Mean ± SD) | Mean FIM Improvement (Mean ± SD) | p-value |
|---|---|---|---|---|---|---|
| 18–50 | 52 | 88.5 ± 13.8 | 106.4 ± 12.7 | 124.2 ± 14.5 | 35.7 ± 12.4 | 0.002*** |
| ≥50 | 56 | 84.1 ± 15.2 | 98.8 ± 14.1 | 113.6 ± 16.2 | 29.5 ± 11.8 | 0.002*** |

***Repeated measures of the ANOVA test were used for both age groups separately.

The Pearson correlation test showed that the two variables are strongly correlated in an inverse relationship (r = -0.42, p=0.004), which means that older patients exhibited a lower rate of recovery. Also, the improvement of the FIM score had a negative correlation with the length of hospital stay (r = -0.36, p=0.003) (Table 5).

**Table 5:** Correlation Between Age, Length of Hospital Stay, and Functional Recovery

| Variables | Pearson Correlation (r) | p-value |
|---|---|---|
| Age vs. FIM Improvement | -0.42 | 0.004**** |
| Hospital Stay vs. FIM Improvement | -0.36 | 0.003**** |

****(Pearson's correlation co-efficient, r, statistical analysis).

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## DISCUSSION

The purpose of this study was to assess how effectively stroke patients recover their functional status with reference to the increase in the Functional Independence Measure (FIM) scores comparing at hospital admission and discharge. The present research, in particular, has considered the impacts of hospitalized physical therapy, age, and other variables related to patients on functional recovery. It was concerned with discovering the variables that were capable of enhancing the recovery from the stroke. The post-stroke functioning may be classified into motor and cognitive function domains, and these domains can be considered as primary predictors of recovery using FIM as a broad concept [13]. In order to measure the extent of improvement achieved with rehabilitation sessions, the study noted the functional recovery of ischemic stroke patients at three important points, i.e., hospitalization, discharge, and three months post the incidence of stroke. Our research found significant overall functional recovery in time, with the mean of FIM scores at admission being 86.3 and 102.7, with significant further improvement of 118.9 at discharge and three months respectively ($p<0.001$). It is relevant to note a past study that was conducted on 1700 patients, and it was revealed that the functional recovery of patients undergoing intensive rehabilitation, as long as sessions are regular, is good [14]. Patients with mild strokes had an FIM score of 102 ± 2 after 35 days in the rehabilitation unit. Patients admitted within 2 weeks of a major stroke had a plateau FIM score of 72 ± 6 after 43 ± 3 days on the rehabilitation unit, compared to the 2–4-week group (FIM = 57 ± 5 after 53 ± 4 days) and the 4–6-week group (FIM = 54 ± 10 after 40 ± 6 days) [15]. Evidence on factors influencing the disability caused by stroke events has shown that age plays a pivotal part in recovery, as they were actively involved in more frequent rehabilitative sessions and were more motivated [16]. However, as much as early start of rehabilitation is found to be significantly effective for recovery, high-intensity rehab sessions are established to be counter-productive among stroke patients [17]. The age-specific stratified analysis conducted in our study revealed that younger patients (18–50 years) exhibited significantly greater functional improvement than their older counterparts (≥50 years) ($p=0.002$). The inverse relationship between age and functional recovery ($r = -0.42$, $p=0.004$) is one of our study's main outcomes. A cohort study conducted on stroke patients employed linear regression to conclude that younger patients exhibited greater and quicker functional gains as compared to the older patients when exposed to post-stroke rehabilitation [18]. In contrast to this reporting, a study concluded that baseline independence among stroke patients has a superior edge in predicting the functional prognosis over age [19]. Additionally, our study found a negative correlation ($r = -0.36$, $p=0.003$) between the length of hospital stay and functional improvement, indicating that longer hospital stays may be linked to worse recovery outcomes. According to a series of studies conducted by Ohta *et al.* early discharge coupled with outpatient rehabilitation produces better long-term motor recovery than extended hospital stays [20]. Stroke recovery is continuous but a complicated process determined by several intrinsic and extrinsic factors, but the extent of motor and cognitive impairments after stroke is the main determinant of intervention, rehabilitation, and recovery [21]. Therefore, the necessity of age-appropriate and patient-specific rehabilitation plans that include rigorous treatment and extended follow-ups in order to optimize the functional improvements is emphasized. Multiple features contribute to the reliability and clinical significance of our current study. These include a follow-up over a period of three months, measurement of functional recovery by FIM for standardized and validated assessment. The most significant strength of the analysis is the stratified analysis by age that provides valuable information on the heterogeneity of the rehabilitation process after stroke. Moreover, anticipatory variables of the hospitalization time might help to customize the rehabilitation plan.

Despite the informative findings, our study has certain limitations. This study could have an impact on the generalizability of the findings due to the low sample size and analytical cross-sectional design, which was conducted in a single facility. Further, the long-term (after three months) follow-up was not incorporated, and this limits the chances of evaluating the long-term functional gains.

## CONCLUSIONS

This study concludes that there was a high level of functional recovery among stroke patients who reported to the Department of Neurology, Services Hospital, based on the Functional Independence Measure during hospitalization, discharge, and the three months after stroke, and whereby the younger age, shorter length of stay, and high baseline FIM scores are independent variables of good outcome.

### Authors' Contribution

Conceptualization: SN
Methodology: SN, QB, MAA
Formal analysis: SN
Writing and Drafting: QB, MAA
Review and Editing: SN, QB, MAA

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

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## Conflicts of Interest

All the authors declare no conflict of interest.

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**Original Article**

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# Comparison of Oral versus Intravenous Fluid Therapy on Amniotic Fluid Index in Women with Oligohydramnios

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## ABSTRACT

Oligohydramnios, characterized by reduced amniotic fluid volume, poses significant risks to fetal growth and pregnancy outcomes. **Objectives:** To compare the effects of oral versus intravenous fluid therapy on AFI in women with oligohydramnios, and to determine the more effective hydration strategy for clinical use. **Methods:** Following ethical approval from the Institutional Review Board of Fatima Jinnah Medical University, a quasi-experimental study was conducted. 60 patients diagnosed with oligohydramnios based on operational criteria were enrolled after obtaining written informed consent. Participants were randomly divided into two groups: Group A received IV hydration, while Group B received oral hydration. Both groups remained admitted for one week, during which AFI was measured at baseline and after the intervention. **Results:** The mean age of participants was 27.67 ± 6.00 years. Baseline AFI was 3.79 ± 0.25 cm, with no significant differences between groups. After one week, Group A (IV hydration) showed a mean AFI of 5.34 ± 0.23 cm, while Group B (oral hydration) achieved a significantly higher mean AFI of 5.69 ± 0.41 cm (p=0.000). Treatment efficacy was reported in 90.0% of Group A and 96.7% of Group B participants (p=0.612). **Conclusions:** The improvement in AFI with oral hydration was slightly better than with IV hydration, but not statistically significant. The two interventions were safe with no maternal or fetal adverse effects. The first option is oral hydration, which is practical, non-invasive, and cost-effective, especially in resource-restricted settings.

## INTRODUCTION

The volume of amniotic fluid is a basic indicator of the intrauterine fetal health and a prerequisite for proper fetal growth and development. The amniotic fluid index (AFI) is an ultrasonography method that is deemed normal with a 5-25 cm range [1]. Oligohydramnios is an AFI lower than 5 cm, which is a condition that is linked to severe adverse neonatal outcomes, such as umbilical cord compression, pulmonary hypoplasia, and fetal distress, as well as a higher risk of intrauterine fetal demise, especially when not detected early or that is sustained [2]. In turn, oligohydramnios is still a major cause of perinatal morbidity and mortality in various healthcare establishments. Population prevalence data on a large scale offer clinical relevance of this condition. The First Look Trial, which included more than 13,000 third-trimester pregnancies in Guatemala, Zambia, Pakistan, and the Democratic Republic of Congo, reported oligohydramnios in an average of one in every 150 pregnancies, highlighting the worldwide incidence of the condition, even in low- and middle-income nations [3]. Such prevalence requires not only clinical but also practical approaches in the framework of common obstetric care management strategies. Different invasive interventions that are being used to improve AFI, including desmopressin, intra-amniotic sealing, transabdominal amnioinfusion, and fetal cystoscopy, have been outlined [4, 5]. These methods are, however, expensive, need special

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skills and long-term hospital care, and can potentially cause fetal risks. Their accessibility and practicality are limited and cannot be used widely, particularly in a resource-strained environment. Maternal hydration has thus been considered as a non-invasive, non-surgical, and low-cost treatment for isolated oligohydramnios. The physiological basis of maternal hydration is that depletion of maternal plasma osmolality maximizes uteroplacental perfusion and fetal renal perfusion, leading to increased fetal urine production and consequent increase in amniotic fluid volume [6, 7]. Due to the close connection between maternal fluid balance and AFI, a number of studies have reported the positive response of AFI to the increased maternal fluid intake [8]. The hydration of the mother can be done either orally or by an intravenous route. Oral hydration usually implies the higher intake of plain water, whereas intravenous hydration involves the use of isotonic or hypotonic fluids like normal saline, Ringer's lactate, or dextrose-containing fluids [9]. Although oral hydration has the benefit of being cheaper, preventing hospitalization, and being more comfortable to the patient, intravenous hydration remains a common practice in most obstetric units [10]. There is still an inconsistency in evidence comparing the efficacy of oral and intravenous hydration. Though there have been studies that have yielded better results in improvement of AFI by oral hydration, others have indicated similar results with the two modalities [11-13].

These contradictions also indicate a significant evidence gap in terms of the best course of maternal hydration, especially in environments where resource allocation, hospital bed space, and cost-effectiveness form a key factor in consideration. Considering the broad application of intravenous hydration despite its logistical drawbacks and the discordant information on the comparative efficacy of oral hydration, an explicit and systematic comparison between the two strategies is clinically justified. This study aimed to compare the changes in amniotic fluid index between oral and intravenous fluids in cases of oligohydramnios during pregnancy, as measured at baseline and after one week of treatment, and the mean change in AFI in the two groups.

## METHODS

This quasi-experimental study was carried out at the Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital, Lahore. The study duration was from November 2024 to January 2025. Ethical approval was taken from the Institutional Review Board of Fatima Jinnah Medical University, Lahore, with ref no: 170-MS-Gynaecology/IRB-ERC. The sample size was calculated using mean AFI levels of 5.3 ± 0.7 and 4.8 ± 0.6 for oral and IV hydration groups, respectively, by taking a 95% confidence interval and 80% power of test, and a 20% dropout rate. For better generalization, the final sample size was increased to 60 patients, with 30 participants in each group (sample size calculated using Open Epi: https://www.openepi.com/SampleSize/SSMean.htm) [14]. A convenient sampling technique was used to enroll the patients. Eligible participants were women aged 16–40 years, with parity <5, gestational age between 32 and 35 weeks (LMP-based), intact membranes, and singleton pregnancies. Women with congenital anomalies, IUGR, hypertension, diabetes, anemia, liver or renal dysfunction, cardiac disease, placental abruption, placenta previa, or a history of similar complications were excluded. Following the ethical approval and written informed consent, this quasi-experimental study recruited 60 pregnant women with oligohydramnios. The subjects were randomized to two intervention groups (sequentially) with a predetermined alternate method of allocation, i.e., the first 30 patients were given oral hydration (Group A), and the next 30 patients were given intravenous hydration (Group B). Group A was treated by IV hydration of 2 L every four hours for one week with Isotonic saline. For group B, the study switched to oral hydration at the same volume and rate. Recruits had to undergo a set of baseline tests for blood sodium, potassium, and chloride to ascertain the baseline level of serum compartment hydration, and then remained confined. All participants had to stay in the hospital for one week to ensure to confirm compliance directly by collecting urine to test osmolality. Participants also had blood drawn for serum urea and electrolytes on alternating days. Signs/ symptoms of overhydration were watched for. The over-hydrated patients had their AFI levels (amniotic fluid index) measured at the end of the week by the same person multiple times from the group. Standard IV treatment was given to those oral group patients by day 3 who had not measured a viable AFI. Among pregnant patients, the effect of treatment was determined as an AFI change following hydration treatment. US assessed AFI at enrollment (before hydration) and at one-week follow-up. AFI change was calculated (in centimeters) by calculating the difference between baseline and follow-up. Effective treatment was considered to be one where the clinical improvement was significant, i.e., an AFI over 5 cm within one week after the treatment was taken. The same trained sonographer measured the primary outcome of AFI for all participants in order to have consistency and to minimize inter-observer variations. Since this was a quasi-experimental study, blinding was not applied; this was aided by using just one sonographer so that the chances of measurement bias were minimized. The participants provided a signed informed consent to allow the researchers to analyze the data with the SPSS version 26.0 analysis program under the provided conditions. For the

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quantitative variables of the participants (age, primary BMI, number of live children, duration of pregnancy in weeks, number of AFI levels), which were provided by SD, the normality of data was assessed by using the Shapiro-Wilk test, and after assessing normality, the independent sample t-test and the paired sample t-test were applied. Chi-square/Fisher's exact test was applied to see the association of study groups and study outcomes. The criteria for p-values to allow significant features were 0.05 or weaker statistically. The results for AFI also had to be stratified relative to their BMI, age, weeks of gestation for and number of children to show any modifier effects.

## RESULTS

A total of 60 women diagnosed with oligohydramnios were enrolled and divided equally into two groups: Group A (IV hydration) and Group B (oral hydration). The baseline characteristics of both groups were statistically the same. Group A had a mean age of 28.27 ± 5.82 years while Group B had a mean age of 27.07 ± 6.23 years (p=0.444). The mean gestational ages were 34.40 ± 1.61 and 34.63 ± 1.69 weeks (p=0.586). The groups also had no statistically significant differences in parity (2.30 ± 1.09 vs. 2.17 ± 1.02; p=0.626), and BMI (26.04 ± 3.59 vs. 25.82 ± 3.83; p=0.816). The mean AFI at time of admission to both groups was also very similar (3.77 ± 0.25 cm vs. 3.81 ± 0.25 cm; p=0.575), supporting the idea that they were the same at baseline (Table 1).

**Table 1:** Comparison of Baseline Characteristics Between the Groups

| Characteristics | Group A (n=30) | Group B (n=30) | p-value |
|---|---|---|---|
| **Age** | | | |
| 16–40 Years | 28.27 ± 5.82 | 27.07 ± 6.23 | 0.444 * |
| 16–30 Years | 18 (60.0%) | 19 (63.3%) | 0.791 ** |
| 31–40 Years | 12 (40.0%) | 11 (36.7%) | – |
| Gestational Age | 34.40 ± 1.61 | 34.63 ± 1.69 | 0.586 * |
| **Weeks** | | | |
| 32–35 Weeks | 19 (63.3%) | 17 (56.7%) | 0.598 ** |
| 36–37 Weeks | 11 (36.7%) | 13 (43.3%) | – |
| **Parity** | | | |
| – | 2.30 ± 1.09 | 2.17 ± 1.02 | 0.626 * |
| 1–2 | 19 (63.3%) | 20 (66.7%) | 0.787 ** |
| 3–4 | 11 (36.7%) | 10 (33.3%) | – |
| **BMI** | | | |
| $kg/m^2$ | 26.04 ± 3.59 | 25.82 ± 3.83 | 0.816 * |
| Normal Weight | 11 (36.7%) | 15 (50.0%) | 0.297 ** |
| Overweight/Obese | 19 (63.3%) | 15 (50.0%) | – |
| **AFI (cm)** | | | |
| At Admission | 3.77 ± 0.25 | 3.81 ± 0.25 | 0.575 * |

*Independent sample t-test. ** Chi-Square test. Taking p-value≤0.05 as significant.

In both groups, AFI improved in the week that followed. Group A was 5.34 ± 0.23, and Group B was 5.69 ± 0.41 cm. The difference between groups was statistically significant (p=<0.001 ). The mean change in AFI from baseline to post-intervention (after 1 week) was 1.56 ± 0.34 cm in Group A and 1.88 ± 0.39 cm in Group B (p=0.001), showing that more improvement was seen with oral hydration (Table 2).

**Table 2:** Comparison of Mean Change in AFI Level Between the Study Groups

| Time Interval | Study Groups | n | Mean ± SD | p-value |
|---|---|---|---|---|
| At Admission | Group A | 30 | 3.77 ± 0.25 | 0.575 |
| | Group B | 30 | 3.81 ± 0.25 | – |
| Post Intervention After 1 Week | Group A | 30 | 5.34 ± 0.23 | <0.001 |
| | Group B | 30 | 5.69 ± 0.41 | – |
| Change in AFI | Group A | 30 | 1.56 ± 0.34 | 0.001 |
| | Group B | 30 | 1.88 ± 0.39 | – |

Independent sample t-test, taking p-value≤0.05 as significant.

Within-group analysis showed that all groups demonstrated significant growth in AFI with treatment. Group A showed AFI from 3.77 ± 0.25 cm to 5.34 ± 0.23 cm (p<0.001), while Group B showed AFI from 3.81 ± 0.25 cm to 5.69 ± 0.41 cm (p<0.001) with respect to study results (Table 3).

**Table 3:** Comparison of Mean AFI Level from Baseline within the Groups after Treatment

| Study Groups | | Mean | p-value |
|---|---|---|---|
| Group A (Pair 1) | AFI at After 1 Week: 5.337 | 0.23 ± 1.43 | <0.001 |
| | AFI at Admission: 3.773 | 0.25 ± 1.43 | |
| Group B (Pair 1) | AFI at After 1 Week: 5.693 | 0.41 ± 1.73 | <0.001 |
| | AFI at Admission: 3.810 | 0.25 ± 1.73 | |

Treatment success was observed in 27 (90.0%) of participants in Group A and in 96.7% (n = 29) of Group B, with neither group showing a significant difference (p=0.612). There were no cases of fluid overload in Group A, while one case (3.3%) was observed in Group B (p=1.000). There were no incidents of treatment failure in either group, with both methods having good tolerability (Table 4).

**Table 4:** Comparison of Various Study Outcomes Between the Groups

| Characteristics | Yes / No | Group A (n=30) | Group B (n=30) | p-value |
|---|---|---|---|---|
| Efficacy Achieved | Yes | 27 (90.0%) | 29 (96.7%) | 0.612 |
| | No | 3 (10.0%) | 1 (3.3%) | – |
| Fluid Overload | Yes | 0 (0.0%) | 1 (3.3%) | 1.000 |
| | No | 30 (100.0%) | 29 (96.7%) | – |
| Treatment Failure | Yes | 0 (0.0%) | 0 (0.0%) | – |
| | No | 30 (100.0%) | 30 (100.0%) | – |

In stratified analysis, oral hydration (Group B) had the highest mean AFI at Week 1 across all subgroups: age, gestational age, parity, and BMI. Among 16-30 years (p=0.001), 31-40 years (p=0.042), those with gestational age 32-35 weeks (p=0.000), parity 1-2 (p=0.001), and both normal weight (p=0.009) and overweight/obese (p=0.007)

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women, the differences were statistically significant. Although the trends aligned with oral hydration in other subgroups, the differences were not statistically significant, likely due to sample size (Table 5).

**Table 5:** Comparison of Mean AFI at Week 1 Between the Groups Stratified for Age, Gestational Age, Parity, and BMI

| Variables | Subgroups | Study Groups | n | Mean ± SD | p-value |
|---|---|---|---|---|---|
| Age | 16–30 Years | Group A | 18 | 5.39 ± 0.16 | 0.001 |
| | | Group B | 19 | 5.73 ± 0.35 | – |
| | 31–40 Years | Group A | 12 | 5.25 ± 0.29 | 0.042 |
| | | Group B | 11 | 5.63 ± 0.52 | – |
| Gestational Age | 32–35 Weeks | Group A | 19 | 5.36 ± 0.22 | <0.001 |
| | | Group B | 17 | 5.80 ± 0.37 | – |
| | 36–37 Weeks | Group A | 11 | 5.30 ± 0.24 | 0.102 |
| | | Group B | 13 | 5.55 ± 0.44 | – |
| Parity | 1–2 | Group A | 19 | 5.34 ± 0.23 | 0.001 |
| | | Group B | 20 | 5.72 ± 0.38 | – |
| | 3–4 | Group A | 11 | 5.33 ± 0.23 | 0.073 |
| | | Group B | 10 | 5.64 ± 0.49 | – |
| BMI | Normal Weight | Group A | 11 | 5.29 ± 0.24 | 0.009 |
| | | Group B | 15 | 5.71 ± 0.44 | – |
| | Overweight/ Obese | Group A | 19 | 5.36 ± 0.22 | 0.007 |
| | | Group B | 15 | 5.68 ± 0.41 | – |

## DISCUSSION

Oligohydramnios, which is characterized by a low amniotic fluid index (AFI), correlates with higher chances of undesirable maternal and fetal events, such as premature delivery, intrauterine growth retardation, and neonatal morbidity. Maternal hydration is a non-invasive measure of optimization of AFI that can be successfully researched. There is both oral and intravenous (IV) fluid supplementation that finds use in clinical practice, but comparative efficacy is a subject of research. This quasi-experimental research paper was designed to investigate the efficacy of oral and IV hydration in enhancing AFI in patients with isolated oligohydramnios and the goal of optimal maternal and fetal outcomes [15]. A total of 60 participants were involved in this investigation, and the mean maternal age was 27.67 + 6.00 years, which is similar to previous studies that show between 26.2 and 26.68 years, although some groups showed maternal ages of 32.2 ± 39.44 years. The average gestational age was 34.52 and was 1.64, and the mean parity was 2.23 and mean BMI was 25.93 and 3.69 kg/m2 as previously reported [13, 16]. AFI was 3.79 +/ -0.25 cm, which agrees with the reported ranges of oligohydramnios (3.3-4.8 cm). After a week of intervention, there was an increase in AFI of 5.34 ± 0.23 cm in the IV hydration group (Group A) and 5.69 ± 0.41 cm in the oral hydration group (Group B), but the difference between the two groups was statistically significant ($p<0.001$). The average change in AFI was 1.56 ± 0.34 cm when hydrated with IV and 1.88 + 0.39 cm when hydrated with oral fluid, which was better with oral fluid. Such findings are in agreement with previous reports, which have noted higher levels of post-intervention AFI in patients who are administered oral hydration [17, 18]. The results of the current research are supported by a systematic review and meta-analysis. The available evidence demonstrates that oral hydration therapy is a promising intervention to improve the amniotic fluid index (AFI) and is a safe and cost-effective intervention to treat oligohydramnios. It is specifically beneficial in contexts with limited resources as its administration is relatively simple, and the intravenous therapy may be limited in accessibility to the hospital. These results support the validity of oral hydration as a primary intervention in the prevention of AFI and the enhancement of maternal and fetal outcomes [19]. Physiological reasons could be used to explain the relatively increased effectiveness of oral hydration. An oral fluid intake activates gastrointestinal absorption and could influence a more gradual and prolonged plasma volume expansion, which stimulates renal perfusion and fetal urine production, a key factor in amniotic fluid volume. On the other hand, IV hydration causes a more acute and temporary intravascular volume increase, which can be temporary and less efficient in the maintenance of long-term increases in AFI [1]. Although in our study, the overall treatment efficacy was slightly better in the oral hydration group (96.7% versus IV hydration 90.0%), the difference was not statistically significant ($p=0.612$). Notably, fluid overload and other unfavorable maternal/fetal outcomes were not observed in any of the participants, which demonstrates the safety of both types of hydration. These data are in line with the previous studies on comparing oral and intravenous maternal hydration in third-trimester oligohydramnios [20].

The shortcomings are that the study has a single-center design, and the sample is small, which could limit the generalizability. Finally, oral and IV hydration strategies are safe and effective in the treatment of AFI in isolated oligohydramnios, with better effectiveness of the first probably due to a prolonged plasma volume expansion and increased fetal urine. The findings offer clinically applicable information on the choice of hydration strategies to attain the best perinatal outcomes. Future studies with larger, multicenter samples and longer follow-up are recommended to confirm the comparative effectiveness of oral versus intravenous hydration in managing oligohydramnios.

## CONCLUSIONS

Oral and intravenous hydration are safe and effective interventions to improve the amniotic fluid index (AFI) of women with oligohydramnios. Even though oral hydration was found to increase AFI slightly better than IV hydration, this difference was found to be not significant. Both

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methods were safe, as no negative effects were found on a maternal or fetal level. Oral hydration is non-invasive, cost-effective, and can be implemented easily, and can, therefore, be regarded as a practical first-line strategy, especially in resource-limited environments.

## Authors' Contribution

Conceptualization: MS
Methodology: ST
Formal analysis: MF
Writing and Drafting: MS
Review and Editing: MS, ST, 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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# Frequency and Association of Dyslipidemia with Clinical and Biochemical Parameters among Patients with Non-alcoholic Fatty Liver Disease

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## ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is increasingly associated with metabolic disorders, particularly dyslipidemia, which contributes to cardiovascular risk and disease progression. Understanding this relationship is essential for early intervention. **Objectives:** To assess the frequency of dyslipidemia and its association with clinical and biochemical parameters in NAFLD patients. **Methods:** A cross-sectional study was carried out at the Department of Medicine, Jinnah Hospital, Lahore, from November 2024 to April 2025. A total of 116 ultrasonographically confirmed NAFLD patients aged 18–70 years were registered using non-probability consecutive sampling. Patients with secondary causes of liver disease, lipid-altering medications, or systemic illnesses were excluded. **Results:** Among the 116 NAFLD participants, the average age was 48.67 ± 11.57 years, and the mean body mass index (BMI) was 28.27 ± 4.60 kg/m$^2$. Dyslipidemia was present in 72 (62.1%) of participants. Females comprised 44 (61.1%) of the dyslipidemic group, and 44 (61.1%) were aged 46–70 years. Diabetes mellitus and ischemic heart disease were significantly associated with dyslipidemia (p=0.016 and p=0.004, respectively). Biochemical markers, including BMI (p=0.002), AST (p=0.012), and ALT (p=0.041), were significantly elevated in dyslipidemic patients. Lipid profile abnormalities, such as total cholesterol, triglycerides, and LDL-C, were significantly higher, while HDL-C was lower (all p<0.001). Dyslipidemia prevalence increased with NAFLD severity grade (p<0.001). **Conclusion:** Dyslipidemia is prevalent in NAFLD and significantly correlates with disease severity and metabolic comorbidities, highlighting the need for integrated lipid and hepatic assessment in clinical management.

## INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) refers to a range of liver disorders marked by fat deposition exceeding 5% of hepatocytes, occurring without notable alcohol intake, viral hepatitis, or other secondary causes of liver disease [1]. Globally, NAFLD affects about 25 to 30% of adults, with similar rates in South Asia [2]. In Pakistan, it is estimated that 14% to 30% of the overall population is impacted by NAFLD, with higher rates (up to 61%) in urban and high-risk groups. Among individuals with metabolic disorders, prevalence is notably elevated: 48–55% in diabetes, 74% in hypertension, and 41–47% in obesity. Even non-obese individuals show a prevalence of 12–25% [3, 4]. Its burden is also rising steadily in South Asian populations, driven by dietary transitions, increasing sedentary lifestyles, as well as the growing occurrence of metabolic syndrome. The condition includes various liver abnormalities, from basic steatosis to more severe forms such as NASH, fibrosis, cirrhosis, and even liver cancer [5]. The pathogenesis of NAFLD shows a strong link with insulin resistance and widespread disturbances in metabolic

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processes. Among the metabolic abnormalities frequently observed in NAFLD, dyslipidemia plays a central role [6]. Individuals with NAFLD commonly exhibit an atherogenic lipid profile. This pattern of dyslipidemia contributes both to liver fat buildup and significantly increases the risk for cardiovascular complications [7, 8]. Although global data have established a strong link between dyslipidemia and non-alcoholic fatty liver disease, evidence from Pakistan remains limited, particularly among patients with ultrasonographically confirmed NAFLD. The association between dyslipidemia and NAFLD has been well documented across various populations. Multiple studies have demonstrated a strong relationship between NAFLD and dyslipidemia. Ullah *et al.* and Waqas *et al.* reported dyslipidemia in 26–29% of NAFLD patients with elevated TC, TG, and low HDL-C [9, 10]. Shaikh *et al.* observed 61.3% low HDL-C and worsening lipid profile with fibrosis ($p<0.01$) [11]. Cigri *et al.* and Dowla *et al.* highlighted significant dyslipidemia in pediatric NAFLD, particularly raised TG and LDL-C with reduced HDL-C [12, 13]. A study has further suggested that the severity of NAFLD, as assessed by ultrasound or liver biopsy, correlates with the degree of lipid derangement and insulin resistance [14]. Despite the increasing recognition of NAFLD and its metabolic implications, there is a relative paucity of data from Pakistan regarding the frequency and pattern of dyslipidemia among individuals with ultrasonographically confirmed NAFLD. Most regional studies remain hospital-based, with limited representation of the broader population. Moreover, while international guidelines recommend routine lipid profiling in NAFLD patients to assess cardiovascular risk, local screening practices remain inconsistent due to limited infrastructure and variable awareness [15-17].

The present study was therefore designed to address this deficiency by determining the frequency of dyslipidemia and evaluating its relationship with disease severity in ultrasonographically confirmed NAFLD patients. Given the rising prevalence of NAFLD and the well-established contribution of dyslipidemia to its progression and associated morbidity, it is imperative to characterize the burden of lipid abnormalities in this patient popula Understanding the frequency and distribution of dyslipidemia among NAFLD patients may facilitate early identification of individuals at higher risk of cardiovascular complications and inform public health strategies for targeted metabolic intervention. This study aims to determine the frequency of dyslipidemia and its associated clinical patterns among patients with NAFLD diagnosed on ultrasonography.

## METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine at Jinnah Hospital Lahore, over a period of 6 months spanning November 2024 to April 2025. Approval for the study was granted by the Institutional Review Board of Jinnah Hospital, Lahore, with ref no: ERB132/3/17-11-2022/S1 ERB and CPSP np: CPSP/REU/MED-2021-055-18180. Eligible participants with NAFLD were recruited through a consecutive non-probability sampling method. The sample size was 116, which was calculated by assuming a proportion of dyslipidemia of 26%, with a 95% confidence level and an 8% margin of error [9]. Adults aged 18 to 70 years of either gender with ultrasonographically confirmed NAFLD and who provided informed consent were included. Exclusion criteria included chronic liver disease of other etiologies (viral hepatitis B/C, autoimmune hepatitis, hemochromatosis, Wilson's disease, drug-induced liver injury), history of alcohol intake, use of lipid-lowering drugs within the past three months, pregnancy or lactation, and chronic systemic illnesses affecting lipid metabolism, such as malignancy, chronic kidney disease, or heart failure. After obtaining informed consent from patients, those meeting the criteria were enrolled consecutively until the required sample size was achieved. At the time of enrollment, baseline demographic data, including age and gender, were recorded. Clinical information, including diabetes mellitus, hypertension, and ischemic heart disease, was obtained from patients' medical records. Ultrasonographic assessment for NAFLD grading was performed using a Samsung HS40 diagnostic ultrasound system equipped with a 3.5 MHz convex transducer, operated by experienced radiologists following standardized protocols. NAFLD was defined as increased hepatic echogenicity compared to the renal cortex, with the absence of secondary causes of liver fat accumulation. The severity of NAFLD was graded using ultrasonographic findings. Grade 0 was considered normal hepatic echogenicity. Grade 1 was characterized by a mild rise in liver echogenicity, while the diaphragm and intrahepatic vessels remained clearly visible. In Grade 2, there was a noticeable rise in liver echogenicity along with partial obscuration of the diaphragm or intrahepatic vessels. Grade 3 exhibited a significant elevation in echogenicity, often accompanied by poor or lost visualization of the diaphragm, intrahepatic vasculature, and the posterior segment of the right hepatic lobe. All participants underwent venous blood sampling following an overnight fast of 8 to 12 hours. Venous blood samples were collected after an overnight fast of 8–12 hours. Serum AST and ALT were measured using the Roche Cobas c311 automated chemistry analyzer (Roche Diagnostics, Germany) based on

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the International Federation of Clinical Chemistry (IFCC) kinetic method. Lipid profile parameters, total cholesterol, triglycerides, LDL-C, and HDL-C, were quantified by enzymatic colorimetric assays on the Roche Cobas c311 platform, employing Roche Diagnostics reagent kits, ensuring internal quality control and calibration before each batch run. Dyslipidemia, which served as the primary outcome, was identified according to predefined criteria, derived from national and international lipid guidelines. A diagnosis of dyslipidemia was established when one or more of the following thresholds were met: total cholesterol ≥200 mg/dL, triglycerides ≥150 mg/dL, LDL-C ≥130 mg/dL, HDL-C <40 mg/dL in men, or <50 mg/dL in women. Each case was monitored and reviewed at the point of laboratory reporting to ensure accurate classification. Data were statistically analyzed using SPSS, version 26.0. Categorical data were presented as frequencies and percentages, while continuous data were presented as mean and standard deviation (SD). Group comparisons between patients with and without dyslipidemia were conducted using the Chi-square test for categorical variables and independent sample t-tests for continuous variables. Associations between categorical variables were assessed using odds ratios with 95% CIs, while continuous variable comparisons were accompanied by mean differences and corresponding 95% CIs. The relationship between dyslipidemia and NAFLD severity grades was analyzed using the Chi-square test, and percentages were computed row-wise to reflect the proportion of dyslipidemia within each NAFLD grade. A p-value <0.05 was considered statistically significant.

## RESULTS

In this study, 116 patients were included with a mean age of 48.67 ± 11.57 years and a mean BMI of 28.27 ± 4.60kg/m$^2$. There was no association between dyslipidemia and age group, with 28 (38.9%) affected patients aged 18–45 years and 44 (61.1%) aged 46–70 years. Gender distribution was also statistically non-significant, with 44 (61.1%) females and 28 (38.9%) males in the dyslipidemic group (p=0.241). In contrast, a statistically significant association was observed for diabetes mellitus, which was present in 49 (68.1%) patients with dyslipidemia versus 20 (45.5%) without (p=0.016). Ischemic heart disease also showed a strong correlation with dyslipidemia (p=0.004), affecting 32 (44.4%) versus 8 (18.2%) patients. No difference was found in hypertension prevalence (p=0.104). BMI was higher in the dyslipidemia group (29.26 ± 4.76 vs. 26.64 ± 3.84kg/m$^2$; p=0.002). AST (41.89 ± 11.45 vs. 36.56 ± 10.08 IU/L; p=0.012) and ALT (54.93 ± 17.09 vs. 48.59 ± 14.18 IU/L; p=0.041) were also significantly raised (Table 1).

**Table 1:** Association of Demographic, Clinical, and Biochemical Variables with Dyslipidemia in Patients with NAFLD (n=116)

| Variables | Subgroup | Dyslipidemia Present (n=72) | Dyslipidemia Absent (n=44) | Test Statistic ($\chi^2$ / t) | Effect Size (OR / Mean Difference, 95% CI) | p-value |
|---|---|---|---|---|---|---|
| Age Group (years) | 18–45 | 28 (38.9%) | 18 (40.9%) | $\chi^2$ = 0.047 | OR = 1.088 (0.506–2.339) | 0.829 |
| | 46–70 | 44 (61.1%) | 26 (59.1%) | | | |
| Gender | Female | 44 (61.1%) | 22 (50.0%) | $\chi^2$ = 1.375 | OR = 1.571 (0.737–3.352) | 0.241 |
| | Male | 28 (38.9%) | 22 (50.0%) | | | |
| Diabetes Mellitus | Yes | 49 (68.1%) | 20 (45.5%) | $\chi^2$ = 5.788 | OR = 2.557 (1.180–5.538) | 0.016* |
| | No | 23 (31.9%) | 24 (54.5%) | | | |
| Hypertension | Yes | 39 (54.2%) | 17 (38.6%) | $\chi^2$ = 2.638 | OR = 1.877 (0.875–4.028) | 0.104 |
| | No | 33 (45.8%) | 27 (61.4%) | | | |
| Ischemic Heart Disease | Yes | 32 (44.4%) | 8 (18.2%) | $\chi^2$ = 8.338 | OR = 3.600 (1.469–8.820) | 0.004* |
| | No | 40 (55.6%) | 36 (81.8%) | | | |
| Age (Years) | – | 47.81 ± 11.73 | 50.09 ± 11.29 | t = 1.033 | MD = 2.285 (–2.099–6.669) | 0.304 |
| BMI (kg/m$^2$) | – | 29.26 ± 4.76 | 26.64 ± 3.84 | t = –3.095 | MD = –2.63 (–4.31 to –0.95) | 0.002* |
| AST (IU/L) | – | 41.89 ± 11.45 | 36.56 ± 10.08 | t = –2.544 | MD = –5.33 (–9.49 to –1.18) | 0.012* |
| ALT (IU/L) | – | 54.93 ± 17.09 | 48.59 ± 14.18 | t = –2.062 | MD = –6.33 (–12.42 to –0.25) | 0.041* |

Chi-square test was used for categorical variables and an independent t-test for continuous variables. A p-value <0.05 was considered statistically significant. OR – odds ratio; CI – confidence interval; MD – mean difference; AST – aspartate aminotransferase; ALT – alanine aminotransferase; BMI – body mass index.

Patients with dyslipidemia exhibited higher lipid parameters compared to those without. The mean total cholesterol level was 216.11 ± 18.74 mg/dL in the dyslipidemia group versus 205.17 ± 36.88mg/dL in the non-dyslipidemia group (p = 0.037). Triglycerides were also elevated in dyslipidemic individuals (201.99 ± 20.58mg/dL) compared to 170.05 ± 24.59mg/dL (p<0.001). LDL-C was markedly raised at 143.67 ± 15.46mg/dL versus 119.73 ± 18.46mg/dL (p<0.001). In contrast, HDL-C was significantly lower in dyslipidemic patients (35.35 ± 4.52mg/dL) than in those without dyslipidemia (41.38 ± 7.93mg/dL) (Table 2).

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**Table 2:** Comparison of Lipid Profile Parameters Between Patients with and without Dyslipidemia (n=116)

| Lipid Parameters | Dyslipidemia Present (Mean ± SD) | Dyslipidemia Absent (Mean ± SD) | t-value | Mean Difference (95% CI) | p-value |
|---|---|---|---|---|---|
| Total Cholesterol (mg/dL) | 216.11 ± 18.74 | 205.17 ± 36.88 | −2.114 | −10.94 (−21.98 to −0.69) | 0.037* |
| Triglycerides (mg/dL) | 201.99 ± 20.58 | 170.05 ± 24.59 | −7.528 | −31.95 (−40.35 to −23.54) | <0.001* |
| LDL-C (mg/dL) | 143.67 ± 15.46 | 119.73 ± 18.46 | −7.513 | −23.94 (−30.25 to −17.63) | <0.001* |
| HDL-C (mg/dL) | 35.35 ± 4.52 | 41.38 ± 7.93 | 5.218 | 6.03 (3.74 to 8.32) | <0.001* |

An independent t-test was used to compare the lipid parameters between patients with and without dyslipidemia. A p-value <0.05 was considered statistically significant.

Dyslipidemia frequency increased with disease severity (p<0.001). In Grade 1, dyslipidemia was observed in 20 (41.7%) versus 28 (58.3%) without. Grade 2 included 28 (66.7%) dyslipidemic and 14 (33.3%) non-dyslipidemic patients. In Grade 3, 24 (92.3%) had dyslipidemia versus only 2 (7.7%) without, indicating a significant association between dyslipidemia and higher NAFLD grade (Table 3).

**Table 3:** Association Between Dyslipidemia and NAFLD Severity Grades

| NAFLD Grade | Dyslipidemia Present (n=72) | Dyslipidemia Absent (n=44) | p-value |
|---|---|---|---|
| Grade 1 (Mild) | 20 (41.7%) | 28 (58.3%) | <0.001* |
| Grade 2 (Moderate) | 28 (66.7%) | 14 (33.3%) | |
| Grade 3 (Severe) | 24 (92.3%) | 2 (7.7%) | |

The Pearson Chi-Square test was used to assess the association between dyslipidemia and NAFLD severity grades.

In this study comprising 116 participants, dyslipidemia was observed in 72 (62.1%) patients, while 44 (37.9%) patients did not have dyslipidemia (Figure 1).

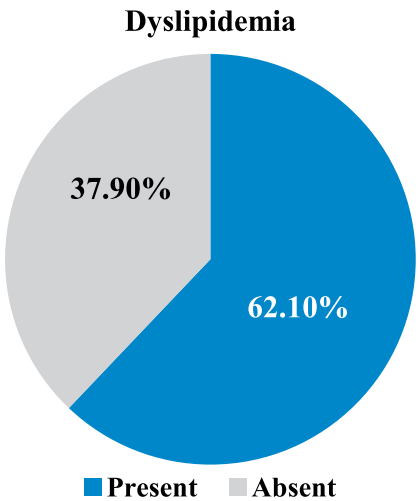


**Figure 1:** Frequency of Dyslipidemia among NAFLD Patients

## DISCUSSION

This study evaluated the association between dyslipidemia and clinical, biochemical, and radiological features of non-alcoholic fatty liver disease (NAFLD) among 116 patients. Age and gender did not show significant associations with dyslipidemia in our study (p=0.829 and p=0.241, respectively). Comparable findings were noted by Ferreira *et al.* and Krishan, where demographic variables like age and sex did not significantly influence the presence of dyslipidemia among NAFLD patients [18, 19]. However, Dowla *et al.* documented age and race-dependent variations, particularly earlier NAFLD onset and higher dyslipidemia rates among Hispanic children, suggesting that population-specific genetic and environmental factors may modulate lipid patterns [13]. In the present study, diabetes mellitus (DM) was significantly more prevalent among dyslipidemic NAFLD patients (68.1% vs. 45.5%, p=0.016), with an odds ratio of 2.557. This finding resonates with studies by Ferreira *et al.* and Méndez-Sánchez *et al.* which identified type 2 diabetes mellitus (T2DM) as an independent predictor of advanced fibrosis and dyslipidemia in NAFLD patients [18, 20]. The interplay of insulin resistance with hepatic lipid metabolism is a well-established driver of steatosis and subsequent liver injury. Ischemic heart disease (IHD) also demonstrated a robust association with dyslipidemia (p=0.004), with an OR of 3.6, underscoring the shared pathophysiological axis between hepatic fat accumulation and atherogenesis. These observations are supported by Dowla *et al.* and Risal *et al.* who emphasized cardiovascular comorbidity as an essential component of the NAFLD metabolic phenotype. Although hypertension showed a higher prevalence among dyslipidemic individuals (54.2% vs. 38.6%), statistical significance was not attained (p=0.104) [13, 21]. In contrast, Méndez-Sánchez *et al.* demonstrated a significant link between hypertension and advanced fibrosis, with hypertension emerging as an independent risk factor (OR 2.59, p=0.014) [20]. The mean BMI in the dyslipidemic group was higher (29.26 ± 4.76 vs. 26.64 ± 3.84kg/m$^2$, p=0.002), reaffirming obesity as a central contributor to both hepatic steatosis and lipid dysregulation. This finding is corroborated by Cigri *et al.* who reported significantly elevated BMI in pediatric NAFLD patients (23.5 vs. 22.1 kg/m$^2$, p<0.001), and Risal et al. where NAFLD patients had significantly higher BMI than controls (26.41 ± 4.03 vs. 23.48 ± 2.85kg/m$^2$, p<0.001) [12, 21]. Similarly, Ferreira *et al.* showed significantly increased BMI and waist circumference in NAFLD individuals [18]. Transaminases were significantly elevated in dyslipidemic NAFLD patients in our study. AST levels were higher (41.89 ± 11.45 vs. 36.56 ± 10.08 IU/L, p=0.012), and ALT values also showed significance (54.93 ± 17.09 vs. 48.59 ± 14.18 IU/L, p=0.041).

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These findings mirror the results of Singh *et al.* and Cigri *et al.* where ALT and AST levels were higher in patients with elevated triglycerides and NAFLD [22, 12]. Dowla *et al.* further highlighted strong correlations between ALT and other metabolic markers, including GGT, TG, and non-HDL-C [13]. Notably, Cigri *et al.* identified ALT as a highly sensitive diagnostic biomarker for NAFLD (AUC = 0.986), with sex-specific cut-off values suggesting the clinical utility of ALT in early screening [12]. Dyslipidemic NAFLD patients exhibited significantly higher total cholesterol (216.11 ± 18.74 vs. 205.17 ± 36.88mg/dL, p=0.037), triglycerides (201.99 ± 20.58 vs. 170.05 ± 24.59mg/dL, p<0.001), and LDL-C (143.67 ± 15.46 vs. 119.73 ± 18.46mg/dL, p<0.001), with HDL-C levels being significantly lower (35.35 ± 4.52 vs. 41.38 ± 7.93mg/dL, p<0.001). These findings are in agreement with Singh *et al.* who reported significantly elevated triglycerides (194.3 ± 104.7 vs. 131.9 ± 53.1 mg/dL) and lower HDL-C in NAFLD patients [22]. Similarly, Méndez-Sánchez *et al.* found triglycerides and LDL-C as independent predictors of fibrosis (OR for TG = 4.96, LDL-C = 3.04, both p<0.05) [20]. Risal *et al.* and Dowla *et al.* also reported lipid derangements, particularly higher TG, LDL-C, and non-HDL-C levels in NAFLD subjects compared to controls or normolipidemic subgroups [13, 21]. The current study's mean LDL-C of 143.67 mg/dL in the dyslipidemic NAFLD group falls well within the elevated range identified in these prior analyses, further validating the link between hepatic fat accumulation and atherogenic lipid patterns. The frequency of dyslipidemia was notably high (62.1%) among NAFLD individuals, consistent with the dyslipidemic burden documented in global and regional literature. The frequency of dyslipidemia in NAFLD in the present study aligns with figures reported by Singh *et al.* (NAFLD n=2436), who observed a dyslipidemia frequency exceeding 60%, and Krishan, where 65% of T2DM patients had NAFLD and a significantly high burden of lipid abnormalities [19, 22]. Similarly, Risal *et al.* identified dyslipidemia in a majority of NAFLD cases compared to controls, particularly low HDL-C and high LDL-C [21]. The link between dyslipidemia and NAFLD likely reflects insulin resistance–driven hepatic lipid accumulation. Increased free fatty acid flux to the liver enhances triglyceride synthesis, while impaired VLDL secretion and reduced HDL formation create an atherogenic lipid profile that perpetuates hepatic steatosis. A significant correlation was observed between the presence of dyslipidemia and NAFLD severity grades (p<0.001), with 33.3% of dyslipidemic patients categorized in Grade 3 compared to only 4.5% among the non-dyslipidemic group. This trend of increasing dyslipidemia with advancing steatosis is supported by Krishan, who observed worsening lipid parameters across NAFLD grades, and by Risal *et al.* whose grade III NAFLD subgroup showed the highest non-HDL-C and atherogenic ratios [19, 21]. The pattern underscores the progressive metabolic derangement associated with steatohepatitis. Furthermore, Méndez-Sánchez *et al.* demonstrated that dyslipidemia not only coexists with but also contributes to fibrosis progression and cirrhosis risk in biopsy-confirmed NASH, with LDL-C and TG emerging as key markers [20]. Given the statistically significant correlations between dyslipidemia and key metabolic and hepatic parameters, early lipid profiling in NAFLD patients is essential. Integration of lipid management into NAFLD care protocols may reduce not only hepatic complications but also the cardiovascular burden, as emphasized by multiple global studies. The study's strength lies in its comprehensive analysis of dyslipidemia in relation to NAFLD severity, incorporating both clinical and biochemical parameters using robust statistical methods. The use of ultrasound grading and detailed lipid profiling enhances diagnostic reliability.

However, limitations include the cross-sectional design, absence of lifestyle variable adjustment, and single-center data collection, potentially affecting generalizability. Absence of liver biopsy restricts histological correlation. Future studies should employ longitudinal designs with larger, multicenter cohorts and incorporate non-invasive fibrosis markers or liver histopathology to validate findings. Investigating therapeutic responses to lipid-lowering agents in NAFLD subgroups may also offer valuable clinical insights.

## CONCLUSIONS

This study demonstrates a high frequency of dyslipidemia (62.1%) among patients with non-alcoholic fatty liver disease, with significant associations observed with diabetes mellitus, ischemic heart disease, elevated body mass index, and worsening hepatic enzyme levels. Dyslipidemia was significantly linked with higher NAFLD grades, suggesting its potential role in disease progression. These findings underscore the importance of routine lipid profiling and metabolic screening in NAFLD patients to guide timely intervention and risk stratification for cardiometabolic complications.

## Authors' Contribution

Conceptualization: AU, UA
Methodology: AA, SS, AB, AU, UA, MIJ
Formal analysis: AA, MIJ
Writing and Drafting: AA, UA, MIJ
Review and Editing: AA, SS, AB, AU, UA, MIJ

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

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## Conflicts of Interest

All the authors declare no conflict of interest.

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**Original Article**

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# Exposure of Acute Gastroenteritis in Relation to Season: A Cross-Sectional Study Based on Demographic Representation of Paediatric Patients with Their Outcomes

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## ABSTRACT

Among children, acute gastroenteritis (viral) is a major concern for public health. In Pakistan, childhood mortality remains fourth largest, with gastrointestinal infections remaining a major cause. **Objectives:** To compare acute gastroenteritis and seasonal variations based on their demographic representation. **Methods:** After informed consent and ethical approval, this cross-sectional (prospective) research was carried out in the Paediatric Ward of Al-Tibri Medical College and Hospital, Karachi, from June 2023 to May 2024. Patients diagnosed with acute gastroenteritis were included, while those with any other diagnosis (such as intestinal obstruction, urinary tract infection, etc.) were excluded. SPSS version 23.0 was used for the analysis of data. To test significance, the chi-square test was applied at a p-value≤0.05. **Results:** Among 377 paediatric cases, 55% were male and 45% female, with 34% infants and 38% between 1-4 years. 72.7% of patients were admitted in the summer and 27.3% in winter, with most being admitted in May 2024 (14%) and least in the month of November 2023 (3%). The majority were discharged alive and healthy (99%). A significant association was observed in patients admitted in each month (p-value<0.001). **Conclusions:** This study showed that acute gastroenteritis in paediatric patients was more common among males and children aged 1–4 years, with a significantly higher number of admissions during the summer months, particularly in May 2024. Despite the seasonal surge, almost all patients recovered well, with 99% discharged alive and healthy.

## INTRODUCTION

Acute gastroenteritis (AGE) in Pediatric patients shows clear seasonal patterns influenced by the causative viral agents. Some infections, such as rotavirus, typically peak in winter and early spring, while others (like adenovirus) are more prevalent in summer and early autumn, with some studies noting dual peaks in cooler months like January and September [1, 2]. Other viruses also peak in winter, with certain genotypes causing more severe symptoms and outbreaks during this season [3]. Some associated with gastroenteritis tend to have higher prevalence during the rainy season in tropical regions [4]. The COVID-19 pandemic and related protective measures have altered the epidemiology of these viruses, reduced some infections, but highlighted the need for ongoing surveillance [5]. Overall, seasonality varies by virus type and geographic region, but winter months generally see increased viral gastroenteritis cases in children, emphasizing the importance of targeted prevention and

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vaccination strategies [6]. The majority of children below 5 years of age commonly have diarrhoea with or without vomiting. It is an acute gastroenteritis (AGE) defining trait. Anorexia, vomiting, diarrhoea, fever, pallor, and stomach cramps are all symptoms of AGE that frequently result in dehydration [1]. It is the second most common infection observed among children <5 years. In countries that are developed, the occurrence of diarrheal illness caused by Acute Gastroenteritis (AGE) has been estimated to range between 0.5 to 1.9 episodes/child/year in infants and children up to 3 years [7]. The main public health concern affects children under the age of five, as well as occasionally children over the age of five [8]. According to reports, viruses are the most frequent cause of AGE [9]. The prevalence of AGE in developed countries is significantly lower than in less developed countries, largely due to improved hygiene, appropriate sanitation systems, and heightened public health education and awareness. Despite this, AGE cases are still reported in both developed and underdeveloped countries [10]. Research has shown that AGE is a major cause of childhood mortality in Pakistan.

Even though there are lots of studies in Pakistan that show the mortality caused by AGE, there is not enough data from different hospitals in different parts of the country [11]. As AGE is still a prevalent issue in developing countries, it is beneficial to investigate the seasonal patterns of presentation of the disease for taking necessary procedures in seasons with a higher AGE burden in order to address the issue and reduce the incidence rate. This study aimed to evaluate the exposure of paediatric patients to AGE based on their demographic representation, their outcomes, the month/season of admission, duration of hospitalization, and the manner in which they were discharged.

## METHODS

A cross-sectional observational study was conducted at the Department of Paediatrics of Al-Tibri Medical College and Hospital, involving 377 paediatric cases who were admitted between June 2023 and May 2024. The study received approval from the Ethical Review Committee of Al-Tibri Medical College and Hospital and Isra University, Karachi, with ref no: IERC/ATMC/02-2021/20, and obtained informed consent from guardians or parents. The study utilized a non-probability, convenience sampling technique to collect data. This study included patients who had been admitted to the Paediatric Ward with an AGE diagnosis. The study included paediatric patients aged between one month and twelve years. Excluded from the study were any other paediatric patients with other illnesses (such as urinary tract infection, appendicitis, intussusception, intestinal obstruction, drug induced gastritis, inflammatory bowel disease etc.) those who had been observed in the Emergency/Intensive Care Unit (ECU) for < 24 hours, those admitted to Paediatric ICU, and those with surgical paediatric conditions (such as appendicitis, intestinal obstruction, intussusception etc.). The study utilized version 23.0 of the Statistical Package for Social Sciences (SPSS) to gather and analyse data. The study employed descriptive statistics to gather and examine information, including variables such as age, gender, duration of hospital stays, hospitalization month, admission season, admission outcome, discharge method, and diagnosis. This study then provided calculations for frequency and percentages. To assess the data's significance, we performed chi-square test or Fisher's exact test where appropriate, and one-way ANOVA keeping p-value<0.05, showing significant difference in presentation of age based on gender and season.

## RESULTS

377 paediatric subjects were admitted during one year, beginning in June 2023 and concluding in May 2024, for acute gastrointestinal disease. Out of the 377 patients, 55 % were male, while 45 % were female. The frequency of male was higher than that of female patients (p=0.45) (Figure 1).

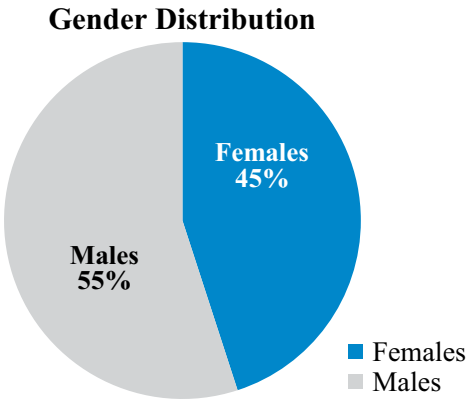


**Figure 1:** Distribution of Pediatric Patients with Acute Gastroenteritis Based on Gender (p=0.45)

The total number of cases was 377, 128 (34%) being infants; 144 (38.2%) being between 1 and 4 years of age; 66, with 17.5% being between 5 and 8 years of age; and 10.3% being between 9 and 12 years of age. There was a non-significant difference in age by season (0.43) (Table 1).

**Table 1:** Categorization of Pediatric Cases of Acute Gastroenteritis According to Age Groups (n=377)

| Age Groups | Frequency (%) | p-value |
|---|---|---|
| Infant | 128 (34%) | 0.43 |
| 1-4 Years | 144 (38.2%) | |
| 5-8 Years | 66 (17.5%) | |
| 9-12 Years | 39 (10.3%) | |

*Chi-square test applied

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According to month wise admission, 29 (7.7%)of patients were admitted in June 2023,34(9%) in July 2023, 39(10.3%) in August 2023, 31 (8.2%) in September 2023, 27 (7.2%) in October 2023, 13 (3.4%) in November 2023, 26 (6.9%) in December 2023, 34 (9.0%) in January 2024, 30 (8.0%) in February 2024, 37 (9.8%) in March 2024, 24 (6.4%) in April 2024, 53 (14.1%) in May 2024, There was a significant relationship between admissions and season (p-value<0.001)(Table 2).

**Table 2:** Frequency Distribution of Patients Admitted to Pediatric Ward Between June 2023 to May 2024

| Month of Admission | Frequency (%) |
|---|---|
| June 2023 | 29 (7.7%) |
| July 2023 | 34 (9.0%) |
| August 2023 | 39 (10.3%) |
| September 2023 | 31 (8.2%) |
| October 2023 | 27 (7.2%) |
| November 2023 | 13 (3.4%) |
| December 2023 | 26 (6.9%) |
| January 2024 | 34 (9.0%) |
| February 2024 | 30 (8.0%) |
| March 2024 | 37 (9.8%) |
| April 2024 | 24 (6.4%) |
| May 2024 | 53 (14.1%) |

In total, 274 children were admitted in summer (72.7%), and 103 in winter (27.3%)(Figure 2).

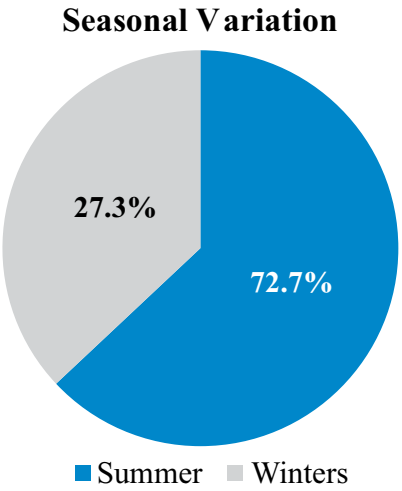


**Figure 2:** Seasonal Distribution of Admitted Patients(n=377)

Out of 377 patients, 373 were discharged alive (98.9%), and only 04 died (1.1%), with a difference of just 0.26 between the two seasons (Figure 3).

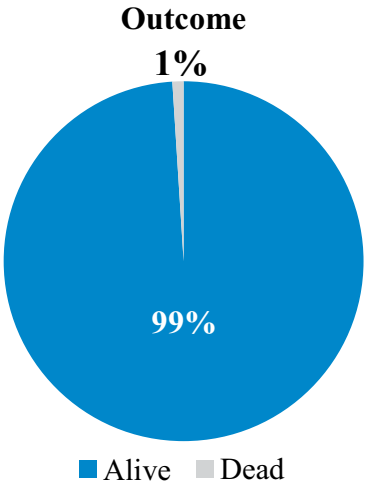


**Figure 3:** Outcome of Admitted Patients(n=377)

## DISCUSSION

In this study, 377 paediatric cases (between 1 month to 12 years) were enrolled in the hospital, of which 208 were male (55.2%), 169 were female (44.8%), and 144 were between 1-4 years of age (38.2%). Infants accounted for 34% of the patients. The majority of the patients' hospital stays were 24- 72 hours, while 104 were 4-7 days (27.6%). The majority of the patients were admitted in the summer, May 2024, among them, 99% were discharged by the attending paediatrician. Viral acute gastroenteritis in children shows distinct seasonal patterns depending on the causative virus: rotavirus peaks mainly in winter and spring, adenovirus shows dual peaks in autumn and winter, and norovirus is most prevalent in winter [3]. Male predominance in viral infections is common but often not statistically significant, consistent with the observed gender distribution in this cohort [6]. These seasonal and demographic patterns highlight the importance of targeted prevention, vaccination, and resource planning for paediatric acute gastroenteritis [12]. Despite the prevalence of AGE cases being reported throughout the year, the AGE incidences by season have never been evaluated. In current research, most patients were admitted during the summer months, with May being the month with the highest number of admissions for gastroenteritis. Studies have indicated that AGE prevalence is higher in areas with low air temperature, particularly during the rainy/post-monsoon season [13]. Research from South Asian regions and other countries has also reported that AGE presentation is consistent throughout the year, with less seasonal variation [14]. Conversely, various studies have reported that AGE prevalence peaks occurred in winters and less frequently in summers [15]. This seasonal pattern aligns with research indicating that viral gastroenteritis cases in children often peak in cooler months, particularly winter and early spring

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[16]. Infections also show seasonal peaks, often with dual peaks in autumn and winter, while some tend to peak during rainy seasons in tropical regions [17]. The significant relationship between admissions and season ($p<0.001$) reflects these viral epidemiological trends, emphasizing the importance of season-aware healthcare planning and preventive measures such as vaccination and hygiene promotion [18]. In current study, higher admissions were encountered during the summer season. This indicates a strong seasonal pattern in paediatric acute gastroenteritis cases, with a significantly higher burden in warmer months [19]. The significant seasonal variation in admissions reflects the diverse epidemiology of causative viruses, which vary by region and climate [20]. Continuous surveillance is essential to monitor these patterns, especially as viral prevalence can shift due to factors like vaccination and public health measures. Understanding these seasonal dynamics supports targeted prevention and healthcare resource allocation for paediatric gastroenteritis.

This study was single-center and cross-sectional, limiting generalizability. Viral etiologies were not confirmed with laboratory testing, and data on environmental or socioeconomic factors were not collected, which may have influenced seasonal patterns. Future research should involve multicenter, longitudinal studies with laboratory-confirmed viral identification to better understand seasonal trends and guide targeted prevention and resource planning for pediatric acute gastroenteritis.

## CONCLUSIONS

This study demonstrates a clear seasonal pattern in the exposure and hospitalization of paediatric patients with acute gastroenteritis, with a significantly higher burden of cases presenting during the summer months compared to winter. Most affected children were between 1 and 4 years of age, with a slight predominance of males. Despite the seasonal surge, clinical outcomes were overwhelmingly favourable, with nearly all patients discharged alive and healthy. These findings highlight the strong influence of seasonal and demographic factors on acute gastroenteritis incidence and underscore the need for heightened preventive strategies and resource preparedness during peak summer months.

## Authors' Contribution

Conceptualization: ES
Methodology: SBK, WA, SKF
Formal analysis: AI, SKF
Writing and Drafting: NS, SBK
Review and Editing: NS, ES, AI, SBK, WA, SKF

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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# Assessment of Symptom Severity, Urinary Flow, and Prostate Volume in Men with Benign Prostatic Hyperplasia: A Cross-Sectional Correlation Study

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## ABSTRACT

Benign prostatic hyperplasia (BPH) is a common cause of lower urinary tract symptoms (LUTS) in ageing men, yet patient-reported symptoms, urinary flow parameters, and prostate size often show inconsistent clinical relationships. Clarifying how these measures relate may improve diagnostic interpretation and clinical decision-making. **Objectives:** To evaluate the correlations among symptom severity (IPSS), peak urinary flow rate (Qmax), and prostate volume in men with BPH. **Methods:** A cross-sectional analytical study was conducted among 56 men aged ≥50 years with clinically diagnosed BPH. Symptom severity was assessed using the International Prostate Symptom Score (IPSS). Uroflowmetry provided Qmax values, and transabdominal ultrasonography measured prostate volume. Pearson correlation coefficients with 95% confidence intervals were calculated to assess associations among variables. **Results:** The mean age of participants was 62.79 ± 6.64 years, and most reported moderate to severe symptoms (mean IPSS 21.79 ± 6.22). No significant correlation was found between IPSS and Qmax ($r = -0.064$, $p = 0.639$; 95% CI −0.32 to 0.20) or between IPSS and prostate volume ($r = 0.216$, $p = 0.110$; 95% CI −0.03 to 0.45). Prostate volume showed a weak, nonsignificant inverse association with Qmax ($r = -0.139$, $p = 0.306$; 95% CI −0.37 to 0.13). **Conclusion:** The absence of significant correlations among IPSS, Qmax, and prostate volume confirms that symptom burden, flow limitation, and gland size represent different dimensions of BPH. Clinical decision-making should therefore integrate these measures collectively rather than interpreting them in isolation.

## INTRODUCTION

Benign prostatic hyperplasia (BPH) is among the most common urological disorders in older men, characterized by progressive enlargement of the prostate gland and resultant bladder outlet obstruction [1]. This enlargement often contributes to lower urinary tract symptoms (LUTS), including urinary frequency, nocturia, and voiding difficulty, all of which negatively impact quality of life [2]. With ageing populations and increasing life expectancy globally, the clinical and economic burden associated with BPH continues to grow [2, 3]. Assessment of BPH routinely involves symptom scoring using the International Prostate Symptom Score (IPSS), uroflowmetry, and ultrasound-based measurement of prostate size [4]. Although these tools are widely used, evidence consistently shows poor

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alignment between patient-reported symptoms, urinary flow parameters, and prostate size [5, 6]. Some men present with significant LUTS despite having normal flow rates and minimal prostatic enlargement, whereas others demonstrate large prostates with minimal subjective symptoms [7]. This inconsistency raises important questions about how well these commonly used measures reflect one another and whether they can reliably guide clinical decision-making. Despite widespread use of IPSS, uroflowmetry, and prostate volume in routine practice, the strength and direction of their interrelationships remain inconsistently reported, particularly within local populations. This lack of reproducible correlation represents a clinically relevant gap, as treatment decisions frequently rely on these measures. This study evaluates the correlations among IPSS, Qmax, and prostate volume, hypothesizing that these variables would demonstrate weak or nonsignificant associations, reflecting distinct pathological and perceptual components of benign prostatic hyperplasia.

Clinical assessment relies on the International Prostate Symptom Score (IPSS), uroflowmetry (Qmax), and prostate volume; however, these parameters frequently show discordant findings across patients. Reported relationships between symptom severity, urinary flow, and prostate size remain inconsistent, with limited reproducible evidence from local populations. This uncertainty complicates clinical decision-making, as management strategies often depend on these measures. This study aimed to evaluate the correlations among IPSS, Qmax, and prostate volume in men with benign prostatic hyperplasia.

## METHODS

This study was designed as a prospectively conducted cross-sectional analytical investigation aimed at determining whether symptom severity, urinary flow parameters, and prostate volume are correlated in men with benign prostatic hyperplasia. The research was carried out in the Department of Urology at Jinnah Postgraduate Medical Centre (JPMC), Karachi, over six months from April 2022 to September 2022. All information was collected prospectively, ensuring clarity of design and alignment with the study objective. Ethical approval for the study was obtained from the Institutional Ethical Review Committee (Ref: CPSP/REU/URO/2019-1861140). Each participant was briefed about the study's purpose and procedures, and written informed consent was secured. Confidentiality was maintained by avoiding personal identifiers, and all study procedures adhered to the Declaration of Helsinki. The sample size was calculated using a correlation-based formula, assuming an expected effect size of r = 0.368 derived from the reported correlation between IPSS and Qmax in a comparable population taken from the Oranusi *et al.* [8]. With a significance level of 0.05 and a statistical power of 80%, the minimum required sample size was 56 participants. Non-probability consecutive sampling was employed to include all eligible patients presenting during the study period, which is appropriate for exploratory correlation analysis in a clinical setting. Men aged 50 years or older with lower urinary tract symptoms and a clinical diagnosis of benign prostatic hyperplasia were included. Individuals with suspected or confirmed prostate cancer, prior prostate or urethral surgery, active urinary tract infection, or neurogenic bladder dysfunction were excluded to avoid confounding influences on urinary flow and symptom scores. Demographic variables and relevant medical history were documented through a structured proforma. Symptom severity was assessed using the International Prostate Symptom Score (IPSS), a validated tool widely used for evaluating LUTS in men with BPH [6]. The IPSS includes seven symptom questions scored 0–5 and one Quality-of-Life (QoL) question scored 0–6, producing a total score ranging from 0 to 35. Symptom severity categories were defined as mild (0–7), moderate (8–19), and severe (20–35). Uroflowmetry was performed using a calibrated electronic uroflow meter, operated by trained personnel. Devices underwent weekly calibration checks, and only voids with a minimum voided volume of ≥150 ml were accepted to ensure reproducibility. When the voided volume was insufficient, the test was repeated after adequate hydration. Measured parameters included Qmax, average flow rate, voided volume, and flow curve characteristics. Prostate volume and post-void residual urine were measured by transabdominal ultrasonography, performed by experienced radiology staff. Prostate volume was calculated using the ellipsoid formula. Data were entered into SPSS version 25.0. Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Normality of IPSS, Qmax, and prostate volume was assessed using the Kolmogorov–Smirnov test. Because distributions approximated normality and IPSS is commonly treated as a quasi-continuous variable in urological correlation studies, Pearson's correlation coefficient was applied. To strengthen interpretation, 95% confidence intervals for correlation coefficients were also calculated. A p-value <0.05 was considered statistically significant.

## RESULTS

A total of 56 men with benign prostatic hyperplasia were included. Normality testing using the Kolmogorov–Smirnov test showed no significant deviation from normal distribution for IPSS (p = 0.21), Qmax (p=0.18), and prostate

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volume (p=0.26). The mean age was 62.79 ± 6.64 years (range 50–77), and the mean BMI was 26.21 ± 2.79 kg/m$^2$. The mean duration of urinary symptoms was 15.27 ± 6.75 months. Diabetes was present in 42.9% of participants, hypertension in 37.5%, smoking history in 19.6%, and prior urinary retention in 17.9% (Table 1).

**Table 1:** Baseline Characteristics of Participants (n=56)

| Variables | n (%) or Mean ± SD | Range |
|---|---|---|
| Age (Years) | 62.79 ± 6.64 | 50–77 |
| BMI (kg/m$^2$) | 26.21 ± 2.79 | 18.3–32.2 |
| Symptom Duration (Months) | 15.27 ± 6.75 | 4–31 |
| Diabetes | 24 (42.9%) | – |
| Hypertension | 21 (37.5%) | – |
| Smoker | 11 (19.6%) | – |
| History of Urinary Retention | 10 (17.9%) | – |

The study summarizes demographic and comorbidity distribution

The mean IPSS score was 21.79 ± 6.22, and most patients fell into the moderate or severe symptom categories. The mean QoL score was 3.95 ± 1.23. Uroflowmetry results showed a mean Qmax of 9.14 ± 2.75 ml/sec and a mean average flow rate of 5.04 ± 1.35 ml/sec. Mean post-void residual urine was 71.71 ± 23.94 ml, and mean prostate volume was 51.00 ± 15.59 ml (Table 2).

**Table 2:** Clinical Characteristics and Symptom Measures (n=56)

| Variables | n (%) or Mean ± SD | Range |
|---|---|---|
| IPSS | 21.79 ± 6.22 | 8–35 |
| IPSS QoL | 3.95 ± 1.23 | 2–6 |
| Qmax (ml/sec) | 9.14 ± 2.75 | 3.2–17.2 |
| Average Flow (ml/sec) | 5.04 ± 1.35 | 1.8–8.2 |
| Post-Void Residual (ml) | 71.71 ± 23.94 | 14–127 |
| Prostate Volume (ml) | 51.00 ± 15.59 | 15.2–88.5 |

The table summarizes symptom severity, flow parameters, and ultrasound measurements.

Regarding IPSS categorization, none of the participants fell into the mild range; 35.7% had moderate symptoms, and 64.3% had severe symptoms (Table 3).

**Table 3:** IPSS Severity Classification

| Severity Category | n (%) |
|---|---|
| Mild (0–7) | 0 (0%) |
| Moderate (8–19) | 20 (35.7%) |
| Severe (20–35) | 36 (64.3%) |

Correlation analysis demonstrated weak and nonsignificant associations between symptom severity, urinary flow, and prostate volume. The correlation between IPSS and Qmax was weak (r = –0.064, p=0.639; 95% CI –0.32 to 0.20). IPSS showed a small, non-significant positive correlation with prostate volume (r = 0.216, p=0.110; 95% CI –0.03 to 0.45). The correlation between prostate volume and Qmax was also weak and non-significant (r = –0.139, p=0.306; 95% CI –0.37 to 0.13) (Table 4).

**Table 4:** Correlation Between IPSS, Qmax, and Prostate Volume (n=56)

| Variable Comparisons | r | p-value | 95% CI |
|---|---|---|---|
| IPSS vs Qmax | –0.064 | 0.639 | –0.32 to 0.20 |
| IPSS vs Prostate Volume | 0.216 | 0.110 | –0.03 to 0.45 |
| Qmax vs Prostate Volume | –0.139 | 0.306 | –0.37 to 0.13 |

A weak negative correlation was observed (r = –0.064), which was not statistically significant (p=0.639). The fitted trendline indicates minimal change in Qmax with increasing symptom score ($R^2$ = 0.0041) (Figure 1).

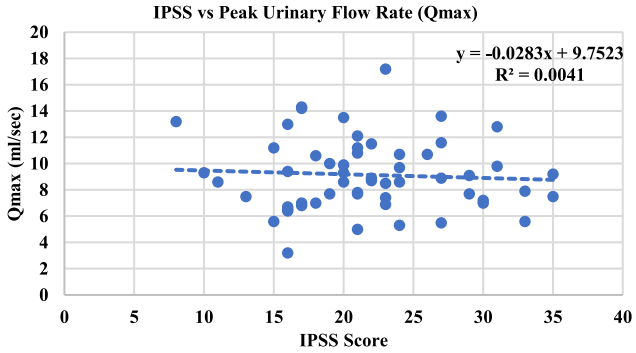


**Figure 1:** Scatter Plot Relationship Between IPSS and Qmax

A weak, non-significant positive correlation was observed (r = 0.216, p=0.110) (Figure 2).

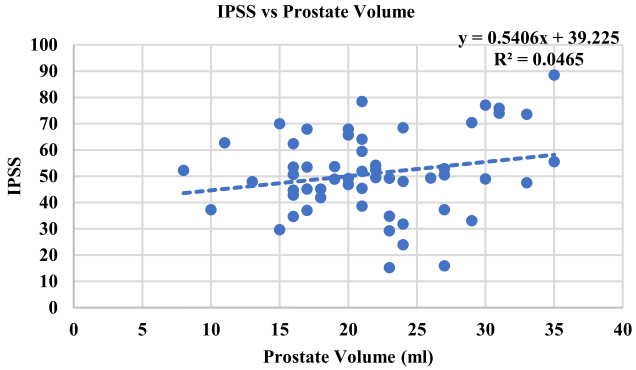


**Figure 2:** Scatter Plot Relationship Between IPSS and Prostate Volume

The correlation was weak and non-significant (r = –0.139, p=0.306) (Figure 3).

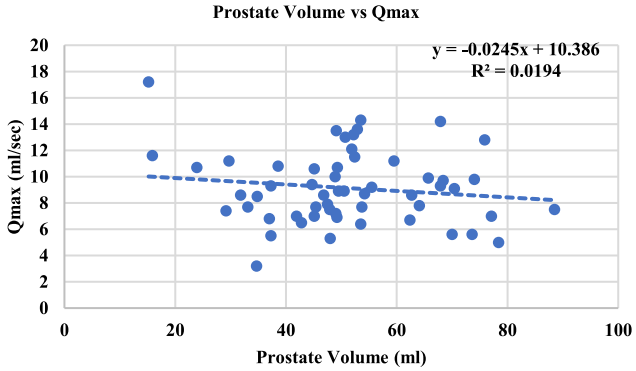


**Figure 3:** Scatter Plot Relationship Between Prostate Volume and Qmax

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## DISCUSSION

This study demonstrated no significant correlations among symptom severity, urinary flow, and prostate volume in men with benign prostatic hyperplasia. From a clinical perspective, the weak associations observed suggest that symptom severity cannot be reliably inferred from either prostate size or urinary flow rate alone. This helps explain why patients with comparable prostate volumes may experience markedly different symptom burdens, and why uroflowmetry parameters often fail to predict perceived disease severity. These findings reinforce the importance of individualized clinical assessment rather than reliance on any single diagnostic indicator when managing men with benign prostatic hyperplasia. These findings reinforce the widely observed mismatch between subjective lower urinary tract symptoms and objective indicators of obstruction. Several studies have similarly reported that IPSS scores do not consistently reflect measured urinary flow rates, suggesting that patient-perceived symptom burden reflects a broader combination of sensory, behavioural, and functional factors rather than flow limitation alone [9, 10]. The weak and nonsignificant association between IPSS and prostate volume observed here follows the pattern described in previous research, where prostate size has shown only modest or clinically negligible relationships with symptom severity [11, 12]. This emphasizes that structural enlargement alone does not determine symptom intensity, as individual variations in bladder behaviour, detrusor activity, and symptom perception play a substantial role in shaping LUTS [13, 14]. Likewise, the small inverse trend between prostate volume and Qmax aligns with findings from larger multicenter datasets, where modest correlations have been reported but explain only a limited proportion of flow variability [15-17]. Flow performance ultimately reflects a combination of detrusor contractility and outlet resistance, and prostate size alone provides an incomplete picture of voiding efficiency. Interpretation of the nonsignificant relationships must consider the study's sample size, which was sufficient to detect moderate but not small effects a limitation shared by similar studies evaluating the interplay of symptoms, flow, and morphology [18-20]. Real-world clinical variability, including comorbidities and hydration status, may also diminish correlation strength. Overall, the findings highlight the multifactorial nature of LUTS in BPH and reinforce that no single parameter reliably captures the complexity of patient experience or obstruction severity. A combined approach using symptom scores, uroflowmetry, and imaging remains essential for comprehensive evaluation.

There are a few limitations of this study, as it was single centered with a limited sample size, which may have reduced the ability to detect small correlations between symptom severity, urinary flow, and prostate volume. Additionally, real-world variability such as comorbidities and hydration status was not controlled, and no advanced functional assessments beyond standard uroflowmetry and imaging were included. Future research should involve larger, multicenter studies incorporating additional functional and urodynamic parameters to better understand the multifactorial relationships among LUTS, flow dynamics, and prostate morphology in BPH patients.

## CONCLUSIONS

This study found no significant correlations among symptom severity, urinary flow, and prostate volume in men with benign prostatic hyperplasia. These results indicate that neither flow rate nor prostate size reliably reflects patient-reported symptoms, underscoring the need to interpret these measures collectively rather than in isolation. Clinical assessment should incorporate symptom scoring, uroflowmetry, and ultrasound findings to provide a balanced understanding of both subjective and objective aspects of BPH. Larger studies with additional functional parameters may help clarify the subtle interactions among symptoms, voiding dynamics, and prostate anatomy.

## Authors' Contribution

Conceptualization: AFP
Methodology: AFP, SAC, MZZK, MM
Formal analysis: MSR, A, MZZK
Writing and Drafting: AFP, MSR, A, MM
Review and Editing: AFP, MSR, SAC, A, MZZK, MM

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**

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# Diagnostic Accuracy of Computed Tomography with Intraoperative Findings in Prediction of Metastatic Cervical Lymph Nodes in Oral Squamous Cell Carcinoma by Taking Histopathology as Gold Standard

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## ABSTRACT

Oral squamous cell carcinoma is a common cancer with a high risk of cervical lymph node metastasis. Accurate identification of metastatic nodes is vital for staging and treatment planning. Computed tomography (CT) is widely used for pre-surgical assessment, while intraoperative lymph node evaluation offers additional diagnostic value. **Objectives:** To assess the diagnostic accuracy of CT and intraoperative findings in predicting metastatic cervical lymph nodes in oral squamous cell carcinoma, using histopathology as the gold standard. **Methods:** A cross-sectional study was conducted at the Department OF Radiology, Dr. Ziauddin University Hospital, Karachi, from November 2023 to November 2024. A total of 323 patients with clinically suspicious oral squamous cell carcinoma underwent CT neck scans and intraoperative lymph node assessment based on size, consistency, shape, and adherence. Histopathology of resected nodes was the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. **Results:** The mean patient age was 51.5 years, with an average lymph node size of 20.9 mm. CT showed sensitivity 97.2%, specificity 84.6%, PPV 76.3%, NPV 98.4%, and accuracy 88.8%. Intraoperative scoring demonstrated sensitivity 89.3%, specificity 88.8%, PPV 80.3%, NPV 94.5%, and accuracy 89.2%. **Conclusions:** Both CT and intraoperative scoring demonstrated high diagnostic accuracy for detecting metastatic cervical lymph nodes. Their combined application is recommended to enhance staging, guide surgery, and improve patient outcomes.

## INTRODUCTION

Oral squamous cell carcinoma (OSCC) is among the most prevalent malignancies of the head and neck, representing over 90% of oral cancers worldwide [1]. It arises from the squamous epithelium of the oral mucosa and is known for its locally aggressive behavior and tendency to metastasize to cervical lymph nodes. Despite advances in treatment modalities, including surgery, radiotherapy, and chemotherapy, survival rates for OSCC remain unsatisfactory, primarily due to late diagnosis and nodal metastasis [2]. Early detection and accurate staging of cervical lymph nodes are therefore critical for optimizing treatment planning and improving patient prognosis. The burden of OSCC is particularly high in South Asia, including Pakistan, where it ranks among the top three cancers in

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incidence [3]. This high prevalence is strongly linked to region-specific risk factors such as tobacco use, betel quid, and areca nut chewing, along with contributory elements like alcohol consumption and poor oral hygiene. The aggressive nature of OSCC, combined with the widespread presence of risk factors, results in a growing incidence and mortality rate [4]. Consequently, early identification of nodal involvement has become a cornerstone of effective management in this population. Cervical lymph node metastasis is a major prognostic indicator in OSCC, with levels I–III most commonly involved [5]. The presence of metastatic nodes, particularly with extracapsular spread, is associated with advanced disease, increased recurrence, and poorer survival outcomes. Clinical examination alone often falls short in detecting small or deep-seated nodal metastases, while reactive nodes can mimic malignancy. To address these challenges, imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasonography are increasingly relied upon, with CT being the most widely used due to its accessibility and detailed anatomical imaging [6]. However, CT has limitations, particularly in differentiating reactive from metastatic lymph nodes based on size alone and in detecting subtle extracapsular spread [7]. Intraoperative assessment during neck dissection provides an additional opportunity to evaluate nodes based on consistency, shape, and adherence to adjacent tissues. Scoring systems have been developed to standardize intraoperative evaluation, and evidence suggests that combining CT findings with intraoperative assessment enhances diagnostic accuracy.

Nevertheless, there is limited local data from Pakistan to validate these approaches in OSCC patients. This study hypothesizes that the integration of CT imaging with intraoperative lymph node scoring improves diagnostic accuracy for detecting metastatic cervical lymph nodes in OSCC patients. This study aimed to determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of CT and intraoperative scoring, using histopathology as the gold standard. Also, to analyze the influence of factors such as age, gender, necrosis, and extracapsular spread on diagnostic performance.

## METHODS

This cross-sectional diagnostic accuracy study was conducted in the Department of Radiology at Dr Ziauddin University Hospital, Karachi, from November 2023 to November 2024. Ethical approval was obtained from the institutional review board before commencement, and the research synopsis was approved by the College of Physicians and Surgeons Pakistan (CPSP) under reference number CPSP/REU/RAD-2022-201-3687. The sample size was calculated using the Open-Epi diagnostic test sample size calculator, which applies the Buderer formula for studies of diagnostic accuracy. The formula considers sensitivity, specificity, disease prevalence, desired precision, and confidence interval. For sensitivity: $n = (Z^2 \times Se \times (1 - Se)) \div (d^2 \times P)$. For specificity: $n = (Z^2 \times Sp \times (1 - Sp)) \div (d^2 \times (1 - P))$. Where: Se = expected sensitivity, Sp = expected specificity, P = prevalence of disease, d = precision (margin of error), Z = 1.96 at 95% confidence interval. Using values from a previous study by Sharma et al. (2021) [8], sensitivity = 92%, specificity = 42%, and prevalence = 70.58%. With a 95% confidence interval and a margin of error of 10%, the required sample size was calculated to be 319 patients. To ensure adequate power, 323 patients were finally included in this study. Inclusion criteria were male and female patients aged between 30 and 70 years presenting with clinically suspicious oral squamous cell carcinoma and undergoing evaluation through computed tomography followed by surgical resection. The age range of 30–70 years was selected to minimize confounding, as oral squamous cell carcinoma is rare in younger patients, while those above 70 often have multiple comorbidities, higher perioperative risk, and reduced likelihood of undergoing curative surgery in our setting. Patients who had received radiotherapy or chemotherapy, those with inoperable disease or distant metastasis, and those who refused surgery were excluded from the study. Tumor stage was recorded according to the AJCC TNM classification, based on clinical and radiological findings. The targeted population for this study was patients with clinically suspected oral squamous cell carcinoma presenting to a tertiary care center for diagnostic evaluation and surgical management. After informed consent was obtained, each patient underwent a CT scan of the neck from the base of the skull to the clavicle. All scans were performed using a 16-slice multidetector Toshiba Alexion (Japan) with intravenous contrast. Radiological features were assessed using predefined malignancy criteria, including short-axis diameter >10 mm, rounded shape (short-to-long axis ratio >0.5), loss of fatty hilum, presence of central necrosis, irregular margins suggesting extracapsular spread, vascular invasion, and nodal conglomeration. It should be noted that CT-based scoring and intraoperative scoring differ in their parameters. CT scoring is based on radiological features such as size, necrosis, and extracapsular spread, whereas intraoperative scoring relies on tactile and visual assessment by the surgeon. Based on these criteria, each lymph node was classified as malignant or non-malignant for analysis. During surgery, intraoperative assessment of lymph nodes was performed by evaluating four key features, including size, consistency,

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shape, and adherence to surrounding structures. Each parameter was scored as 1 if present and 0 if absent, with a total score ranging from 0 to 4. A score of 3 or more was considered suggestive of malignancy, while scores between 0 and 2 were considered non-malignant. This cutoff was adapted from surgical practice experience and available literature, though formal external validation is still warranted. All resected lymph nodes were submitted for histopathological examination, which served as the gold standard for confirmation of metastatic involvement. Specimens were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 4–5 µm thickness, and stained with hematoxylin and eosin (H&E). Each node was examined microscopically for metastatic deposits, nodal necrosis, and extracapsular spread. Immunohistochemistry was performed if the morphology was equivocal. Information was gathered through a standardized proforma and subsequently entered into SPSS version 23.0 for statistical evaluation. Descriptive statistics were generated to summarize demographic and clinical characteristics. Sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were computed for both CT and intraoperative scoring using established formulas. Stratified analyses were performed according to age, gender, presence of necrosis, and extracapsular spread to control potential confounders and evaluate diagnostic performance within subgroups. Chi-square test was applied to compare proportions, and p-values <0.05 were considered statistically significant. Receiver operating characteristic (ROC) curve analysis was also performed to determine the diagnostic performance of CT and intraoperative scoring, with the area under the curve (AUC) calculated.

## METHODS

A total of 323 patients with clinically suspected oral squamous cell carcinoma were included. The mean age was 51.51 ± 10.92 years, and the mean lymph node size on CT was 20.87 ± 5.82 mm. Among the participants, 187 (57.9%) were male and 136 (42.1%) female. Tumor staging revealed 160 patients (49.5%) with T1, 113 (35.0%) with T2, 39 (12.1%) with T3, and 11 (3.4%) with T4. Central necrosis was observed in 62 patients (19.2%), while extracapsular spread was detected in 64 patients (19.8%) (Table 1).

**Table 1:** Patient Demographics and Clinical Characteristics (n=323)

| Variables | Mean ± SD | Median | IQR |
|---|---|---|---|
| Age (Years) | 51.51 ± 10.92 | 55 | 16 |
| Lymph Node Size (mm) | 20.87 ± 5.82 | 24 | 10 |

Comparison of CT findings with histopathology showed that 106 lymph nodes (32.8%) were true positives, 181 (56.0%) true negatives, 33 (10.2%) false positives, and 3 (0.9%) false negatives. The sensitivity and specificity of CT were 97.2% (95% CI: 92.1–99.4) and 84.6% (95% CI: 79.1–89.2), respectively. Positive predictive value (PPV) was 76.3% (95% CI: 68.2–83.2), negative predictive value (NPV) was 98.4% (95% CI: 95.5–99.7), and overall diagnostic accuracy was 88.8% (95% CI: 84.8–92.1). The association between CT and histopathology was statistically significant ($\chi^2 = 142.6$, $p<0.001$) (Table 2).

**Table 2:** : CT Scan Results Compared with Histopathology (n=323)

| CT Result | Histopathology Positive | Histopathology Negative | Total | % of Total | $\chi^2$ | p-value |
|---|---|---|---|---|---|---|
| Positive | 106 (32.8%) | 33 (10.2%) | 139 | 43.0% | 142.6 | <0.001 |
| Negative | 3 (0.9%) | 181 (56.0%) | 184 | 57.0% | | |
| Total | 109 (33.7%) | 214 (66.3%) | 323 | 100% | | |

Chi-square test applied; level of significance $p<0.01$. The ROC curve for CT demonstrated an AUC of 0.91 (95% CI: 0.87–0.95), confirming excellent diagnostic performance (Figure 1).

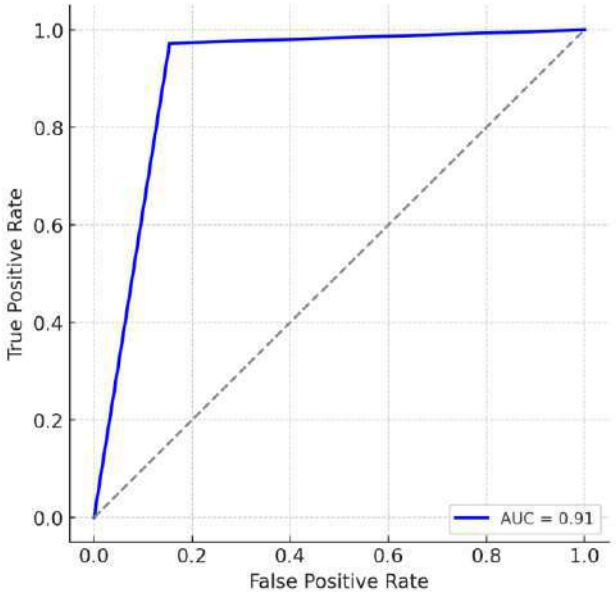


**Figure 1:** ROC Curve of CT vs Histopathology

Intraoperative scoring based on lymph node size, consistency, shape, and adherence showed variable distribution. Scores of 0 included 189 nodes (all histopathology negative, 58.5% of total); score 1 included 1 positive case (0.3%); score 2 included 10 positive and 1 negative case (3.4%); score 3 included 74 positive and 24 negative cases (30.3%); and score 4 included 24 nodes, all histopathology positive (7.4%) (Table 3).

**Table 3:** Distribution of Intraoperative Scores vs Histopathology (n=323)

| Score | Histopathology Positive | Histopathology Negative | Total | % of Total |
|---|---|---|---|---|
| 0 | 0 (0%) | 189 (58.5%) | 189 | 58.5% |
| 1 | 1 (0.3%) | 0 (0%) | 1 | 0.3% |
| 2 | 10 (3.1%) | 1 (0.3%) | 11 | 3.4% |

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| | | | | |
|---|---|---|---|---|
| 3 | 74 (22.9%) | 24 (7.4%) | 98 | 30.3% |
| 4 | 24 (7.4%) | 0 (0%) | 24 | 7.4% |
| Total | 109 (33.7%) | 214 (66.3%) | 323 | 100% |

When applying a cutoff score of ≥3 for malignancy, intraoperative scoring yielded 98 true positives (30.3%), 190 true negatives (58.8%), 24 false positives (7.4%), and 11 false negatives (3.4%). Sensitivity was 89.3% (95% CI: 82.0–94.3), specificity 88.8% (95% CI: 83.7–92.9), PPV 80.3% (95% CI: 71.7–87.1), NPV 94.5% (95% CI: 90.5–97.2), and diagnostic accuracy 89.2% (95% CI: 85.4–92.3). The association between intraoperative scoring and histopathology was statistically significant ($\chi^2$ = 165.8, p<0.001)(Table 4).

**Table 4:** Intraoperative Scoring (≥3) Compared with Histopathology (n=323)

| Intraoperative Score | Histo-pathology Positive | Histo-pathology Negative | Total | % of Total | $\chi^2$ | p-value |
|---|---|---|---|---|---|---|
| ≥3 (Malignant) | 98 (30.3%) | 24 (7.4%) | 122 | 37.8% | 165.8 | <0.001 |
| 0–2 (Non-malignant) | 11 (3.4%) | 190 (58.8%) | 201 | 62.2% | | |
| Total | 109 (33.7%) | 214 (66.3%) | 323 | 100% | | |

Chi-square test applied; level of significance p < 0.01. The ROC curve for intraoperative scoring demonstrated an AUC of 0.89 (95% CI: 0.84–0.94), reflecting high diagnostic performance (Figure 2).

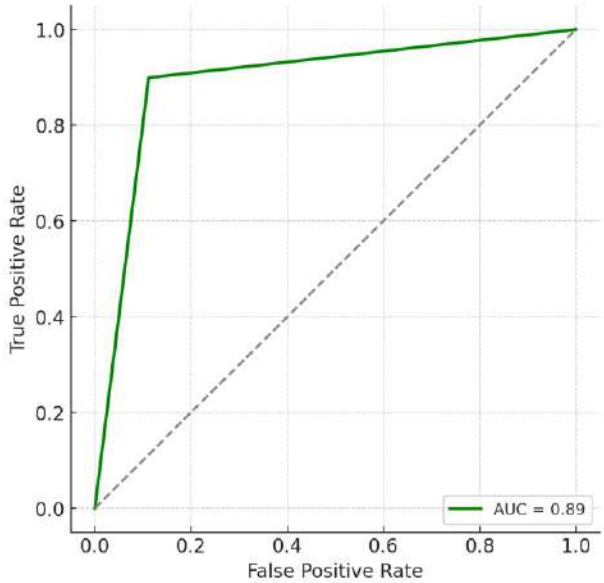


**Figure 2:** ROC Curve of Intraoperative Scoring vs Histopathology

When comparing diagnostic performance, CT demonstrated higher sensitivity (97.2% vs. 89.3%) and NPV (98.4% vs. 94.5%), while intraoperative scoring showed comparable specificity (88.8% vs. 84.6%) and overall accuracy (89.2% vs. 88.8%)(Figure 3).

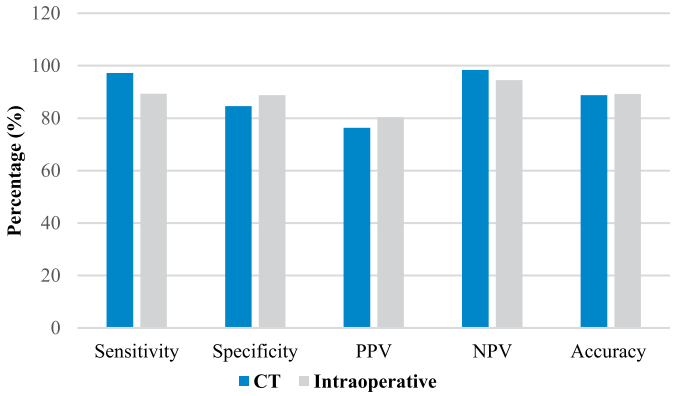


**Figure 3:** Comparative Diagnostic Performance: CT vs Intraoperative Scoring

## DISCUSSION

Oral squamous cell carcinoma (OSCC) remains a significant health burden worldwide and is particularly prevalent in South Asia, including Pakistan [9]. The presence of metastatic cervical lymph nodes is a well-established prognostic factor and directly influences survival and treatment planning. Accurate and timely identification of nodal metastasis is therefore critical [10]. In the present study, both computed tomography (CT) and intraoperative lymph node scoring were evaluated against histopathology as the gold standard. A statistically significant association was observed between both modalities and histopathological findings (p<0.001), confirming their diagnostic reliability [11]. The sensitivity of CT was 97.2%, consistent with previously published data, where CT demonstrated high accuracy for detecting metastatic nodes using size criteria, central necrosis, and extracapsular spread. Specificity was slightly lower, reflecting the tendency of reactive or inflammatory nodes to mimic metastatic involvement. These findings echo prior studies that also highlighted false positives as a limitation of CT [12]. The predictive values further support the utility of CT in clinical decision-making. With an NPV of 98.4%, CT can confidently rule out nodal metastasis, minimizing unnecessary neck dissections in negative patients [13]. This observation is in line with earlier reports, where CT reliably excluded metastasis when nodes appeared normal radiologically [14]. Intraoperative lymph node scoring, based on parameters such as size, consistency, shape, and adherence, demonstrated a sensitivity of 89.3% and specificity of 88.8% [15]. These values, though slightly lower in sensitivity compared to CT, were statistically significant (p<0.001) and comparable with other studies that support the role of intraoperative evaluation as an adjunct to preoperative imaging [16]. Importantly, intraoperative scoring provided additional tactile and visual cues of firmness and adherence that are not available on imaging. Such real-time information is

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particularly relevant for assessing extracapsular spread, where intraoperative adherence findings may supplement radiological suspicion [17]. The overall diagnostic accuracies of CT (88.8%) and intraoperative scoring (89.2%) were nearly identical, a finding corroborated by previous literature [18]. This reinforces the concept that both modalities are complementary: CT is invaluable for preoperative planning, while intraoperative scoring adds real-time confirmation and may guide the extent of neck dissection. From a clinical perspective, the implications are noteworthy. In low-resource settings such as Pakistan, where access to advanced imaging or PET-CT may be limited, combining CT with intraoperative scoring represents a cost-effective and practical approach [19]. The ability to make intraoperative judgments reduces dependence on expensive imaging modalities and provides surgeons with an evidence-based framework to tailor the extent of surgery. This is particularly beneficial in resource-constrained environments, where avoiding both under- and over-treatment is crucial for patient outcomes and healthcare efficiency. Extracapsular spread (ECS), observed in nearly one-fifth of patients in this study, remains a major prognostic concern [20]. While CT may suggest ECS through radiological features such as irregular margins, intraoperative findings of nodal adherence can serve as a real-time surrogate marker, helping surgeons anticipate the need for more extensive resections and adjuvant therapy [21]. False positives and negatives observed with both modalities underline the importance of a combined strategy. While CT may misclassify reactive nodes, and intraoperative scoring may misinterpret firm reactive nodes as malignant, their combined use reduces the likelihood of diagnostic error. These findings parallel those of international studies emphasizing the need for multimodal approaches [22].

The strengths of this study include a relatively large sample size and the use of histopathology as the gold standard, while limitations involve its single-center design and the absence of interobserver reliability testing. Future studies incorporating multi-institutional data and evaluating observer variability would further strengthen the evidence base. Another limitation is that the intraoperative scoring cutoff (≥3) was adapted from surgical practice experience and available literature, and while it performed well in this cohort, it requires formal external validation in larger, multicenter studies.

## CONCLUSIONS

In this study, computed tomography demonstrated a sensitivity of 97.2%, specificity of 84.6%, and diagnostic accuracy of 88.8% for detecting metastatic cervical lymph nodes in oral squamous cell carcinoma, while intraoperative scoring showed a sensitivity of 89.3%, specificity of 88.8%, and accuracy of 89.2%. Both methods showed statistically significant associations with histopathology and comparable overall diagnostic performance.

## Authors' Contribution

Conceptualization: KH
Methodology: KH, SA, BI, AK, M, BS
Formal analysis: SA, AK, BS, PD
Writing and Drafting: KH, BS, V, M
Review and Editing: KH, SA, BI, AK, M, BS, PD

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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# Gender Identification Based on Dental Micro-Esthetics: A Study of Dental Professionals' Perceptions

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## ABSTRACT

Dental micro-aesthetic traits are linked to gender-specific features in dentistry, but their reliability for gender identification remains controversial. **Objectives:** To assess the correlation between accurate gender identification and micro-aesthetic dental traits through the evaluation of frontal intraoral photographs by observers, specifically dental undergraduates, graduates, and postgraduates. **Methods:** A cross-sectional study was conducted at Lahore Medical and Dental College (June 2024 to May 2025) with 376 participants (99% response rate). Participants evaluated 10 anonymous frontal intraoral photographs for gender identification via a questionnaire. Descriptive statistics, chi-square tests, and logistic regression analyzed associations between accuracy and clinical experience (>3 vs. ≤3 years), using SPSS version 25.0. Photographs were selected for variability in micro-aesthetic traits. **Result:** The mean accuracy score was 5.38 ± 1.72 out of 10, with 58.8% scoring 4–6. Accuracy varied significantly (23.94% for Q8 to 70.21% for Q3, $p<0.05$). Males had higher accuracy of achieving correct answers ($p=0.033$), indicating that males were more likely to score above the median score of 5. Experienced clinicians prioritized tooth size ($p=0.005$) and triangular canines ($p=0.017$). Logistic regression showed experience-based differences in the correct identification of specific female photographs (OR = 0.564 for Q7, $p=0.033$; OR = 2.583 for Q9, $p<0.001$). **Conclusions:** Dental micro-aesthetic traits provide only moderate accuracy for gender identification due to considerable overlap and observer bias. Targeted education on trait variability is recommended.

## INTRODUCTION

The study of dental morphology for gender determination has gained traction in recent years, offering applications in both forensic and clinical dentistry. Tooth morphology plays a key role in smile aesthetics and overall facial harmony. Treatment planning now increasingly considers societal standards of beauty—such as balance, proportion, and harmony—framed through macro-esthetic, mini-esthetic, and micro-esthetic elements. Dental micro-esthetics focus on tooth shape, size, color, alignment, gingival characteristics, and texture, which collectively influence smile attractiveness [1-3]. A key question is whether mini-aesthetic traits exhibit sexual dimorphism. The "theory of temperament" suggests that tooth shape may reflect emotional characteristics, such as sanguine (dynamic) or melancholic (sensitive), though its clinical validity is debated [2]. Gender-based stereotypes often associate women with rounded, ovoid teeth and men with angular, square forms, influencing dental education and prosthetic design, despite studies finding no consistent biological correlation between tooth morphology and

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gender [2, 4]. Specific micro-aesthetic features have been frequently investigated in relation to gender differentiation and aesthetic perception. Tooth size is generally larger in male than in female, with canines often regarded as the most sexually dimorphic teeth, although overlap limits their diagnostic value [5]. In addition, the morphology of the maxillary central and lateral incisors has also been examined, with males more frequently presenting larger crown dimensions in height and width compared to females, though variability remains substantial. Tooth color also contributes to esthetic perception, with female dental students more often preferring lighter shades, while male dental students tend to report a higher need for orthodontic treatment and ceramic veneers [6]. The presence of anterior restorations has also been noted in desired treatments, particularly tooth-colored restorations among students from lower-income households, though mismatched color or contour has not been explicitly identified as reducing esthetic acceptance. Other features, such as alignment and gingival display, significantly influence attractiveness ratings. Incisal alignment plays a critical role, as midline deviations combined with gingival display reduce esthetic scores, whereas coincident midlines yield higher ratings across both dentists and laypersons [7]. In a Romanian sample, gingival exposure between 0–3 mm was most frequently selected by dentists as ideal for an esthetic smile (70.4%), while excessive gingival exposure (median 4 mm) was considered the least attractive [8]. Gingival pigmentation significantly influences smile esthetics, with laypersons often rating smiles with less pigmentation as more attractive, potentially differing from dental professionals' more critical assessments [9]. In contrast, soft tissue features, such as lips and gingiva, play a critical role in gender differentiation, as deep learning analyses of intraoral photographs reveal that these features are more distinguishable than hard tissue features like teeth for identifying gender differences [10]. While oral hygiene conditions are not directly addressed in gender differentiation studies, Zhou *et al.* further demonstrated that gender-related morphological differences are more pronounced in the mandibular region compared to the maxillary region [10]. Oral pigmentation and dental conditions—including caries, crowding, missing teeth, and restorations—also reduce esthetic acceptance, with dental professionals being more critical than laypersons. Calheiros-Lobo *et al.* showed that dental professionals more accurately identify morphological anomalies like lateral incisor agenesis than laypeople, implying that training enhances sensitivity to aesthetic traits [11]. Negruțiu *et al.* stated that gingival exposure significantly affects smile perception, with varying preferences noted between dentists and laypersons [8]. However, Mahn *et al.* reported gender misidentification based on presumptions about tooth shape, such as rounded being feminine or squarish being masculine, highlighting the unreliability of morphology alone [4]. Najafi *et al.* additionally highlighted how different professional roles assess gingival display and midline discrepancies, reflecting varying degrees of aesthetic awareness [7]. Despite these associations, significant gaps remain in the literature. Results vary across populations and are often shaped by cultural expectations. Tooth morphology alone has shown only moderate predictive accuracy for gender identification, with some studies reporting results close to chance [4]. Due to these limitations, it is necessary to investigate not only biological dimorphism but also how dental professionals perceive and utilize these micro-aesthetic traits in practice. This study WAS designed to enhance dental education by determining whether specific morphological features should be prioritized in didactic and clinical training as gender-specific traits. Since gender-specific dental characteristics are not universally consistent—male may present with rounded teeth and female with squarish ones—overreliance on these distinctions could lead to misjudgments.

Moreover, little is known about how reliably dental professionals at different training levels can identify gender based on these traits alone. This uncertainty highlights a gap between theoretical assumptions and practical perception in dentistry. This study aimed to assess the correlation between accurate gender identification and micro-aesthetic dental traits through the evaluation of frontal intraoral photographs by dental undergraduates, graduates, and postgraduates.

## METHODS

This cross-sectional descriptive study was conducted from June 2024 to May 2025 in Lahore Medical and Dental College, Lahore. The study was approved by the college's Institutional Review Board, LMDC/FD/1549/23. The study population consisted of dental professionals, including dental undergraduates, graduates, and postgraduate trainees, who evaluated anonymous frontal intraoral photographs to determine the gender of the photographs based on dental micro-esthetics. Participants were eligible if they were aged 20- 30 years and provided informed consent. Those with previous training in forensic odontology were excluded. The study utilized a non-probability convenience sampling method. The study utilized a non-probability convenience sampling method. The single-proportion formula $n=Z21-\alpha/2p(1-p)/d^2$, where p was the anticipated proportion, d was the margin of error, and $Z1-\alpha/2$ the standard normal value for a two-sided 95% confidence level. Using p=0.538 (frequency of correct

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identification), d=0.05, and Z=1.96, the required sample was n= 382 [2]. Allowing for a 5% non-response/dropout, the adjusted target was 402 participants. The questionnaire used in this study was adapted from Qali *et al.* which assessed gender identification using intraoral photographs [2]. The adapted tool retained the core structure of Qali *et al.* (10 anonymized frontal intraoral photographs) but was expanded with additional demographic and clinical experience items to suit our educational context [2]. Face and content validity were established by subject experts, who reviewed all items for relevance and clarity. The questionnaire was pilot-tested on 20 dental professionals; minor wording changes were made based on their feedback. Internal consistency reliability was assessed using Cronbach's alpha and showed acceptable values ($\alpha \geq 0.71$). The final questionnaire consisted of four sections: (1) demographic data (age, gender), (2) current academic level (undergraduate, graduate, postgraduate) and years of clinical experience, (3) 10 unlabeled frontal intraoral photographs in which participants selected whether each dentition was male or female, and, (4) 10 statements on morphological features distinguishing male and female dentitions that participants reported using in routine practice. Section 3- Gender-identification photographs: 10 anonymized frontal intraoral photographs of maxillary and mandibular anterior teeth (5 male and 5 female dentitions), cropped to show only teeth and gingiva, were presented in random order to the participants. For each photograph (Q1–Q10), participants answered the question: "In your opinion, this dentition belongs to:" with response options "Male" and "Female." Each correct response was scored as 1 and each incorrect response as 0, giving a total accuracy score ranging from 0 to 10, where higher scores indicate greater accuracy. For interpretation, scores of 0–3 were classified as low accuracy, 4–6 as moderate accuracy, and 7–10 as high accuracy. Section 4- Morphological feature use: Ten items addressed, which micro-aesthetic features participants routinely use to distinguish male from female dentitions in everyday practice. Items covered the following features: tooth color, tooth size, pigmentation of mucosa, canine shape, incisal alignment, incisal crowding, presence of diastema, anterior restorations, poor oral hygiene, and maxillary central/lateral crown morphology. Each statement was phrased in the form "I use [feature] to help differentiate between male and female dentitions" and rated on a 3-point Likert scale (agree, neutral, disagree). All participants provided informed consent before enrollment, with the right to withdraw from the study at any time. The survey was distributed both physically within the department and digitally through online platforms. Participants had seven days to complete the questionnaire, with a reminder sent after one week for non-respondents. Once collected, the data were entered into SPSS statistical software for analysis. Data were analyzed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., NY, USA). Descriptive statistics (frequencies, percentages, means, and standard deviations) were computed for participant characteristics and questionnaire responses. For the 10-item accuracy score, scores 0–3 was classified as low, 4–6 as moderate, and 7–10 as high accuracy. For inferential analyses, the total accuracy score was further dichotomized at the median (≤5 vs. >5) to create a binary accuracy variable. Chi-square tests were used to examine associations between this dichotomized accuracy variable and categorical participant characteristics (gender, age group, qualification, and clinical experience). For questionnaire photograph-specific performance, the proportion of participants who correctly identified each photograph (Q1–Q10) was calculated. Two-sided binomial tests against a 50% expected accuracy (chance level) were used to obtain p-values, and 95% confidence intervals were computed for each proportion. For each of the 10 photographs in the questionnaire, separate binary logistic regressions were performed with clinical experience (>3 years vs. ≤3 years) as the dependent variable and correct/incorrect responses for each intraoral photograph as independent variables. Thus, for each photograph, a 2×2 contingency structure (correct vs. incorrect by >3 vs. ≤3 years of experience) underpinned the odds ratios. Odds ratios (ORs) with 95% confidence intervals (CIs) and p-values were reported. Associations between clinical experience (>3 vs. ≤3 years) and responses to each of the 10 morphological feature items (agree, neutral, disagree) were also examined using chi-square tests of independence.

## RESULTS

A total of 376 responses were received, giving a response rate of 94%. 190 (50.5%) undergraduates, 131 (34.8%) graduates, and 55 (14.6%) postgraduates. Out of the total participants, 258 (68.6%) were female, and 118 (31.4%) were male. The mean age of participants was 24.05 ± 2.83 years. 290 (77%) participants had 3 years or less of clinical experience, and 86 (23%) had more than 3 years' experience. The average mean score of correct answers of the participants was 5.38 ± 1.72 (range 0–10). Using the predefined categories, 56 (14.9%) had low accuracy (scores 0–3), 221 (58.8%) had moderate accuracy (scores 4–6), and 99 (26.3%) had high accuracy (scores 7–10). Overall, when dichotomized at the median, 189 (50.3%) participants scored 5 or less, and 187 (49.7%) scored more than 5. The results present the distribution of participant characteristics according to accuracy scores dichotomized at ≤5 and >5. Chi-square test for gender showed a significant association, p=0.033, indicating that

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males are more likely to score above the median score of 5 (Table 1).

**Table 1:** Association Between Participant Characteristics and Dichotomized Accuracy Score

| Variables | Low Accuracy (>5), n (%) | High Accuracy (>5), n (%) | p-value |
|---|---|---|---|
| **Gender** | | | |
| Male | 50 (42.4%) | 68 (57.6%) | 0.033* |
| Female | 139 (53.9%) | 119 (46.1%) | |
| **Age** | | | |
| 20–25 Years | 138 (50.2%) | 137 (49.8%) | 0.910 |
| 26–30 Years | 51 (50.5%) | 50 (49.5%) | |
| **Qualification** | | | |
| Undergraduate | 98 (51.6%) | 92 (48.4%) | 0.582 |
| Graduate | 62 (47.3%) | 69 (52.7%) | |
| Postgraduate | 29 (52.7%) | 26 (47.3%) | |
| **Clinical Experience** | | | |
| ≤3 Years | 147 (50.7%) | 143 (49.3%) | 0.665 |
| >3 Years | 42 (48.8%) | 44 (51.2%) | |

*Indicated statistical significance at p≤0.05

The study shows accuracy for each photograph (Q1–Q10). Q1–Q10 correspond to the 10 anonymized frontal intraoral photographs (5 male and 5 female dentitions) presented in random order, and the accuracy reported for each item represents the proportion of participants who correctly identified the sex of that specific photograph. The proportion of correct responses, 95% confidence intervals, and two-sided binomial test p-values against a 50% chance level are reported. All p-values were <0.05, indicating that the accuracy for each photograph differed significantly from random guessing. Accuracy varied across photographs, being highest for Q3 (70.21%), Q4 (66.76%), and Q10 (65.69%), and lowest for Q8 (23.94%). The "Correct Answer" column specifies the true gender of each anonymized photograph (5 male, 5 female in random order) (Table 2).

**Table 2:** Accuracy for Gender Identification for Each Photograph (Q1 to Q10)

| Question | True Gender of Dentition in the Photograph | Correct Responses, n (%) | Incorrect Responses, n (%) | 95% CI for % Correct | p-value v/s 50% Accuracy[a] |
|---|---|---|---|---|---|
| Q1 | Female | 236 (62.77%) | 140 (37.23%) | 57.9–67.7 | <0.001* |
| Q2 | Male | 153 (40.69%) | 223 (59.31%) | 35.7–45.7 | <0.001* |
| Q3 | Male | 264 (70.21%) | 112 (29.79%) | 65.6–74.9 | <0.001* |
| Q4 | Female | 251 (66.76%) | 125 (33.24%) | 62.0–71.5 | <0.001* |
| Q5 | Male | 218 (57.98%) | 158 (42.02%) | 53.0–63.0 | 0.002* |
| Q6 | Female | 224 (59.57%) | 152 (40.43%) | 54.6–64.6 | <0.001* |
| Q7 | Female | 212 (56.38%) | 164 (43.62%) | 51.3–61.4 | 0.015* |
| Q8 | Male | 90 (23.94%) | 286 (76.06%) | 19.6–28.3 | <0.001* |
| Q9 | Female | 149 (39.63%) | 227 (60.37%) | 34.7–44.6 | <0.001* |
| Q10 | Female | 247 (65.69%) | 129 (34.31%) | 60.9–70.5 | <0.001* |

[a]Two-sided binomial test against 50% expected accuracy (chance level). *Indicates the statistical significance with p-value <0.05. Note: Each item (Q1–Q10) corresponds to one anonymous intraoral photograph depicting either a male or a female dentition, not both. The column "True gender of dentition in photograph" therefore reflects the actual gender of the dentition shown to participants. Percentages represent the proportion of participants who correctly identified that gender.

Separate binary logistic regression models were performed with clinical experience (>3 years vs. < 3 years) as the dependent variable and correct/incorrect response for each photograph as the predictor. Only Q7 and Q9 emerged as significant. Participants who correctly identified the female dentition in Q7 had 43.6% lower odds of having >3 years of clinical experience (OR = 0.564, 95% CI 0.333–0.954, p=0.033)). In contrast, those who correctly identified the female dentition in Q9 had 2.58 times higher odds of having >3 years of experience (OR = 2.583, 95% CI 1.522–4.384, p<0.001). These odds ratios are based on 2×2 tables of correctness (correct vs. incorrect) by experience group. The 10 morphological feature items corresponded directly to the questionnaire statements "I use -feature- to help differentiate between male and female dentitions" (rated agree/neutral/disagree). Their endorsement frequencies and the chi-square tests for differences by clinical experience are summarized. Overall, tooth size was the most frequently endorsed feature, followed by maxillary central/lateral crown morphology and mucosal pigmentation. Chi-square analysis indicated that features such as size, triangular canines, incisal alignment, incisal crowding, diastema, anterior restorations, and poor oral hygiene were used differently by clinicians, indicating that clinical experience shapes which specific cues clinicians rely on for gender judgements. In contrast, broader characteristics such as tooth color, mucosal pigmentation, and maxillary crown morphology were endorsed by all participants, suggesting that these cues are viewed as relevant by all clinicians (Table 3).

**Table 3:** Prominent Features Used to Distinguish Between Male and Female Dentition

| Morphological Feature | Agree, n (%) | Disagree, n (%) | Neutral, n (%) | Chi-Square (Clinical Experience) |
|---|---|---|---|---|
| Tooth Color | 127 (33.8%) | 118 (31.4%) | 131 (34.8%) | $\chi^2 = 3.274$, p=0.195 |
| Size | 274 (72.9%) | 26 (6.9%) | 76 (20.2%) | $\chi^2 = 10.573$, p=0.005* |
| Pigmentation of Mucosa | 213 (56.6%) | 42 (11.2%) | 121 (32.2%) | $\chi^2 = 0.429$, p=0.807 |
| Triangular Canines | 195 (51.9%) | 57 (15.2%) | 124 (33.0%) | $\chi^2 = 8.169$, p=0.017* |
| Incisal Alignment | 153 (40.7%) | 82 (21.8%) | 141 (37.5%) | $\chi^2 = 6.245$, p=0.044* |
| Incisal Crowding | 89 (23.7%) | 142 (37.8%) | 145 (38.6%) | $\chi^2 = 22.374$, p<0.001* |
| Incisal Diastema | 101 (26.9%) | 136 (36.2%) | 139 (37.0%) | $\chi^2 = 6.473$, p=0.039* |

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| | | | | |
|---|---|---|---|---|
| Anterior Restoration | 107 (28.5%) | 158 (42.0%) | 111 (29.5%) | $\chi^2 = 17.213$, p<0.001* |
| Poor Oral Hygiene | 139 (37.0%) | 128 (34.0%) | 109 (29.0%) | $\chi^2 = 10.586$, p=0.005* |
| Maxillary Central/ Lateral Crown | 215 (57.2%) | 46 (12.2%) | 115 (30.6%) | $\chi^2 = 2.152$, p=0.341 |

* Indicates statistical significance at p≤0.05

## DISCUSSION

The results of this study offer significant insights into the capacity of dental professionals and students to identify gender using dental micro-aesthetic traits, highlighting both the potential and limitations of these features in clinical and forensic dentistry. With a mean accuracy score of 5.38 ± 1.72 for gender identification from 10 intraoral photographs, the findings determined moderate success, with notable inconsistencies in accuracy across photographs. This variability indicates that some dental images presented clearer gender-specific cues, while others were ambiguous, underscoring the challenges of relying on micro-aesthetic traits for gender determination. A significant association between participant gender and accuracy (p=0.033) indicated that male were more likely to score above the median (5 marks), which is in contrast to Alam *et al.* who stated that females were more likely to notice aesthetic impacts [3]. Social media significantly influences female patients' perceptions of dental aesthetics, with increased exposure to dental content on platforms like Snapchat and Instagram driving a preference for aesthetic treatments such as bleaching and veneers [12]. Cheng *et al.* found gender-based differences in aesthetic perception, with female laypeople showing a stronger preference for parallel smile arcs and reduced gingival and incisor display, suggesting differing aesthetic sensitivities compared to male participants and professionals [13]. This pattern suggests that gender identification accuracy is shaped not only by dental morphology but also by participants' preconceived concepts of gendered aesthetics, potentially reinforced through dental training or cultural influences on facial profile preferences [14, 15]. Clinical experience variably affected performance. Logistic regression showed that correct identification of Q7 (female) was associated with lower odds of having >3 years of experience (OR = 0.564, p=0.033), suggesting subtler cues in Q7 challenged experienced clinicians reliant on features like canine size [5, 6]. In contrast, Q9 likely included clearer cues, such as gingival exposure or tooth alignment, which more experienced clinicians were trained to recognize with greater precision [8, 16]. The results demonstrated that experienced clinicians prioritized tooth size and canine morphology for gender identification, consistent with forensic evidence showing significant sexual dimorphism in canine dimensions and ridge prominence [5, 17]. Less experienced participants may rely on general esthetic features such as tooth color and alignment, findings consistent with El Mourad *et al.* who reported that dental students often focus on these aspects in self-assessments of their own smiles.[6] However, such features may be less useful for gender identification tasks that require attention to more sexually dimorphic traits [6, 16]. These findings have important implications for dental education. The moderate accuracy (58.8% scoring 4–6) and reliance on gendered stereotypes suggest that current curricula may overemphasize simplistic morphological associations, such as rounded teeth for female and angular teeth for male [2, 4]. Dental training should incorporate modules on sex and gender differences in oral health, recognizing that both biological and sociocultural factors influence oral health outcomes and care-seeking behaviors [18]. Addressing cognitive biases is also critical, as participants' perceptions may be shaped by assumptions rather than objective evidence [19]. Nakhapaksirat *et al.* stated that targeted interventions like workshops and reflective case discussions help dental students transition to independent practice by equipping them with skills to recognize and manage cognitive biases, thereby promoting evidence-based clinical decision-making [19]. Furthermore, incorporating advanced visual aids like intraoral scans, as demonstrated by Schulz-Weidner et al. and Menon and Kumar, forensic techniques such as 3D scanning, can enhance training by improving students' ability to interpret subtle aesthetic and morphological cues [20, 21]. In forensic dentistry, the study highlights the limitations of using dental micro-aesthetics for gender identification. Ajmal *et al.* confirmed sexual dimorphism in canine morphology but noted trait overlap, reducing reliability, as seen in the low accuracy for Q8 [5]. This aligns with findings from Viciano *et al.* and Heng *et al.* which highlight that while odontometric analysis and dental morphology display measurable dimorphism, significant trait variability necessitates the use of multimodal methods, including advanced imaging, to improve the accuracy of sex estimation [22, 23]. Stojilković *et al.* highlight that dental aesthetics significantly impact psychosocial well-being and self-esteem, with varying perceptions of traits like tooth alignment or color influencing personal and social confidence.[24] This psychosocial dimension, as noted by Campos *et al.* underscores the need for dentists to consider how patients' aesthetic perceptions may influence the interpretation of dental traits in gender identification [25]. Advanced imaging like CBCT and OPG has been evaluated for forensic sex estimation, with CBCT offering higher accuracy due to its 3D visualization of dental and craniofacial structures, though limited by cost and accessibility [26]. Integrating dental traits with other forensic markers, such as cranial features, could enhance

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gender determination.

This study was single center with a limited sample size and used only intraoral photographs, which may not capture the full spectrum of dental micro-aesthetic traits. Participant performance may have been influenced by prior training, personal biases, and cultural perceptions of aesthetics, limiting generalizability. Future research should involve larger, multicenter samples, including advanced imaging techniques (e.g., CBCT, 3D scans), and integrating multimodal forensic markers to improve the accuracy and reliability of gender identification from dental traits.

## CONCLUSIONS

This study showed that dental professionals and students moderately succeeded in identifying gender using tooth shape and size. They correctly identified gender in about half the intraoral photographs, with accuracy varying widely from low to high. Male participants generally performed better than female participants, suggesting that personal biases may influence how dental features are interpreted. Experienced professionals focused on tooth size and canine shape, but accuracy depended on trait clarity, while less experienced dentists relied on less reliable features like tooth color. These findings show that dental features can help identify sex, but are not always dependable due to overlapping traits and individual biases.

## Authors' Contribution

Conceptualization: MIR, NF
Methodology: AFB
Formal analysis: MUDA, UWJ, SRK
Writing and Drafting: AFB, AAB
Review and Editing: AFB, MUDA, UWJ, MIR, NF, AAB, SRK

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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# Frequency of Congenital Anomalies in Newborns

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## ABSTRACT

Congenital abnormalities (CA) are anatomical or performance-based anomalies that express themselves during the in-utero growth and may be diagnosed during pre-birth, during delivery, and post-birth. **Objective:** To review the incidence of birth defects in infants. **Methods:** The descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Civil Hospital, Karachi, during a period of two years, i.e., March 2017 to March 2019. This study had 213 pregnant women. After birth, there was the identification of congenital anomalies in the newborns by visual examination, and other factors were established by the history of the patient or medical records. All the data were recorded on a pre-determined proforma template. **Results:** The average age of the participants was 27.381 ± 4.08. The most common congenital anomalies were anencephaly (19.7%), hydrocephalus (15.5%), absence of ear/figure/toe/scrotum/arm/leg/limbs (9.4%), cleft lip and cleft palate (8.9%), meningomyelocele (7%), and talipes (8%). The causal variables were maternal age 30 years and above (20.2%), paternal age 35 years and above (19.7%), maternal diabetes mellitus (20.2%), consanguinity marriage (20.2%), maternal infection during pregnancy (8.9%), and maternal folic acid supplementation (61.5%). These are said to be descriptive and not causal. **Conclusions:** This study highlights the rate of congenital anomalies and the types of congenital anomalies. Its results touch on the importance of routine antenatal care and prenatal screening to intervene and manage affected pregnancies at an earlier stage.

## INTRODUCTION

Congenital abnormalities (CA) are anatomical or performance-based abnormalities (e.g., endocrine or sensory functional conditions like congenital deafness or visual impairment) that appear during in utero growth and could be diagnosed prenatally, at birth, or later on [1]. The WHO indicates that congenital defects occur in approximately 6 percent of live births in the world. They cause 17-42 percent of deaths in infants, and there is variability in the deaths in various regions and different countries [2]. A study by Shahid et al. in Pakistan has shown that congenital abnormalities were a major cause of high perinatal mortality rate, and the Pakistan Health and Demographic Survey 201718 states that the perinatal mortality rate in Pakistan has been consistently high over the last decade at 75 per 1,000 births [3]. CA is a result of the abnormal development process that is inherent in which the development of a tissue or organ is arrested or slowed down prematurely [4]. Congenital anomalies have been the major cause of spontaneous miscarriage, stillbirth, perinatal mortality, and long-term disability that cause significant challenges to affected persons, their families, and to healthcare systems [5]. The anomalies can be associated with one organ or a combination of organ systems and have various possible causes. Nevertheless, the cause that lies behind the whole situation is not known in about half of all cases. Among those with an identifiable cause, about 20–25% are believed to result from a combination of genetic and environmental factors. Recent

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studies have expanded our understanding of monogenic disorders frequently associated with congenital anomalies, while emerging methods have also uncovered non-Mendelian genetic factors, including interactions between genes and environmental exposures [6]. The prevalence of congenital anomalies is strongly influenced by genetic, environmental, and socioeconomic factors. According to the WHO, the majority of severe congenital disorders occur in low- and middle-income countries [7]. Gastrointestinal tract and abdominal wall anomalies are among the most frequently observed congenital anomalies, ranking as the fourth most common structural anomalies after those affecting the heart, nervous system, and urogenital tract [8]. In a systematic review and meta-analysis study by Staniczek *et al.* adolescents and young women living in socioeconomically poor neighborhoods were reported to be more susceptible to giving birth to children with congenital anomalies. This increased danger is due to the lack of access to vaccination services, insufficient folic acid consumption, and little preconception and antenatal care. Also, young women who are exposed to maternal infections are especially at risk of giving birth to children with congenital abnormalities [9]. Geda *et al.* performed a meta-regression analysis and identified that maternal illness, unidentified drug use, low birth weight, khat chewing, exposure to chemicals, and never use of folic acid were statistically significant factors that could lead to the risk of congenital anomalies in low-resource settings [10]. High-quality antenatal care, skilled attendance at birth, and appropriate management of small and sick newborns play a vital role in reducing the incidence of congenital anomalies and neonatal mortality. Integrating the prevention and management of congenital anomalies into existing maternal, reproductive, and child health services is essential for improving outcomes [11].

This study aimed to determine the most common congenital anomaly in newborns and identify the causative factors in our population, so that preventable measures taken to prevent the most frequent congenital anomaly and prenatal diagnosis can be made to take any decision for intervention. A congenital anomaly was defined as the presence of any of the following conditions, which were identified by visual examination: hydrocephalus, characterized by an enlarged head with prominence of the forehead; anencephaly, defined by a small head with no prominence of the forehead; cleft lip, which is the partial fusion of the upper lip; cleft palate, the partial fusion of the upper jaw; talipes, where the foot is twisted from its normal shape and position; spina bifida, which is a malformation of the vertebral column through which meninges may or may not protrude; and omphalocele, the protrusion of the intestine through a defect in the abdominal wall that is covered by a membrane. The research aimed to identify the frequency of congenital anomalies in newborns and the causes behind these anomalies.

## METHODS

This descriptive cross-sectional study was undertaken at Unit 2 of the Department of Obstetrics and Gynecology, Civil Hospital Karachi, during the span of two years, from March 2017 to March 2019, following approval of the research proposal by CPSP (CPSP Letter number CPSP/REU/OBG-2015-183-7029). The sample size was determined using the Open Epi sample size calculator tool with a prevalence of 5.26% [5], a margin of error of 3%, and a 95% confidence interval, resulting in an estimated sample size of 213. Formula: $n=Z2 \times p \times (1-p) / d^2$. Where n is the required sample size, Z=1.96for a 95% confidence interval, p=0.0526 (prevalence of congenital anomalies [5]), and d=0.03 (absolute precision). Substituting these values: n = (1.96) 2 x 0.0526 x (1 – 0.0526) / (0.03)2. n=213 (Thus, the minimum required sample size was 213 participants). Participants were selected by consecutive sampling with a non-probability sampling technique. Maternity age was limited to 19 45 years, both primigravida and multipara women, and gestational age of over 20 weeks. Those who were pregnant with twins or below 20 gestational weeks were excluded. In order to start data collection, the College of Physicians and Surgeons of Pakistan were consulted. All women who followed the inclusion criteria provided informed consent. These women were already in the delivery room in the Department of OBGYN, Unit 2 of Civil Hospital Karachi. Congenital anomalies of the newborns were detected by observing the babies after delivery. The medical history and records were used to get the maternal and pregnancy-related factors. Data such as maternal demographic information, obstetric history, health status, and other clinical findings were collected. A review of the prenatal ultrasound scans, where available, was also done to determine and categorize congenital abnormalities before birth. Maternal infection during pregnancy was documented in relation to clinical history, medical records, and any laboratory testing that was performed. Commonly suspected congenital pathogens (parvovirus B19, varicella, herpes simplex virus, syphilis, and Toxoplasma) were also included in the infections. Not every infection could be serologically confirmed because of the restrictions of routine testing in the hospital. History and prescription records were used to document the folic acid supplementation. Descriptive statistics were utilized to investigate the relationships between maternal infections, folic acid supplementation, and congenital abnormalities, but due to the low number of confirmed infections, they could not perform a robust correlation analysis. All the data were entered into a pre-

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coded proforma and processed to identify the nature and the frequency of congenital anomalies as well as to investigate the relationship with maternal or pregnancy factors. The assessments were all carried out under the guidance of a consultant who has a background of more than five years. To analyze the data, SPSS version 22.0 was employed. Quantitative variables, such as the age of the mother, paternal age, pregnancies, and gestational age, were calculated in terms of the mean and the standard deviation. Qualitative variables like the factors that contribute to the occurrence of congenital anomalies (maternal age, paternal age, consanguinity, folic acid intake, infections, and diabetes) and the nature of congenital anomalies were determined in terms of frequency and percentage. The variables such as gestational age and parity were stratified to determine the effect of these variables on the outcome.

## RESULTS

A total of 213 expectant mothers were included in the study, with a mean maternal age of 27.38 ± 4.08 years, a mean paternal age was 31.99 ± 5.57 years, a mean parity was 3.22 ± 1.89, and a mean gestational age was 32.17 ± 4.85 weeks, as summarized in table 1.

**Table 1:** Descriptive Statistics of Characteristics of Patients

| Variables | Mean ± SD | 95% Confidence Interval |
|---|---|---|
| Maternal Age (Years) | 27.38 ± 4.08 | 26.83-27.94 |
| Paternal Age (Years) | 31.99 ± 5.57 | 28.54-35.44 |
| Parity | 3.22 ± 1.89 | 2.95-3.49 |
| Gestational Age (Weeks) | 32.17 ± 4.85 | 31.52-32.83 |

Among these 213 newborns, 161 (75.6%) were born to multigravida women and 52 (24.4%) to primigravida women. Single congenital anomalies were observed in 175 (82.2%) newborns, while multiple anomalies occurred in 38 (17.8%). The frequency of congenital anomalies in newborns is presented in table 2.

**Table 2:** Frequency of Congenital Anomalies in Newborns

| Congenital Anomaly | n (%) |
|---|---|
| Anencephaly | 42 (19.7%) |
| Hydrocephalus | 33 (15.5%) |
| Cleft Lip | 10 (4.7%) |
| Talipes | 17 (8.0%) |
| Omphalocele | 7 (3.3%) |
| Gastroschisis | 4 (1.9%) |
| Meningomyelocele | 15 (7.0%) |
| Cleft Palate | 4 (1.9%) |
| Encephalocele | 2 (0.9%) |
| Meningocele | 6 (2.8%) |
| Hydrops Fatalis | 7 (3.3%) |
| Absence of Ear/Figure/Toe/scrotum/Arm/Leg/Limbs | 20 (9.4%) |
| Cleft Lip + Cleft Palate | 19 (8.9%) |
| Hydrocephalus +Cleft lip + Cleft palate | 3 (1.4%) |
| Hydrocephalus + Talipes | 7 (3.3%) |
| Hydrocephalus + Encephalocele | 4 (1.9%) |
| Meningocele + Talipes | 3 (1.4%) |
| Hydrocephalus + Polydactyl | 2 (0.9%) |
| Other | 8 (3.8%) |

As this study only included affected newborns and did not include a comparison group of unaffected newborns, these data are descriptive only, and no causal associations can be inferred. Maternal and pregnancy-related factors among newborns with congenital anomalies included maternal age >30 years (20.2%), paternal age ≥35 years (19.7%), diabetes (20.2%), consanguineous marriage (20.2%), infections during pregnancy (8.9%), and folic acid supplementation (61.5%), as summarized in table 3.

**Table 3:** Frequency of Maternal and Pregnancy-Related Factors Among Newborns with Congenital Anomalies

| Factors | Frequency (%) |
|---|---|
| **Maternal Age (Years)** | |
| ≤ 30 Years | 170 (79.8%) |
| >30 Years | 43 (20.2%) |
| **Paternal Age (Years)** | |
| <35 Years | 171 (80.3%) |
| ≥35 Years | 42 (19.7%) |
| **Diabetic Mellitus** | |
| Yes | 43 (20.2%) |
| No | 170 (79.8%) |
| **Consanguineous Marriage** | |
| Yes | 43 (20.2%) |
| No | 170 (79.8%) |
| **Infection During Pregnancy** | |
| Yes | 19 (8.9%) |
| No | 194 (91.1%) |
| **Folic Acid Supplementation** | |
| Yes | 131 (61.5%) |
| No | 82 (38.5%) |

This table presents the frequency and percentage of various maternal and pregnancy-related factors observed in newborns with congenital anomalies. The factors are reported as associations and are not established as causes.

On analysis of the 213 newborns, certain congenital anomalies were observed to vary with gestational age and maternal parity. Anencephaly (22.6% vs 11.1%, p=0.006), talipes (5.7% vs 14.8%, p=0.032), meningomyelocele (9.4% vs 0%, p=0.019), and absence of limbs (6.3% vs 18.5%, p=0.008) differed significantly between neonates delivered at <35 weeks and those ≥35 weeks. Encephalocele was significantly more frequent among primigravida than among multigravida (3.8% vs 0%, p=0.012), whereas most other anomalies showed no significant differences by parity. Regarding maternal and pregnancy-related factors, none of the factors were significantly associated with

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gestational age. However, maternal age >30 years (p=0.003), paternal age ≥35 years (p= <0.001), and maternal diabetes (p=0.029) were significantly associated with the occurrence of congenital anomalies when stratified by parity. Other factors, including consanguinity, infection during pregnancy, and folic acid supplementation, did not show significant associations, as shown in Table 4.

**Table 4:** Congenital Anomalies and Associated Factors

| Variables | Group 1 | Group 2 | p-value | Significant | Comparison Basis |
|---|---|---|---|---|---|
| Anencephaly | <35 Weeks: 22.6% | ≥35 Weeks: 11.1% | 0.006 | Yes | Gestational Age |
| Talipes | <35 Weeks: 5.7% | ≥35 Weeks: 14.8% | 0.032 | Yes | |
| Meningomyelocele | <35 Weeks: 9.4% | ≥35 Weeks: 0% | 0.019 | Yes | |
| Absence of Limbs | <35 Weeks: 6.3% | ≥35 Weeks: 18.5% | 0.008 | Yes | |
| Encephalocele | Primigravida: 3.8% | Multigravida: 0% | 0.012 | Yes | Maternal Parity |
| Other Anomalies by Parity | No Significant Difference | No Significant Difference | >0.050 | No | Maternal Parity |
| Maternal Factors (GA Association) | No Factor Significant | – | – | No | Gestational Age |
| Maternal Age >30 Years | Associated | – | 0.003 | Yes | Parity-Stratified |
| Paternal Age ≥35 Years | Associated | – | <0.001 | Yes | |
| Maternal Diabetes | Associated | – | 0.029 | Yes | |
| Consanguinity | Not Associated | – | >0.050 | No | |
| Infection During Pregnancy | Not Associated | – | >0.050 | No | |
| Folic Acid Supplementation | Not Associated | – | >0.050 | No | |

## DISCUSSION

Congenital anomalies are characterized by structural or functional defects present at birth, which frequently lead to significant morbidity and mortality [12]. Congenital anomalies occur in about 3% to 4% of births and are a major cause of perinatal and infant morbidity and mortality [13]. In many high-income settings, routine antenatal care includes two ultrasound scans: one performed at 11–14 weeks of gestation to confirm fetal viability, determine gestational age, and detect multiple pregnancies, and another at 18–20 weeks to screen for major congenital anomalies [14]. Regarding morbidity, congenital malformations represent 12% of all pediatric admissions to hospitals. Patients with congenital malformations tend to have extended hospitalizations and increased medical costs as compared to other patients [15]. In addition to other associated risks, major congenital fetal abnormalities increase the likelihood of malpresentation, particularly breech presentation, and are a risk factor for delivery by cesarean section [16]. Congenital anomalies (CAs) are estimated to affect 3-6% of newborns globally and are linked to hundreds of thousands of deaths. Additionally, socioeconomic disadvantage, health disparities, and misinformation can hinder prevention efforts. A substantial proportion of CAs are caused by genetic factors, including chromosomal abnormalities or single-gene disorders [17]. The most frequently observed congenital anomalies include heart defects, neural tube defects, Down syndrome, cleft lip and palate, clubfoot, hydrocephalus, anencephaly, and others [18]. In a study conducted by Ahn *et al.* and Loane *et al.* it was seen that women in the older maternal age group were more likely to have children with congenital anomalies compared to those aged 20–34 years. However, there was no significant increase in the likelihood of congenital anomalies in women under 20, except for abdominal defects, when compared to those in the 20–34-year age group [18, 19]. This investigation aimed to find out the frequency of congenital anomalies in newborns and the factors contributing to them. A total of 231 pregnant women, aged 19-45 years, were included in the study. Both younger and older maternal ages can elevate the likelihood of birth defects, which presents a significant public health concern [9, 5]. The mean age of the women in our research population was 27.38 ± 4.08 years. The literature that has been available has discussed the implications of maternal age on pregnancy and how it is related to the occurrence of congenital anomalies among newborns. The average age of women at birth has been observed to increase by a noteworthy margin in the last few decades. More couples are getting their first children when the maternal age is 30 or more to 35 years. Some of the studies have attributed delayed childbearing to several pregnancy and fetal complications, which provide guidelines on how to manage these high-risk pregnancies. The strongest among congenital anomalies is the relationship between chromosomal abnormalities (CA) and advanced maternal age (AMA), which has already developed a strong relationship that has influenced the current pattern of screening by professionals worldwide, and it is constantly being improved [20]. In one study by Pethő *et al.* it was found that some non-chromosomal anomalies (NCAs) are closely related to the maternal age and a definite case of

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high or low maternal age that increases the risk of developing an NCA, but the specific age ranges differ depending on the anomaly. On the basis of these findings, the introduction of better screening procedures is suggested. The guidelines are not currently combined with maternal age-related recommendations to fetal echocardiography or fetal neurosonography, which may prove to be useful in the detection of the corresponding NCAs. Also, it should not be limited to the old mothers alone, but the very young mothers age group should be considered as well. [20]. It has been reported in the past that the incidence of malformations is significantly high among multiparous women [18]. Our findings also confirm this position, which shows that there is a positive relationship between birth order and the occurrence of birth anomalies. Notably, 75.5% of the women in our study were multiparous. The trends and frequency of congenital disorders can change over the course of time or across different geographic locations, influenced by a sophisticated interplay of hereditary, ecological, socio-cultural, racial, and ethnic factors, both known and unknown [19]. In the current study, there were 82.16% single anomalies and 17.84% multiple anomalies. The commonest congenital anomalies were anencephaly 19.7%, Hydrocephalus 15.5%, Absence of Ear/Figure/Toe/scrotum/Arm/Leg/Limbs 9.4% Cleft Lip plus Cleft Palate 8.9%, meningomyelocele 7%, and talipes 8%. Our study revealed that the central nervous system (CNS) was the most frequently affected, followed by the ear, fingers, toes, scrotum, arms, legs, and musculoskeletal system, in that order of frequency. This aligns with a study conducted in Saudi Arabia, which also found the central nervous system (CNS) to be the most frequently affected, with the musculoskeletal and renal systems following in prevalence [9]. Likewise, a study conducted in Iran identified disorders of the CNS, musculoskeletal system, gastrointestinal system, urogenital system, and chromosomal abnormalities, listed in order of decreasing frequency [20]. A study conducted in India found that the central nervous system (CNS) ranked first, followed by the musculoskeletal system and then the cardiovascular system (CVS) [20]. Similarly, another study found CNS anomalies to be the most common [21]. In a study conducted by Asemi et al. it was found that anomalies of the nervous system (24.1%) and cardiovascular system (21.1%) were the most frequent. Spina bifida was the most common central nervous system anomaly, while unspecified heart malformations (17.1%), other cardiovascular malformations (18.7%), and patent ductus arteriosus (11.7%) were the most prevalent cardiovascular anomalies [22]. In our study, the responsible factors were Maternal age>30 (20.2%), paternal age ≥35 (19.7%), diabetic mellitus (20.2%), consanguineous marriage (20.2%), infection during pregnancy (8.9%), and folic acid supplementation (61.5%). Consanguineous marriages are reported to significantly contribute to the occurrence of congenital malformations [23]. In the current study, the prevalence of congenital anomalies was higher among newborns born to consanguineous marriages, which aligns with findings from studies conducted in Qatar, Morocco, and India [24-26]. Our study found that mothers exceeding the age of 30 had a higher likelihood of giving birth to newborns with congenital malformations. This is in agreement with a study report by Fernandes *et al.* who reported that advanced maternal age (above 40 years old) and multiple pregnancies were major risk factors associated with a high probability of live births with the occurrence of congenital anomalies [27]. Maternal diabetes has long been considered an important factor in neural tube defects (NTDs), but this association is hardly investigated in multivariate analyses. It was determined in a study that complications of pregnancy by type 2 diabetes were associated with a significant incidence of congenital anomalies, and the incidence was increased in mothers with maternal HbA1c levels above normal [28]. Thus, in women with existing diabetes, a high dose folate therapy of up to 5 mg/day is prescribed, and it is necessary to be included in a personalized preconception care plan [29]. Although there is a high likelihood of recurrent malformations occurring congenitally, the preventive measures are not prevalent among developing countries such as India. This implies that there is a requirement for good preventive measures against congenital abnormalities in this area. Raising the awareness of the importance of maternal care in the course of pregnancy, initiating educational programs on the topic of congenital malformations, and emphasizing the dangers of consanguinity marriages are among the key steps to reduce the incidence of congenital malformations and the associated health issues.

This study was descriptive, single-centered, and cross-sectional, limiting the ability to establish causal relationships. Laboratory confirmation of anomalies and genetic testing were not performed, and potential confounding factors such as environmental exposures and socioeconomic status were not fully assessed. Future research should involve larger, multicenter, prospective studies with genetic and laboratory evaluations, along with public health interventions targeting maternal health, consanguinity, diabetes management, and folic acid supplementation, to improve early detection, prevention, and management of congenital anomalies.

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## CONCLUSIONS

This group of 213 newborns with congenital anomalies was of 82 percent single anomalies, the most common ones being anencephaly (19.7) and hydrocephalus (15.5). Descriptive characteristics of the maternal and pregnancy were presented, though it is not possible to point out causal or statistical dependencies because the study was descriptive. The common characteristics in the affected pregnancies were maternal age ≤30 years (79.8%), diabetes (20.2%), consanguinity (20.2%), and absence of folic acid supplementation (38.5%), but these do not imply causal relationships. There is a need to provide enhanced surveillance and early detection of congenital anomalies to enhance antenatal counselling and neonatal care planning.

## Authors' Contribution

Conceptualization: AI
Methodology: AI, NN, AB
Formal analysis: FNB, HMI
Writing and Drafting: FNB, RB, ZK
Review and Editing: AI, FNB, RB, NN, AB, HMI, ZK

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**

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# Diagnostic Accuracy of Colour Doppler Ultrasound in Antenatal Diagnosis of Morbidly Adherent Placenta, Taking Operative Finding as Gold Standard

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## ABSTRACT

Morbidly adherent placenta (MAP), often linked to prior cesarean delivery, is a serious obstetric condition requiring timely Doppler ultrasound diagnosis despite variable specificity. **Objectives:** To evaluate the diagnostic accuracy of Color Doppler ultrasound (CDUS) for antenatal detection of MAP, using intraoperative findings as the reference standard. **Methods:** This was a comparative analytical study with a retrospective review of patient data conducted in the Department of Diagnostic Radiology at Aga Khan University spanning April to August 2025 and included pregnant women via consecutive sampling identified as being at risk for MAP. Each participant underwent an antenatal ultrasound assessment, and the sonographic findings were subsequently compared with operative findings. Diagnostic indices such as sensitivity, specificity, positive and negative predictive values, as well as overall accuracy, were determined. **Results:** Color Doppler ultrasound exhibited strong diagnostic performance in detecting MAP, achieving a sensitivity of 98.10 % (95% CI: 93.29-99.77) and a specificity of 55.56 % (95% CI: 35.33-74.52). The point receiver operating characteristic (ROC) curve demonstrated an area under the curve (AUC) of 0.89, indicative of excellent discriminatory capacity. Diagnostic accuracies were observed as 90.48% for accreta ($p<0.001$), 89.19% for increta ($p<0.001$), and 79.17% for percreta ($p<0.001$). Subgroup analysis showed the same accuracy in women aged ≤35 years (98.08%) and those >35 years (98.08%). **Conclusions:** Doppler ultrasound showed high diagnostic accuracy for MAP with excellent ROC performance and consistent sensitivity across maternal age and gestational subgroups.

## INTRODUCTION

Morbidly adherent placenta (MAP) refers to an abnormal implantation of the placenta in which the chorionic villi invade the uterine wall either partially or completely, encompassing the subtypes placenta accreta, increta, and percreta [1]. Although uncommon, MAP is associated with severe, life-threatening maternal complications and remains a major contributor to emergency obstetric hysterectomy worldwide. In Pakistan, it ranks as the third leading indication for emergency hysterectomy, following uterine rupture and postpartum uterine atony [2, 3]. According to international data from the American College of Obstetricians and Gynecologists, the incidence of morbidly adherent placenta (MAP), also referred to as placenta accreta spectrum (PAS), is estimated at approximately 1 in 2500 deliveries, though more recent studies report rates ranging from 1 in 2500 to 1 in 1100 deliveries, with maternal mortality reaching up to 10% [1]. The rising global incidence has been closely linked to increasing cesarean delivery rates, with recent estimates indicating a pooled prevalence of about 0.17% worldwide and local hospital-based data showing rates as high as 3 per 1000 deliveries [4]. Placenta accreta accounts for

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nearly 80% of PAS cases, increta for about 15%, and percreta for roughly 5% [5, 6]. The most firmly established risk factors include placenta previa and a history of prior cesarean section [7, 8]. Several studies have examined the diagnostic accuracy of color Doppler ultrasound (CDUS) for antenatal detection of MAP. A study conducted in Multan reported a sensitivity of 87.5%, specificity of 98.36%, and overall diagnostic accuracy of 97.1% [9]. Kamankesh *et al.* demonstrated sensitivity and specificity of 97.7% and 86.2%, respectively [10], while Nawab *et al.* reported corresponding values of 85.7% and 83.3% [11]. Similarly, research at Ganga Ram Hospital, Lahore, found MAP in 14.38% of deliveries, with sensitivity, specificity, PPV, NPV, and accuracy of 86.96%, 98.54%, 90.91%, 97.83%, and 98.13%, respectively [12]. However, previous studies, both international and local, showed notable variability in diagnostic performance [10, 12]. Although ultrasound remains the first-line imaging tool for suspected MAP, the absence of standardized diagnostic criteria contributes to inconsistency in accuracy and interpretation, posing challenges in clinical decision-making. In Pakistan, standardized and consistent evidence regarding the diagnostic performance of CDUS for MAP is limited. This gap may lead to delayed recognition or misdiagnosis in high-risk pregnancies. Considering the rising incidence of MAP and its strong association with maternal morbidity and mortality, reliable antenatal diagnostic strategies are essential. Based on existing evidence suggesting the diagnostic potential of ultrasonography in detecting abnormal placentation, this study hypothesizes that color Doppler ultrasound provides high diagnostic accuracy in identifying morbidly adherent placenta (MAP) when compared with intraoperative findings. To test this hypothesis, the study aims to determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of color Doppler ultrasound for the antenatal detection of MAP. The results are expected to inform gynecologists and radiologists on the appropriate application of ultrasound in suspected cases, improve early diagnosis, and ultimately help reduce maternal morbidity and mortality.

In Pakistan, locally standardized and consistent evidence regarding the performance of CDUS in detecting MAP remains limited. This lack of reliable local data may contribute to delayed diagnosis and suboptimal peripartum management. This study aimed to evaluate the diagnostic accuracy of color Doppler ultrasound for antenatal detection of morbidly adherent placenta using intraoperative findings as the reference standard.

## METHODS

This comparative analytical study with a retrospective review was conducted in the Department of Diagnostic Radiology at Aga Khan University Hospital, Karachi, from April to August 2025. The sample size was calculated using previously reported diagnostic parameters, assuming a sensitivity of 85.7% and specificity of 83.3% as reported by Nawab et al. [11], and a prevalence of Placental adherence of 36.4% based on Elbery et al. [13], With a 10% margin of error and a 95% confidence level, the minimum required sample size was estimated to be 132 participants, calculated using an online sample size calculator developed by Arifin (https://wnarifin.github.io/ssc/sssnsp.html), which is specifically designed for studies evaluating sensitivity and specificity through consecutive sampling. Cases were identified from the hospital's record and all cases that met the predefined inclusion criteria, antenatal suspicion of MAP on Doppler ultrasound, and subsequent operative confirmation at delivery, were included until the required sample size was achieved. Eligible participants were women aged 18–49 years with suspected placental adherence, identified based on third-trimester bleeding or pelvic pain. On color Doppler ultrasound, morbidly adherent placenta (MAP) was diagnosed according to established sonographic criteria, including loss of the utero-placental clear zone, disruption of the serosa–bladder interface, and the presence of turbulent placental lacunae with high-velocity flow [14, 15]. Intraoperative confirmation was established when direct visualization of villous attachment to or invasion of the myometrium was observed. Participants with gestational diabetes, chronic hypertension, cardiovascular disease, or other systemic comorbidities were excluded to minimize potential confounding effects on placental vascularity and Doppler flow patterns. This design-based exclusion was applied during participant selection to ensure diagnostic uniformity. All other demographic variables (maternal age, parity, gravidity, and gestational age) were analyzed descriptively to assess potential distributional differences across diagnostic categories. After obtaining Ethical Review Committee (ERC) approval (Reference No: 2025-10604-33865) and written informed consent from the Institutional Review Committee (IRC), baseline demographic and clinical data were collected from patient records and structured interviews at the time of the ultrasound examination. All Doppler assessments were performed using a GE Voluson E8 ultrasound system (GE Healthcare, Chicago, IL, USA) equipped with a 2–5 MHz curvilinear transducer. Standardized scanning parameters included a pulse repetition frequency (PRF) of 0.9–1.2 kHz, a wall filter optimized for low-flow sensitivity, and color gain adjusted just below the noise threshold to enhance visualization of placental vascularity. All sonographic and clinical findings were recorded on a structured proforma immediately after each examination, with operative

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confirmation obtained at delivery for diagnostic correlation. Data were analyzed using SPSS version 26.0, with quantitative variables reported as mean ± SD or median (IQR) and categorical variables as frequencies and percentages. Diagnostic accuracy of Doppler was determined using a 2 × 2 contingency table to calculate sensitivity, specificity, PPV, NPV, and overall accuracy based on true positive, false positive, true negative, and false negative results. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the discriminative ability of color Doppler ultrasound in detecting MAP. The area under the curve (AUC) with 95% confidence intervals was computed using the nonparametric DeLong method. Statistical significance for AUC values was determined using the SPSS ROC Curve function (Analyze → ROC Curve). Effect modifiers such as age, gestational age, parity, gravida, booking status, previous cesarean section, and family history of MAP were controlled through stratification, with post-stratification diagnostic accuracy recalculated. Associations were determined using the chi-square test, with $p<0.05$ considered statistically significant.

## RESULTS

The mean age of study participants was 36.21 ± 5.07 years. Age distribution was evenly divided, with 66 (50.0%) of women aged ≤35 years and 66 (50.0%) older than 35 years. The median gestational age was 36 weeks (IQR: 4.00); among them, 81 (61.36%) delivered at <37 weeks, while 51 (38.64%) delivered beyond 37 weeks of gestation. Regarding parity, the majority were multiparous (≥2 births, 111 (84.1%), while 11 (8.3%) were nulliparous and 10 (7.6%) were primiparous. Gravidity was equally distributed between multigravida (G2–G4, 66 (50.0%) and grand multigravida (>5, 66 (50.0%). A history of previous cesarean section was reported in 103 (78.0%) of women, compared to 29 (22.0%) without such a history. Finally, only 9 (6.8%) had a positive family history, whereas the vast majority, 123 (93.2%), reported no relevant family history. The study presents detailed baseline demographic and clinical characteristics of the study cohort (Table 1).

**Table 1:** Baseline Characteristics of the Study Population

| Characteristics | | Descriptive Statistics, n (%) |
|---|---|---|
| Age (Mean ± SD) | | 36.21 ± 5.07 |
| Age Groups | ≤35 Years | 66 (50.00%) |
| | >35 Years | 66 (50.00%) |
| Gestational Week Median (IQR) | — | 36 (4.00%) |
| Gestational Groups | <37 Weeks | 81 (61.36%) |
| | >37 Weeks | 51 (38.64%) |
| Parity | Nulliparous Parity=0 | 11 (8.30%) |
| | Primiparous Parity=1 | 10 (7.60%) |
| | Multiparous Parity= >2 | 111 (84.1%) |
| Gravida | Multigravida (G2-G4) | 66 (50.00%) |
| | Grand Multigravida (>5) | 66 (50.00%) |
| Residence | Urban | 99 (75.00%) |
| | Rural | 33 (25.00%) |
| Booking status | Yes | 93 (70.50%) |
| | No | 39 (29.50%) |
| Previous C Section | Yes | 103 (78.0%) |
| | No | 29 (22.0%) |
| Family History | Yes | 9 (6.80%) |
| | No | 123 (93.20%) |

Ultrasound identified 15 true negatives (55.6%), with 2 false positives (1.9%), and detected 103 true positives (98.1%), with 12 false negatives (44.4%). Sensitivity was 98.10%, specificity 55.56%, PPV 89.57%, NPV 88.24%, and overall accuracy 89.39% ($p<0.001$) (Table 2).

**Table 2:** Diagnostic Performance of Ultrasound for the Detection of MAP Compared with Operative Findings

| Category | | MAP-Operative Findings | | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Overall Accuracy (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | Absent | Present | | | | | | |
| MAP on CDUS | Absent | 15 (55.60%) | 2 (1.90%) | 98.10 (93.29-99.77) | 55.56 (35.33-74.52) | 89.57 (84.91-92.91) | 88.24 (64.60-96.86) | 89.39 (82.85-94.08) | <0.001 |
| | Present | 12 (44.40%) | 103 (98.10%) | | | | | | |

Note: Subgroups with small sample sizes (e.g., n=2 false positives and n=12 false negatives) yield wide confidence intervals and should be interpreted with caution due to limited precision and potential instability of estimates.

The results present the diagnostic performance of ultrasound for placenta accreta, increta, and percreta. For placenta accreta, sensitivity was 90.48% and specificity 91.80%, with a PPV of 88.37%, NPV 93.33%, and overall accuracy 91.26% ($p<0.001$). For placenta increta, sensitivity was 89.19% and specificity 90.91%, with PPV 84.62%, NPV 93.75%, and accuracy 90.29% ($p<0.001$). For placenta percreta, sensitivity was 79.17% and specificity 97.47%, with PPV 90.48%, NPV 93.90%, and accuracy 93.20% ($p<0.001$) (Table 3).

**Table 3:** Diagnostic Accuracy of Ultrasound in Detecting Different Types of MAPS Compared with Operative Findings

| MAP on CDUS | | MAP-Operative Findings | | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Overall Accuracy (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | Absent | Present | | | | | | |
| Acreta | Absent | 56 (91.80%) | 4 (9.50%) | 90.48 (77.38-97.34) | 91.80 (81.90-97.28) | 88.37 (76.54-94.65) | 93.33 (84.60-97.27) | 91.26 (84.06-95.93) | <0.001 |
| | Present | 5 (8.20%) | 38 (90.50%) | | | | | | |

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| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Increta | Absent | 60 (90.90%) | 4 (10.80%) | 89.19 (74.58-96.97) | 90.91 (81.26-96.59) | 84.62 (71.78-92.24) | 93.75 (85.56-97.43) | 90.29 (82.87-95.25) | <0.001 |
| | Present | 6 (9.10%) | 33(89.20%) | | | | | | |
| Percreta | Absent | 77 (97.50%) | 5 (20.80%) | 79.17 (57.85 92.87) | 97.47 (91.15-99.69) | 90.48 (70.43-97.43) | 93.90 (87.58-97.11) | 93.20 (86.50-97.22) | <0.001 |
| | Present | 2 (2.50%) | 19 (79.20%) | | | | | | |

Findings show high ultrasound sensitivity (>96%) across subgroups, with specificity ranging widely from 0% to 100%. Overall accuracy exceeded 86% in most categories, while p-values were statistically significant (<0.05) for all subgroups except family history (p=0.236) (Table 4).

**Table 4:** Diagnostic Accuracy of Ultrasound According to Maternal and Clinical Characteristics

| Category | Subgroups | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Accuracy (95% CI) | p-value |
|---|---|---|---|---|---|---|---|
| Age Groups (Years) | ≤35 (n=26) | 98.08 (89.74-99.95) | 64.29 (35.14-7.24) | 91.07 (83.46-95.37) | 90.00 (55.41-98.49) | 90.91 (81.26-96.59) | <0.001 |
| | >35 (n=25) | 98.08 (89.74-99.95) | 46.15 (19.22-74.87) | 87.93 (81.48-92.35) | 85.71 (44.12-97.85) | 87.69 (77.18-94.53) | <0.001 |
| Gestational (Weeks) | <37 (n=81) | 98.39 (91.34-99.96) | 57.89 (33.50-79.75) | 88.41 (81.81-2.82) | 91.67 (60.26-8.76) | 88.89 (79.95-94.79) | <0.001 |
| | >37 (n=51) | 97.67 (87.71-99.94) | 50.00 (15.70-84.30) | 91.30 (83.93-95.46) | 80.00 (33.83-96.90) | 90.20 (78.59-96.74) | <0.001 |
| Gravida | Multigravida (n=66) | 100 (93.40-100) | 58.33 (27.67-84.83) | 91.53 (84.68-95.47) | 100 (59.04-100) | 92.42 (83.20-97.49) | <0.001 |
| | G-Multigravida (n=66) | 96.08 (86.54-99.52) | 53.33 (26.59-78.73) | 87.50 (80.25-92.34) | 80.00 (48.69-94.40) | 86.36 (75.69-93.57) | <0.001 |
| Parity | Nulliparous-P (n=11) | 100 (69.15-100) | 100 (2.50-100) | 100 (69.15-100) | 100 (2.50-100) | 100 (71.51-100) | <0.001 |
| | Primiparous-P (n=10) | 100 (66.37-100) | 0.00 (0.00-100) | 90.00 (90.00-90.00) | – | 90.00 (55.50-99.75) | – |
| | Multiparous-P (n=111) | 97.67 (91.85-99.72) | 56.00 (34.93-75.60) | 88.42 (83.05-92.25) | 87.50 (63.01-96.64) | 88.29 (80.81-93.61) | <0.001 |
| Residence | Urban (n=99) | 98.70 (92.98-99.97) | 50.00 (28.22-71.78) | 87.36 (81.97-91.31) | 91.67 (60.02-98.77) | 87.88 (79.78-93.58) | <0.001 |
| | Rural (n=33) | 96.43 (81.65-99.91) | 80.00 (28.36-99.94) | 96.43 (82.37-99.36) | 80.00 (35.72-96.64) | 93.94 (79.77-99.26) | <0.001 |
| Booking-Status | Booked (n=93) | 98.59 (92.40-99.96) | 59.09 (36.35-79.29) | 88.61 (64.29-98.95) | 92.86 (64.29-98.95) | 89.25 (81.11-94.72) | <0.001 |
| | Un-Booked (n=39) | 97.06 (84.67-99.93) | 40.00 (5.27-85.34) | 91.67 (18.00-94.80) | 66.67 (18.00-94.80) | 89.74 (75.78-97.13) | 0.004 |
| Previous C Section | Yes (n=103) | 97.56 (91.47-99.70) | 61.90 (38.44-81.89) | 90.91 (85.27-94.53) | 86.67 (61.36-96.38) | 90.29 (82.87-95.25) | <0.001 |
| | No (n=29) | 100 (85.18-100) | 33.33 (4.33-77.72) | 85.19 (76.56-91.01) | 100 (15.81-100) | 86.21 (68.34-96.11) | 0.004 |
| Family History | Yes (n=9) | 100 (47.82-100) | 25.00 (0.63-80.59) | 62.50 (48.63-74.59) | 100 (2.50-100) | 66.67 (29.93-92.51) | 0.236 |
| | No (n=123) | 98.00 (92.96-99.76 | 60.87 (38.54-80.29) | 91.59 (86.73-94.78) | 87.50 (63.07-96.63) | 91.06 (84.56-95.45) | <0.001 |

The ROC curve was constructed using the observed operating point (sensitivity = 98.10%, specificity = 55.56%), connecting the coordinates (0, 0) to the operating point and subsequently to (1, 1). The resulting AUC was 0.89, reflecting good diagnostic accuracy. The shaded region illustrates the 95%CI, while the diagonal dashed line represents the line of no discrimination (Figure 1).

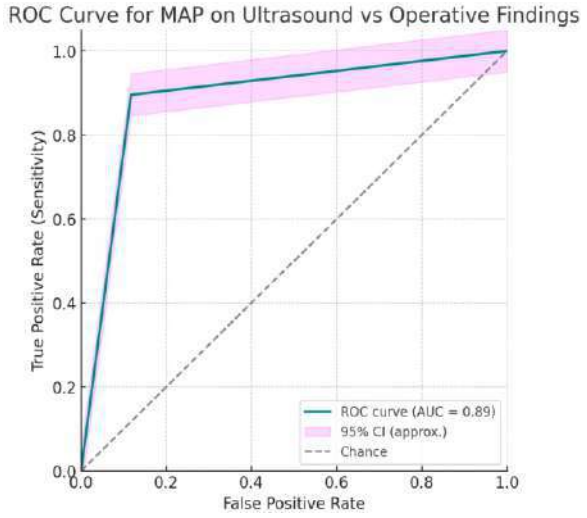


**Figure 1:** Receiver Operating Characteristic (ROC) Curve Depicting Diagnostic Performance of Ultrasound in Detecting MAP

## DISCUSSION

Ultrasound remains the cornerstone for the prenatal diagnosis of abnormal placental adherence, owing to its wide availability, non-invasive nature, and real-time assessment of placental morphology and vascularity. It demonstrates consistently high sensitivity in detecting abnormal placental adherence; however, its specificity can vary considerably depending on operator expertise, equipment quality, and the diagnostic criteria applied. In our study, the approximated ROC operating point revealed a sensitivity of approximately 87.3%, specificity of 86.96%, and an AUC of ~0.89, aligning well with recent systematic meta-analyses that report pooled ultrasound sensitivity in the 86% range (95% CI: 78-92%) and specificity around 63% (95% CI: 55-70%) [16]. Nonetheless, the nearly 98% sensitivity observed in our diagnostic comparison of ultrasound versus operative findings exceeds typical pooled results. This elevated performance likely reflects our cohort's high prevalence of PAS risk factors, primarily previous cesarean sections (78%), which can artificially inflate predictive metrics [17]. Additionally, our use of an imaging procedure performed by trained sonographers may contribute to this superior accuracy, consistent with data showing that ultrasound scoring systems improve diagnostic reliability [18, 19]. In contrast to the high

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specificity reported in previous studies, such as Kamankesh *et al.* (86.2%) [10], Jauniaux *et al.* (≥90%) [20], and Nawab *et al.* (83.3%) [11]. The present study demonstrated a lower specificity (55.6%). This discrepancy may be attributed to the high prevalence of risk factors, particularly previous cesarean deliveries, in our cohort, which increased the likelihood of false-positive interpretations. Furthermore, the absence of a standardized scoring system, as emphasized in the FIGO guidelines [20], may have led to overdiagnosis based on isolated sonographic markers (e.g., placental lacunae, loss of clear zone). Operator vigilance in a high-risk referral setting may also have contributed to prioritizing sensitivity over specificity, thereby reducing the latter. Structured scoring systems, such as those evaluated by Zlotin *et al.* demonstrated remarkable accuracy, achieving AUC values of around 0.93, with pooled sensitivity and specificity exceeding 85% [19]. Peng *et al.* systematic review supports these findings, noting optimal performance in studies utilizing scoring frameworks [21]. These results affirm the advantages of standardized imaging protocols in ultrasound diagnostics. Although MRI offers comparable diagnostic performance with reported sensitivity and specificity in the high 80s to low 90s, its principal value lies in clarifying placental invasion in posterior or lateral PAS, locations where ultrasound has limitations [14, 22]. This supports the widely accepted clinical strategy of using ultrasound as the initial modality and reserving MRI for equivocal or anatomically challenging cases. The specificity variation observed across clinical subgroups, particularly low specificity in primiparous or family-history subgroups, likely stems from small sample sizes in these categories. Such small numbers (n<20) result in wide confidence intervals and unstable estimates, a known limitation in single-center observational research [17]. Future investigations with larger, more diverse cohorts would help strengthen the reliability of subgroup analyses and improve generalizability. Overall, the high sensitivity and AUC reported in our results substantiate ultrasound's continued role as an effective primary diagnostic tool for PAS, particularly within high-risk populations. Nevertheless, integrating MRI for select cases and adopting structured ultrasound scoring systems are sound approaches to optimize prenatal risk stratification and facilitate surgical planning [18, 23].

The study's diagnostic estimates may be influenced by the high prevalence of PAS risk factors, particularly previous cesarean delivery, which can inflate sensitivity and reduce specificity. Additionally, lack of a standardized ultrasound scoring system and small subgroup sizes may have led to variability in specificity and unstable subgroup estimates. Future studies should focus on multicenter, prospective efforts to validate ultrasound scoring systems across diverse populations, and on establishing standardized diagnostic definitions for PAS. Several large-scale collaborative studies have evaluated the diagnostic performance of scoring systems and imaging criteria for PAS [21, 24]. They provide the evidence base for why future multicenter, prospective, and standardized research is needed.

## CONCLUSIONS

Color Doppler ultrasound demonstrated high sensitivity and strong overall diagnostic accuracy for detecting morbidly adherent placenta. While specificity showed moderate variability, the test maintained consistent performance across maternal age and gestational subgroups. These findings confirm the reliability of Doppler ultrasound as an effective antenatal diagnostic tool for a morbidly adherent placenta.

## Authors' Contribution

Conceptualization: MK
Methodology: NN, MS, MY, SS[1], SS[2]
Formal analysis: MK
Writing and Drafting: MK, NN
Review and Editing: MK, NN, MS, MY, SS[1], SS[2]

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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# Frequency of Postpartum Depression in Patients Undergoing Caesarean Section

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## ABSTRACT

Postpartum depression (PPD) is a common mental health disorder affecting women after childbirth, but its risk varies across clinical and obstetric contexts. However, evidence regarding the association between CS-related maternal, socioeconomic, surgical, and neonatal factors and the development of PPD remains inconsistent. **Objectives:** To determine the frequency of PPD among women undergoing Caesarean section and its association with education level, socioeconomic status, type of Caesarean section, complications, history of mental health issues, and neonatal complications. **Methods:** This descriptive cross-sectional study was conducted at the Combined Military Hospital (CMH) Quetta from February 2025 to June 2025. A total of 91 postpartum women who delivered via Caesarean section were included using non-probability consecutive sampling. Data were collected using the Edinburgh Postnatal Depression Scale (EPDS) with a cutoff score of ≥13 to define PPD. Statistical analysis was performed using SPSS version 26.0, and associations between PPD and categorical variables were assessed using the chi-square test. **Results:** The mean age of participants was 32.14 ± 8.34 years, and the average parity was 2.52±1.68. Postpartum depression was identified in 22 (24%) women. Stratified analysis showed no statistically significant association between PPD and education level (p=0.864), socioeconomic status (p=0.493), type of Caesarean section (p=0.978), complications (p=0.656), history of mental health issues (p=0.794), or neonatal complications (p=0.895). **Conclusions:** The prevalence of PPD among women undergoing Caesarean section was 24%. However, no significant associations were found with maternal, socioeconomic, surgical, or neonatal factors (all p>0.05). Routine screening and psychological support are essential to address PPD effectively.

## INTRODUCTION

Postpartum depression (PPD) is a significant public health concern, affecting the mental health of new mothers globally. It is characterized by mood swings, irritability, anxiety, and depressive symptoms occurring within the postpartum period, usually peaking within the first six weeks after childbirth. PPD is multifactorial, arising from a combination of biological, psychological, and social determinants that interact to influence vulnerability. Biologically, the abrupt decline in estrogen and progesterone after delivery, dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis, and surgery-related inflammatory responses—particularly following Caesarean section (CS) can contribute to mood disturbances and reduced stress tolerance. Psychologically, prior anxiety or depression, negative birth experiences, perceived loss of control during labour, and poor coping mechanisms are known contributors. Socially, inadequate family support, lower socioeconomic status, interpersonal conflict, and neonatal illness or NICU admission can exacerbate maternal stress and increase the risk of PPD [1]. Among the various factors associated with PPD, the mode of delivery, particularly Caesarean section (CS), has emerged as a critical determinant in recent years [2]. C-sections, either elective or emergent, are conducted to protect the mother and/or child in certain obstetrical conditions. Yet the psychological implications

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of this surgical procedure, particularly PPD, remain to be fully investigated. According to some reports, women who undergo CS may have a higher risk of suffering PPD than women with spontaneous vaginal delivery (SVD) [3]. This risk may be mediated by mechanisms such as surgical morbidities, postoperative pain, delayed mobilization, and disappointment with unmet birth expectations [4]. Higher rates of CS worldwide have increased the importance of studying its psychological effects. According to the WHO, cesarean section rates above 10–15% are not medically justified, but in most countries these rates have risen sharply, underscoring the importance of investigating CS sequelae, including PPD [5]. Cultural and social attitudes toward the preferred mode of delivery may also add psychological burden, especially in settings where vaginal delivery is culturally expected [6]. Recent evidence has emphasized a stronger relationship between emergency CS and PPD, compared with elective CS or vaginal delivery. The urgency and unpredictability of emergency CS may heighten psychological stress and loss of control, increasing susceptibility to PPD [7]. Elective CS, although planned, can still affect psychological well-being as women may experience anticipatory anxiety or reduced autonomy during the childbirth process [8]. Furthermore, other maternal and contextual contributors, including pre-existing mental health conditions, socioeconomic disadvantage, inadequate support systems, and neonatal complications, have been consistently linked to PPD [9]. Their interaction with the surgical aspects of CS warrants particular attention, as postoperative recovery, physical limitations, and neonatal outcomes may intensify psychological vulnerability. Recent research also implicates inflammatory and neuroendocrine mediators in the development of PPD following CS, suggesting potential biological pathways linking surgical stress to postpartum mood disorders [10]. Understanding the incidence and risk factors of PPD among women undergoing CS is essential for designing targeted preventive interventions. Prompt recognition and appropriate management of PPD can prevent long-term adverse outcomes for both mother and child. Integrating mental health screening into routine obstetric and postoperative care may therefore improve maternal well-being and overall outcomes [11].

Despite extensive research on postpartum depression (PPD), the specific contribution of Caesarean section (CS) to PPD risk remains poorly defined, with inconsistent findings across studies. Many earlier investigations compare CS to vaginal delivery but do not adequately differentiate between elective and emergency CS, nor do they simultaneously examine maternal, socioeconomic, surgical, and neonatal variables within CS populations. Moreover, most available literature focuses on general postpartum cohorts, limiting the understanding of how CS-related factors such as operative complications, postoperative pain, surgical stress, and neonatal morbidity interact with psychosocial determinants to influence PPD. This creates a clear gap in the evidence regarding which subgroups of CS patients may be more vulnerable and which clinical or social factors meaningfully predict PPD in this higher-risk surgical population. By examining these variables collectively within a uniform CS cohort, the study addresses the gap in identifying multidimensional predictors of PPD after CS, enabling more precise screening and more tailored postpartum psychological support strategies for this increasingly common mode of delivery. This study aimed to specifically target women undergoing Caesarean section to determine the frequency of PPD and evaluate its association with education level, socioeconomic status, type of CS, perioperative complications, history of mental health issues, and neonatal outcomes.

## METHODS

This descriptive cross-sectional study was conducted at the Combined Military Hospital (CMH) Quetta from February 2025 to June 2025. The sample size was calculated using the reported frequency of postpartum depression (6.3%) from a study by Yousafzai *et al.* with a 95% confidence level and a margin of error (d) of 5%. The calculated sample size was 91 patients [12]. (This prevalence was the best available estimate from the local literature at the time of protocol development and was used solely for planning purposes. Although the observed PPD prevalence in our study was higher (24%), sample size calculations are based on anticipated rather than actual prevalence; the achieved sample of 91 participants still provides a meaningful estimate of PPD frequency, albeit with a wider confidence interval than originally intended.) A non-probability consecutive sampling technique was employed to recruit participants who met the inclusion criteria. The study included postpartum women aged 18–45 years who underwent Caesarean section within the past six weeks and provided written informed consent. Women with known psychiatric disorders before pregnancy, severe postpartum complications requiring intensive care, or those who declined to participate were excluded. The study was conducted after obtaining approval (Approval No. CMH QTA-IERB/69/2025) from the hospital's ethical review committee, and written informed consent was obtained from each participant before inclusion. Data collection was done using a structured questionnaire that recorded demographic variables, obstetric history, and neonatal outcomes. The presence of postpartum depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS), with a predefined cutoff score of

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≥13 to identify cases of depression. A cutoff score of ≥13 was used on the EPDS, as this threshold has been shown to provide optimal sensitivity and specificity for detecting probable postpartum depression in clinical and research settings. International guidelines and multiple validation studies recommend ≥13 as the standard cutoff for identifying women at risk of major depressive symptoms, including studies validating the EPDS in South Asian and similar populations. Postpartum depression was defined as a positive screening result on the EPDS (score ≥13) within six weeks postpartum. The type of Caesarean section was classified as elective or emergency based on the indication for surgery. Complications during or after surgery included infections, hemorrhage, or any other adverse events noted in the medical record. Neonatal complications included low birth weight (<2.5 kg), admission to the neonatal intensive care unit (NICU), or other adverse neonatal outcomes. Data were entered and analyzed using statistical software SPSS version 26.0. Descriptive statistics summarized the data, with categorical variables presented as frequencies and percentages, and continuous variables as means ± standard deviations. The frequency of postpartum depression was calculated as the proportion of women who screened positive for depression out of the total sample size. Associations between PPD and categorical variables were assessed using the chi-square test. The p-value <0.05 was taken as significant. "Effect size measures such as Cramér's V or odds ratios were not calculated, as the analysis was primarily exploratory and focused on identifying associations rather than quantifying their magnitude."

## RESULTS

A total of 91 participants were included in the study. The mean age of the participants was 32.14 ± 8.34 years, and the average parity was 2.52 ± 1.68. Out of 91 patients, postpartum depression was found in 22 (24%; 95% CI: 15.4%–32.6%) patients (Figure 1).

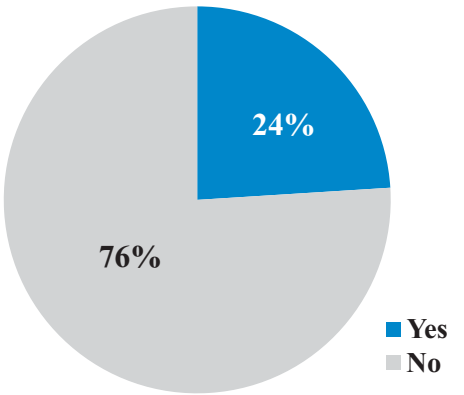


**Figure 1:** Frequency of Postpartum Depression

The study provides a stratified analysis of postpartum depression with various maternal, neonatal, and socioeconomic factors. Education Level: Among women with postpartum depression, 8 (36.4%) had a primary level of education, 10 (24.4%) had secondary education, and 4 (20.0%) had higher education. In contrast, among women without postpartum depression, 22 (63.6%) had primary education, 31 (75.6%) had secondary education, and 16 (80.0%) had higher education. The association between education level and postpartum depression was not statistically significant (p=0.864). Socioeconomic Status: Postpartum depression was observed in 8 (23.5%) women from the low socioeconomic group, 13 (27.7%) from the middle socioeconomic group, and 1 (10.0%) from the high socioeconomic group. Among women without postpartum depression, 26 (76.5%) were from the low group, 34 (72.3%) from the middle group, and 9 (90.0%) from the high group. There was no significant relationship between socioeconomic status and postpartum depression (p=0.493). Type of Caesarean Section: Postpartum depression was reported in 9 (24.3%) women who had elective Caesarean sections and in 13 (24.1%) who had emergency Caesarean sections. Among those without postpartum depression, 28 (75.7%) underwent elective Caesarean sections, and 41 (75.9%) underwent emergency Caesarean sections. This factor showed no statistically significant association with postpartum depression (p=0.978). Complications: Among women with postpartum depression, 5 (20.8%) experienced complications during or after surgery, while 17 (25.4%) did not have complications. For women without postpartum depression, 19 (79.2%) had complications, and 50 (74.6%) did not. The presence of complications was not significantly associated with postpartum depression (p=0.656). History of Mental Health Issues: Postpartum depression was observed in 3 (21.4%) women with a history of mental health issues and in 19 (24.7%) without such a history. Among women without postpartum depression, 11 (78.6%) had a history of mental health issues, while 58 (75.3%) did not. This variable did not show a significant association with postpartum depression (p=0.794). Neonatal Complications: Postpartum depression was noted in 7 (23.3%) women whose neonates had complications and in 15 (24.6%) whose neonates did not. In women without postpartum depression, 23 (76.7%) had neonates with complications, while 46 (75.4%) did not. Neonatal complications were not significantly associated with postpartum depression (p=0.895) (Table 1).

**Table 1:** Association of Postpartum Depression with Maternal, Socioeconomic, Surgical, and Neonatal Factors

| Variables | Category | Postpartum Depression Yes, n (%) | Postpartum Depression No, n (%) | Total n (%) | p-value |
|---|---|---|---|---|---|
| Education Level | Primary | 8 (36.4%) | 22 (63.6%) | 30 | 0.864 |
| | Secondary | 10 (24.4%) | 31 (75.6%) | 41 | |
| | Higher | 4 (20.0%) | 16 (80.0%) | 20 | |

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| | | | | | |
|---|---|---|---|---|---|
| Socioeconomic Status | Low | 8 (23.5%) | 26 (76.5%) | 34 | 0.493 |
| | Middle | 13 (27.7%) | 34 (72.3%) | 47 | |
| | High | 1 (10.0%) | 9 (90.0%) | 10 | |
| Type of Caesarean Section | Elective | 9 (24.3%) | 28 (75.7%) | 37 | 0.978 |
| | Emergency | 13 (24.1%) | 41 (75.9%) | 54 | |
| Complications | Yes | 5 (20.8%) | 19 (79.2%) | 24 | 0.656 |
| | No | 17 (25.4%) | 50 (74.6%) | 67 | |
| History of Mental Health Issues | Yes | 3 (21.4%) | 11 (78.6%) | 14 | 0.794 |
| | No | 19 (24.7%) | 58 (75.3%) | 77 | |
| Neonatal Complications | Yes | 7 (23.3%) | 23 (76.7%) | 30 | 0.895 |
| | No | 15 (24.6%) | 46 (75.4%) | 61 | |

## DISCUSSION

This research explored the occurrence of postpartum depression (PPD) and examined whether maternal, socioeconomic, surgical, and neonatal factors had any bearing on its development. The observed a 24% prevalence of PPD among women who underwent Caesarean section. However, no statistically significant links were identified between PPD and variables such as educational background, economic standing, type of Caesarean procedure, post-surgical complications, mental health history, or neonatal issues. These outcomes both echo and diverge from earlier findings in the literature, highlighting the complex and multifactorial nature of PPD. A study by Yousafzai *et al.* reported that PPD occurred far more frequently in patients who experienced emergency C-sections (76.6%) than in those who delivered vaginally or via elective surgery [12]. This indicates that the stress and unpredictability of emergency procedures might act as psychological triggers. Although our study did not replicate these differences between elective and emergency deliveries, the stress-related mechanisms discussed by Yousafzai *et al.* remain a credible explanation for such trends [12]. Khan *et al.* found a higher PPD prevalence of 36.69%, emphasizing the necessity of early identification and support systems [13]. They also noted a greater vulnerability to PPD among women aged 18 to 35. Our lower prevalence (24%) and lack of significant association may be due to differences in population characteristics and study design. Unlike Khan *et al.* age was not included as a primary analytic variable in our study [13], and our sample included a wider age range, which may have diluted the age-related effects observed in their cohort. Similarly, Malik *et al.* reported a substantially higher PPD prevalence among women undergoing Caesarean section (58%), suggesting a strong link between CS and postnatal depression [14]. Our findings differ, as we did not observe a significant association between the type of CS and PPD. This discrepancy may reflect differences in sampling techniques, cultural context, postpartum support systems, or methodological variations such as the timing of PPD assessment. Malik *et al.* used a smaller, more homogeneous sample, whereas our study included a broader CS population with mixed indications and postoperative experiences, which may have influenced the observed outcomes [14]. In contrast, Selvam et al. reported a lower PPD prevalence (12%) in primiparas, with a higher rate of PPD following vaginal delivery compared to Caesarean section [15]. Such divergent findings among studies may reflect differences in social norms, institutional care standards, family support systems, and the psychological meaning attached to childbirth methods in each cultural setting. Their findings emphasize the significance of contextual and sociocultural factors on PPD, rather than the delivery method alone [16, 17]. A study by Moameri *et al.* found a small but significant relationship between Caesarean delivery and PPD, particularly in emergency cases [18]. Our analysis did not replicate this association, possibly due to the smaller sample size, different population characteristics, and variations in perioperative practices. Additionally, Dousti *et al.* and Doke *et al.* emphasized the role of psychological factors—such as antenatal anxiety and perceived loss of control—which were not specifically assessed in our study and may partly explain the differences in results [19, 20].

The study may be limited by the cross-sectional design and reliance on self-reported screening tools, which restrict causal inference and may introduce reporting bias. Additionally, important psychological variables such as antenatal anxiety, perceived social support, and stress levels were not assessed, potentially masking meaningful associations. Future studies should incorporate longitudinal follow-up with detailed psychosocial assessments to better identify predictors and trajectories of postpartum depression after Caesarean delivery.

## CONCLUSIONS

This study identified postpartum depression (PPD) in 24% of women who delivered via Caesarean section, fulfilling the primary objective of determining its frequency in this population. In addressing the second objective, no statistically significant associations were observed between PPD and maternal factors (education and history of mental health issues), socioeconomic status, surgical characteristics (elective vs. emergency CS and postoperative complications), or neonatal outcomes. These findings suggest that the variables assessed in this study may not be the key determinants of PPD among women undergoing Caesarean section and that other psychosocial or contextual influences not measured here may play a more substantial role. The results underscore the importance of routine mental health screening and supportive postpartum care for all women undergoing Caesarean section to ensure early identification and intervention for depressive symptoms.

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## Authors' Contribution

Conceptualization: SI
Methodology: UA, ZS
Formal analysis: ZS
Writing and Drafting: UA, SBM
Review and Editing: SI, UA, SBM, ZS

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**

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# Physiological Joint Stability and Clinical Outcomes of Braided Suture Techniques in Posterior Cruciate Ligament Reconstruction

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## ABSTRACT

PCL plays a critical role in maintaining the stability of the posterior knee joint, highlighting the importance of accurate diagnosis and effective treatment for such injuries. **Objectives:** To determine the stability of the knee joint in patients with posterior cruciate ligament rupture after the autologous hamstring and braided suture reconstruction. **Methods:** A Quasi-experimental study was conducted from June 2024 to June 2025 at Shahida Islam Medical Complex. This study included 120 patients with posterior cruciate ligament rupture and was divided into control (group A) and study group (Group B)(n=60 each). Group A underwent single-bundle autologous hamstring reconstruction, while group B underwent the same procedure with an added braided thread treatment. Evaluations were performed both before and after surgery, including assessments of complications, joint mobility, gait analysis, knee joint stability (tested with the KT2000), and knee function as measured by Rasmussen scoring. **Results:** Group B showed significantly better treatment rates compared to Group A ($p<0.05$). One year after the surgical operations, Group B exhibited notable improvements in stride speed, joint function, stride length, and Rasmussen scores ($p<0.05$). The cases also showed significantly reduced gait asymmetry and favorable outcomes from the KT2000 test $p<0.05$). **Conclusions:** The combination of autologous reconstruction of the hamstring tendon single bundle by using braided thread enhances clinical outcomes for individuals with PCL tears. This treatment significantly improves joint stability and knee function over the long term, demonstrating its effectiveness as a promising therapeutic option.

## INTRODUCTION

Cruciate ligament ruptures are among the most prevalent knee joint injuries in sports. Posterior cruciate ligament (PCL) injuries, though less frequent than anterior cruciate ligament injuries, still present significant clinical challenges [1]. Physiologically, the PCL is a key restraint to posterior tibial translation and contributes to rotational control and joint congruence, particularly in deep flexion [2]. The PCL plays a critical role in maintaining the stability of the posterior knee joint, highlighting the importance of accurate diagnosis and effective treatment for such injuries [3]. Surgical intervention is a well-established method for addressing cruciate ligament ruptures, but the outcomes of different surgical approaches can vary significantly, particularly concerning their impact on joint stability [4]. In recent years, reconstruction of single-bundle autologous hamstring tendons for PCL injuries has gained attention, proving to be effective in initial treatment phases [5, 6]. While early outcomes indicate good stability,

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studies have suggested that long-term stability of the graft diminishes over time, thus necessitating further advancements in treatment methods to maintain graft stability over extended periods [5]. Braided sutures, a non-absorbable material, have seen increased use in surgeries due to their superior tissue compatibility and strength [6-8]. Despite their growing application, there is limited research on the use of braided sutures in the context of posterior cruciate ligament reconstruction, particularly regarding their influence on joint stability. The results will offer valuable information on the effectiveness of this combined method, assisting in the development of optimal treatment plans for patients undergoing PCL reconstruction surgical operations.

Braided sutures offer high tensile strength and durability, but their role as an adjunct in PCL reconstruction has not been adequately evaluated, particularly in terms of long-term joint stability. The lack of comparative evidence on this combined technique represents a relevant clinical gap. This study aimed to assess the effect of single-bundle hamstring reconstruction augmented with braided sutures on postoperative knee joint stability in patients with PCL tears.

## METHODS

The quasi-experimental study was conducted at Shahida Islam Medical Complex from June 2024 to June 2025, after taking ethical approval with IRB no: SIMC/ET.C./0055/24. The sample size was calculated with Open Epi version 3.01 (open-source epidemiologic calculator) by estimating a 1.0-mm difference in posterior tibial translation between groups as measured by the KT2000 arthrometer at a 30-lb load [6]. Using an expected standard deviation of 1.5 mm from previous studies, a two-sided α of 0.05, and 80% power, a minimum of 36 patients per group was required. Allowing for an anticipated 20–25% loss to follow-up, we aimed to recruit 60 patients per group. The patients were 20-65 years old, diagnosed with PCL rupture and undergoing PCL reconstruction. The rupture was diagnosed clinically by the drawer test and further confirmed by MRI. Individuals with other ligament injuries, a history of knee joint disease or trauma, previous knee surgery, bilateral injuries, or chronic illnesses were excluded from the study. After obtaining written informed consent, the study population was divided into two groups, control (Group A) and cases (Group B), based on the patient's choice of ongoing departmental PCL reconstruction surgeries. Before making the choice, patients were thoroughly informed about the surgery procedure and its outcome in their language and were assured they understood it well. Group A underwent reconstruction of the single-bundle hamstring reconstruction (autologous). Patients were given epidural anesthesia and the double Endo-Button technique following standard preoperative assessments. The knee was accessed using an anterolateral arthroscopic portal to allow optimal visualization and precise instrumentation. The portal was positioned approximately 1-2 cm distal and 1-2 cm anterior to the lateral femoral epicondyle for clear access to the knee joint. The arthroscope was inserted through this portal for comprehensive examination of the adjacent tissues and structures. In cases of meniscal injuries, repairs were performed before the PCL reconstruction. The autogenous hamstring tendon of the patient was then harvested, braided, and sutured at both ends to form a four-strand graft with a 9mm diameter. The tibial tunnel was carefully created using a reverse drill to ensure precise tunnel placement. For tibial fixation, an interference screw (or the specific device used in your procedure) was inserted to secure the graft at the tibial insertion point. This was done after passing the autogenous hamstring tendon through the tibial and femoral tunnels, ensuring a stable and secure fixation. The graft was tightened with the knee in an extended position to restore the stability of the joint. In Group B, the braided suture technique was employed to enhance the strength and stability of the graft. The braided suture (Ethicon thread) was woven into the hamstring tendon by creating a flat knot. The tendon was braided to the desired length and wrapped around the braided wire to form a robust four-strand graft with a total diameter of 9mm. The suture was securely tied to ensure optimal graft tension and stability. This incorporation of the braided suture allowed for enhanced fixation and durability of the graft within the tibial and femoral tunnels. All other steps in the procedure were identical to those performed in Group A (Figure 1).

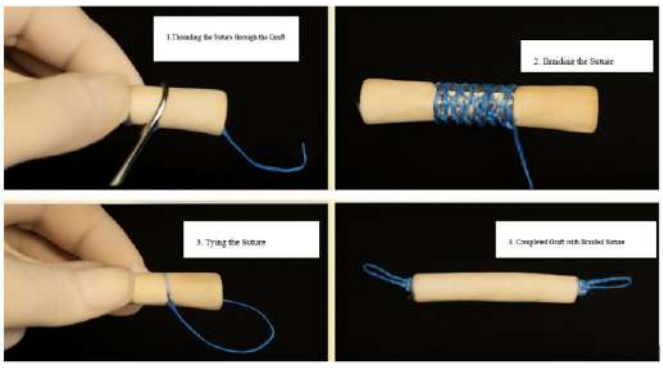

**Figure 1:** Step-wise Approach for Group B Surgery

The primary outcomes assessed included the overall treatment success rate (excellent and good outcomes), complication rate, gait, knee joint activity, and stability (by the KT2000 test). The treatment outcomes for both populations of patients were evaluated using the scoring system of the knee joint function developed by the Special Surgery Hospital (SSH) in New York, USA. This scoring

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system comprises 6 positive points and 1 negative point, with a maximum possible score of 100. The classification system is as follows: scores of more than 85 points are considered Very Good, from 70 to 84 points are considered good, from 60 to 69 points are considered medium, and scores below 59 points are considered bad outcomes [6, 9]. Complication rates, including infections, vascular injuries, nerve injuries, and flexion limitations, were calculated for all populations during hospital stay. The Joint activity for both populations was measured both before and 12 months after surgery. Key indicators, such as the maximum flexion in the knee joint and the range of motion, were assessed using plain radiographic measurements. A 3D gait analysis system was also employed to evaluate gait parameters, including speed of walking, the stride length, and gait asymmetry index, before the surgery and 1 year after the surgery. The Rasmussen score was used to evaluate Knee joint function, which assesses five aspects: pain, mobility, extension of the knee, range of motion of the joint, and joint stability. Each aspect is scored up to 6 points, with higher scores indicating better knee function [7]. The posterior translation of the tibia at 15, 20, and 30 pounds, preoperatively and one year postoperatively, was determined by the KT2000 arthrometer. Displacements in forward and rear were measured, and the average of three readings was recorded. All evaluations and tests were performed by two experienced professionals. The data were analyzed using the 26.0 version of SPSS. In descriptive statistics, continuous variables were shown as the Mean ± SD, and categorical variables were expressed as a percentage (%). To compare the populations, an independent sample t-test was used for continuous variables, while the Chi-square test was applied to examine the association between categorical variables. Baseline characteristics of participants who completed follow-up and those lost to follow-up were qualitatively compared to assess potential attrition bias. A p-value of <0.05 was considered statistically significant.

## RESULTS

The study population was statistically age, gender, and BMI matched. Qualitative inspection of baseline demographic and clinical variables showed no noticeable differences between participants who completed follow-up and those lost to follow-up. Because no postoperative data were available for patients lost to follow-up, additional statistical analysis was not possible. Further, the difference between disease duration, lesion location, and the cause of injury was also non-significant in both groups (p>0.05) (Table 1).

**Table 1:** Baseline Characteristics of the Study Population

| Parameters | Group A (n=60) | Group B (n=60) | T-score | p-value |
|---|---|---|---|---|
| **Gender, n (%)** | | | | |
| Male | 40 (66.67%) | 40 (66.67%) | 0.17 | 0.674 |
| Female | 20 (33.33%) | 20 (33.33%) | | |
| **Age** | | | | |
| Years | 36.39 ± 10.02 | 36.63 ± 11.26 | 0.113 | 0.904 |
| **BMI** | | | | |
| $Kg/m^2$ | 24.09 ± 3.11 | 25.42 ± 2.56 | 0.071 | 0.968 |
| **Course of Disease** | | | | |
| Months | 5.36 ± 1.69 | 5.34 ± 1.81 | 0.163 | 0.864 |
| **Injury Side** | | | | |
| Right | 21 (35%) | 22 (36.67%) | 0.038 | 0.837 |
| Left | 39 (65%) | 38 (63.33%) | | |
| **Cause of Injury** | | | | |
| Accidental | 38 (63.33%) | 41 (68.33%) | 0.161 | 0.682 |
| Natural | 22 (36.67%) | 19 (31.67%) | | |

An independent sample t-test was applied, and p-values of <0.05 were taken as statistically significant.

At final follow-up, the proportion of patients rated as very good or good was high in both groups (Group A: 86.7%, Group B: 90.0%). The difference between groups was not statistically significant ($\chi^2 = 0.36$, p=0.55) (Table 2).

**Table 2:** Comparison of the Rates of Treatment and Complication Rate Post-Reconstruction in the Study Population

| Parameters | Group A (n=60) | Group B (n=60) | $\chi^2$/p |
|---|---|---|---|
| Very Good | 33 (55%) | 36 (60%) | – |
| Good | 19 (31.67%) | 18 (30%) | – |
| Mediocre | 7 (11.67%) | 5 (8.33%) | – |
| Bad | 1 (1.67%) | 1 (1.67%) | – |
| Very Good and Good Rate | 52 (86.67%) | 54 (90%) | 0.36/0.55 |
| Infectious | 1 (1.67%) | 0 (0%) | 1.02/0.316 |
| Vascular Damages | 1 (1.67%) | 1 (1.67%) | 1.03/0.32 |
| Flexion Is Limited | 2 (3.33%) | 1 (1.67%) | 2.04/0.154 |

Before surgery, there was no statistically significant difference in the joint activity indexes between the two populations (p>0.05). However, 12 months after surgery, the joint activity indexes in the study population were significantly higher compared to the control population, with this difference being statistically significant (p<0.05). Before surgery, statistically, there were no significant differences observed in the gait parameters among the populations. However, one year after the surgery, the study population confirmed significantly greater speed of walking and stride length, while the gait asymmetry index was significantly reduced in the study population. Before the surgery, statistically, no significant difference was observed in the Rasmussen scores between populations. However, one year after the surgery, the Rasmussen score was significantly higher in the study population as compared to the control population. Before surgery,

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statistically, there were no significant differences found in the results of the KT2000 test among the groups; however, one year after the surgery, the study population showed significantly lower results of the KT2000 test than those in the control population (Table 3).

**Table 3:** Comparison of Joint Activity Indicators (In Degrees), Gait Parameters, Rasmussen Scores, Forward and Posterior Displacement Before and After Surgery in the Study Population

| Parameters | | Group A | Group B | $\chi^2$ | p-value |
|---|---|---|---|---|---|
| Before and After Surgery | | 60, 49 | 60, 54 | | |
| Motion Range for Knee | Before Reconstruction | 86.79 ± 2.86 | 85.85 ± 3.05 | 0.104 | 0.918 |
| | 1 Year After Reconstruction | 106.82 ± 3.19 | 106.79 ± 3.36 | 4.676 | <0.001 |
| Flexion of the Knee Maximum | Before Reconstruction | 90.33 ± 2.73 | 89.76 ± 2.76 | 0.146 | 0.841 |
| | 1 Year After Reconstruction | 106.29 ± 3.16 | 109.65 ± 3.22 | 5.075 | <0.001 |
| Stride Length (m) | Before Reconstruction | 0.64 ± 0.11 | 0.64 ± 0.10 | 1.083 | 0.282 |
| | 1 Year After Reconstruction | 1.17 ± 0.12 | 1.23 ± 0.14 | 2.555 | 0.012 |
| Speed of Walking (m/s) | Before Reconstruction | 1.11 ± 0.13 | 0.98 ± 0.11 | 0.922 | 0.354 |
| | 1 Year After Reconstruction | 1.25 ± 0.12 | 1.34 ± 0.14 | 2.577 | 0.012 |
| Gait Asymmetry Index | Before Reconstruction | 0.33 ± 0.07 | 0.32 ± 0.08 | 0.788 | 0.432 |
| | 1 Year After Reconstruction | 0.08 ± 0.04 | 0.07 ± 0.03 | 6.056 | <0.001 |
| Pain | Before Reconstruction | 3.11 ± 0.62 | 3.26 ± 0.29 | 0.333 | 0.722 |
| | 1 Year After Reconstruction | 5.51 ± 0.25 | 5.26 ± 0.39 | 2.98 | 0.002 |
| Mobility | Before Reconstruction | 2.72 ± 0.43 | 2.62 ± 0.41 | 0.385 | 0.682 |
| | 1 Year After Reconstruction | 5.22 ± 0.45 | 5.29 ± 0.26 | 2.599 | <0.001 |
| Extension of the Knee | Before Reconstruction | 2.92 ± 0.46 | 2.92 ± 0.23 | 1.033 | 0.289 |
| | 1 Year After Reconstruction | 5.32 ± 0.22 | 5.42 ± 0.25 | 2.753 | 0.005 |
| Range of Motion for the Joint | Before Reconstruction | 2.72 ± 0.25 | 2.72 ± 0.26 | 0.279 | 0.762 |
| | 1 Year After Reconstruction | 4.25 ± 0.21 | 4.62 ± 0.40 | 3.142 | 0.003 |
| Joint Stability | Before Reconstruction | 2.23 ± 0.25 | 1.93 ± 0.26 | 1.439 | 0.140 |
| | 1 Year After Reconstruction | 5.12 ± 0.39 | 5.32 ± 0.25 | 3.353 | 0.001 |
| 15 Pounds* | Before Reconstruction | 3.36 ± 0.62 | 3.52 ± 0.52 | 1.276 | 0.191 |
| | 1 Year After Reconstruction | 2.58 ± 0.54 | 2.32 ± 0.52 | 2.288 | 0.013 |
| 20 Pounds* | Before Reconstruction | 6.62 ± 1.92 | 6.52 ± 2.02 | 0.146 | 0.865 |
| | 1 Year After Reconstruction | 3.52 ± 0.72 | 3.32 ± 0.62 | 2.149 | 0.023 |
| 30 Pounds* | Before Reconstruction | 9.12 ± 2.22 | 9.22 ± 2.32 | 0.26 | 0.777 |
| | 1 Year After Reconstruction | 4.52 ± 1.12 | 4.22 ± 1.02 | 1.142 | 0.241 |
| 15 Pounds** | Before Reconstruction | 0.72 ± 0.12 | 0.76 ± 0.12 | 0.969 | 0.319 |
| | 1 Year After Reconstruction | 0.71 ± 0.05 | 0.65 ± 0.06 | 3.718 | <0.001 |
| 20 Pounds** | Before Reconstruction | 1.95 ± 0.26 | 2.02 ± 0.25 | 0.999 | 0.305 |
| | 1 Year After Reconstruction | 1.36 ± 0.16 | 1.21 ± 0.14 | 5.491 | <0.001 |
| 30 Pounds** | Before Reconstruction | 3.38 ± 0.38 | 3.37 ± 0.37 | 0.127 | 0.881 |
| | 1 Year After Reconstruction | 1.42 ± 0.7 | 1.31 ± 0.27 | 2.085 | 0.028 |

Note: Forward and posterior displacement represent anterior and posterior tibial translation, respectively, measured using the KT2000 arthrometer under 15-, 20-, and 30-pound loads. *Forward displacement (15 lb / 20 lb / 30 lb), mm. **Posterior displacement (15 lb / 20 lb / 30 lb), mm

## DISCUSSION

The present study included age, gender, and BMI-matched controls and cases, as previous literature has shown different study outcomes due to these variables (Table 1). Although loss to follow-up occurred, baseline variables appeared similar between groups, suggesting that attrition was unlikely to substantially bias the outcome estimate. A study reported that obesity was linked to poorer functional outcomes after knee surgery, suggesting a potential correlation that was not observed in the current study population [10, 11]. Gender differences have been observed in several studies as influencing joint recovery, particularly in ACL injuries, where females tend to experience worse outcomes in terms of functional recovery [10-12]. A recent study found that patients who underwent certain types of advanced rehabilitation post-surgery exhibited significantly better outcomes in terms of mobility and function [7]. Some studies report that the overall efficacy of treatment can be highly dependent on pre-existing health conditions, especially chronic conditions like arthritis or diabetes, which might not have been

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considered as potential confounders in this study [13]. The study group at post-operative follow-up of 12 months showed significantly better outcomes in terms of knee flexion and motion range. A study on ACL reconstruction patients found significant improvements in knee flexion and range of motion in the first year after surgery [14]. Similarly, another found that post-surgical rehabilitation significantly influences the range of motion [12]. These results are aligned with the study's findings, highlighting the effectiveness of proper surgical techniques and rehabilitation. However, a recent study noted that joint stiffness remains a prevalent issue even after surgical procedures, particularly in patients with longer disease duration, which could have confounded results if not properly controlled [15]. Previous studies have also shown that Joint stability is closely linked to gait parameters, making the need for durable knee joint stability particularly critical in patients with PCL rupture, which has been validated by the current study findings [10]. One-year post-surgery, the present study population showed significantly greater stride length and walking speed, with reduced gait asymmetry. A study demonstrated that improved gait parameters (speed and stride length) in post-surgical knee patients were predictive of better functional outcomes in the long term [4]. Another study also identified improved gait speed and symmetry as important indicators of successful recovery in musculoskeletal injuries [8]. In the current study, significant improvements in the Rasmussen score were found in the study group after one year, particularly for pain, mobility, and joint stability. In contrast, a study indicated that while improvements in the Rasmussen score are often observed, the degree of improvement can vary widely based on the initial severity of joint damage and patient adherence to post-operative rehabilitation [16]. This could imply that patient-related factors may play a larger role in recovery than the intervention itself. Inter-group differences in gait parameters and KT2000 measures were statistically significant, but the absolute magnitudes were small. Reported MCIDs for gait speed in knee surgery populations are typically on the order of 0.10–0.20 m/s [17]; the current study showed an inter-group difference of ~0.09 m/s. The KT2000 differences were <1 mm, below the 3–5 mm thresholds often cited as clinically relevant for side-to-side laxity [18]. These findings suggest that the braided-suture technique yields subtly superior mechanical stability and gait performance, but the clinical effect size is modest and should be interpreted accordingly. Baseline joint activity indices were comparable; the superior recovery observed in Group B may be explained by the biomechanical and physiological advantages of braided-suture augmentation [19]. The non-absorbable braided suture functions as an internal brace, sharing tensile load with the graft and limiting early graft elongation, particularly at the tibial killer-turn, where peak stress is highest [20]. More consistent posterior tibial control helps maintain normal joint kinematics and reduces abnormal shear forces on healing tissues. This stable mechanical environment likely supports more effective neuromuscular activation, proprioceptive recovery, and symmetrical gait during rehabilitation, contributing to higher joint activity scores in Group B. These mechanisms remain theoretical, as graft strain and rehabilitation parameters were not directly measured. Given these findings, in case of PCL rupture, it is plausible to strengthen the graft in the autologous hamstring tendon by incorporating braided threads, which could help control graft laxity and provide long-term stability. However, related studies on this approach remain limited.

This study was single center with a modest sample size, and some follow-up loss occurred, potentially limiting generalizability. Another limitation is that graft strain, neuromuscular activation, and rehabilitation adherence were not directly measured, and pre-existing comorbidities such as arthritis or diabetes were not controlled, which may have influenced outcomes. Future research should involve larger, multicenter trials with long-term follow-up, incorporating objective measurements of graft biomechanics, rehabilitation adherence, and functional outcomes to validate the advantages of braided-suture augmentation in PCL reconstruction.

## CONCLUSIONS

Posterior cruciate ligament reconstruction with single-bundle hamstring(autologous) and braided sutures combined demonstrated better clinical outcomes. The use of braided sutures improved mechanical stability and knee joint function, which is critical for the overall rehabilitation of PCL rupture. This combined treatment method may present an effective alternative for better recovery in PCL reconstruction.

## Authors' Contribution

Conceptualization: MS, SF, SI, RR
Methodology: MS, SF, SI, RR
Formal analysis: MS, SF, SI, RR
Writing and Drafting: MS, SF, SI, RR
Review and Editing: MS, SF, SI, RR

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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# Diagnostic Accuracy of Red Cell Distribution Width in Diagnosing Early-Onset Neonatal Sepsis in Term Newborns

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## ABSTRACT

Inflammation in neonatal sepsis triggers cytokine-driven disruption of erythropoiesis, producing a mix of immature and damaged red cells. **Objectives:** To determine the diagnostic accuracy of RDW for early onset neonatal sepsis (EONS) in term newborns, taking culture-proven EONS as the gold standard. **Methods:** This prospective validation study was conducted at the Department of Neonatology of Children's Hospital, Institute of Child Health, Multan. A total of 147 term neonates with suspected EONS were enrolled consecutively. Neonates with asphyxia, meconium aspiration, major congenital malformations, or hemolytic disease were excluded. Clinical and laboratory data, including RDW, were collected. Blood, urine, and cerebrospinal fluid cultures were performed as per CLSI guidelines. EONS was confirmed by positive blood culture. A cutoff value of RDW ≥17% was used for labelling EONS. Data were analyzed using SPSS version 25.0, and the diagnostic accuracy of RDW was calculated, taking culture-proven neonatal sepsis as the reference standard. **Results:** The mean postnatal age was 3.7±1.4 days. The mean RDW was 16.9 ± 1.9%. RDW of ≥17% was observed in 54.4% of the neonates. Culture confirmed EONS was diagnosed in 59.9%. RDW showed sensitivity of 84.1% (95% CI: 74.8-91.0%), specificity of 89.8% (95% CI: 79.2-96.2%), positive predictive value of 92.5%, negative predictive value of 79.1%, and diagnostic accuracy of 86.4%. The area under the ROC curve was 0.87 (95% CI: 0.81 – 0.93, p<0.001). **Conclusions:** RDW ≥17% demonstrated high diagnostic accuracy as an early predictor of culture-confirmed EONS in term neonates.

## INTRODUCTION

The terminology "neonatal sepsis," which refers to the systemic illnesses that affect neonates during the initial twenty-eight days of life, includes bloodstream infections (BSIs) or septicemia, pneumonia, meningitis, urinary tract infections, and bone/joint infections [1]. The condition, if manifested in the initial 72 hours of life, is known as Early Onset Sepsis (EOS), while sepsis that is developed after that time is known as Late Onset Sepsis (LOS) [2]. Neonatal sepsis occurs in conjunction with or as a consequence of a suspected or proven infective process [3]. Blood cultures have a long turnaround time and only identify sepsis in one-third of suspected infants, despite being the gold standard for diagnosing neonatal sepsis [4]. The result may be negative if the test is performed before the increase in C-Reactive Protein, which happens only 6 to 8 hours after the infection begins [5]. Microscopic analysis of the degree of anisocytosis is connected with the Red Cell Distribution Width (RDW), a quantitative measure of red cell volume variability [6]. A larger RDW indicates anisocytosis, while a normal RDW indicates the absence of anisocytosis. RDW can be described as the coefficient of variation (CV) of red cell volume measurements in percentage. RDW shows if

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the size of the red cell volume is constant. As the RDW rises, so does the volume heterogeneity and the irregularity in red blood cell size [7]. Because proinflammatory cytokines affect the synthesis of red blood cells, RDW is elevated in sepsis [8]. Research has shown that infection and inflammation increase RDW. Deka A *et al.* examined 100 babies, 50 of whom had sepsis and the other 50 of whom were healthy. Fifty percent of babies had neonatal sepsis. They found that newborn sepsis could be diagnosed with 93.5% accuracy, 86% sensitivity, and 87% specificity at an RDW cut-off level of 17.25% [9]. Similarly, 110 neonates (55 with EOS and 55 controls) were investigated by Nargis *et al.* They concluded that, using Youden's index, the critical cutoff point of RDW was 18.55, with a diagnostic accuracy of 94.45%, a sensitivity of 94.55%, and a specificity of 96.36% for the diagnosis of EOS [10]. Cytokine-induced inflammation suppresses erythropoietin activity and disturbs iron metabolism, leading to the production of red cells of variable sizes (anisocytosis). This variability increases RDW, which reflects underlying inflammatory stress and impaired erythropoiesis.

A timely diagnosis of neonatal sepsis is essential to its enhanced outcome since it is a frequent cause of morbidity and death among infants. There is limited research on RDW in newborns and its relation to neonatal sepsis. To diagnose and treat newborn sepsis as early as possible, RDW, as an effective predictor, shall be used to guide the treatment of pediatricians and neonatologists. The research will aid in generating evidence among septic neonates who are admitted to our facility. It will lead to the use of RDW as a helpful predictive tool to treat and diagnose neonatal sepsis as early as possible by treating doctors. This study aimed to find the diagnostic value of RDW in neonatal sepsis.

## METHODS

This prospective validation study was performed at the Department of Neonatology in Children's Hospital (CH) and The Institute of Child Health (ICH), Multan, from 1st January 2024 to 30th June 2024 after approval from the Institutional Ethics Review Committee (2148 CH&ICH Multan). A total of 147 term neonates, admitted within 7 days of postnatal life due to suspected early onset neonatal sepsis, were consecutively included in the study after informed consent was provided by the parents. Neonates with a history of perinatal asphyxia, meconium aspiration, major congenital malformation, and ABO / RH – isoimmunization were excluded from the study. Baseline characteristics of neonates, including postnatal age, gestational age, gender, mode of delivery, and weight on admission (kg), were recorded. Through aseptic technique, five millilitres of venous blood were drawn on admission for complete blood counts and red cell distribution width. CBC analysis was performed on an autoanalyzer (Model: Sysmex XN-2000, features: 3-part differential) in the hematology section. All neonates had blood and urine cultures obtained on admission before the first dose of antibiotics as per hospital protocol. Based on clinical manifestations and indications, neonates were subjected to chest x-rays (Model: Toshiba Rotanode, Type: Floor-mounted digital radiography systems) and cerebrospinal fluid examination and cultures. CSF examination and culture were performed after lumbar puncture, where cerebrospinal fluid is aseptically collected from the L3–L4 or L4–L5 interspace using a sterile spinal needle. The fluid was divided into sterile tubes for biochemical, cytological, and microbiological analysis. For culture, a portion was inoculated immediately onto blood and chocolate agar and incubated in the laboratory to identify bacterial growth and sensitivity. All cultures were performed in the microbiology section as per The Clinical & Laboratory Standards Institute (CLSI) guidelines. Rephrase and divide into small sentences so that the meaning becomes clear. Neonates ≤7 days of age were evaluated for early-onset sepsis if they had at least one maternal risk factor. These included maternal fever (T ≥101 °F) within 72 hours before delivery, foul-smelling liquor, or rupture of membranes for more than 24 hours. Clinical suspicion was raised when a neonate exhibited three or more features: temperature instability (>100.5 °F or <96 °F), weak cry, poor feeding, lethargy, capillary refill time >3 seconds, decreased tone, reduced neonatal reflexes, apnea, respiratory rate >60/min, or heart rate <80 or >160/min. EONS was confirmed if a pathogen was detected from the blood, urine, or cerebrospinal fluid in a newborn with suspicion of EONS. The sample size was calculated through one sample sensitivity and specificity formula through online software https://wnarifin.github.io/ssc/sssnsp.html. The sample size required was 147 neonates based on 86% sensitivity and 87% specificity of RDW, 50 percent prevalence of EONS, 8 percent precision, and 95 percent confidence [10]. The data were analyzed with the help of SPSS version 25.0. The Shapiro-Wilk test was used to identify numerical data as normally distributed. The descriptive statistics were performed as mean, standard deviation, and frequency (percentages) of numerical and categorical variables, respectively. RDW (%) cut-off value of 17 or more, as reported in literature previously, was taken to classify EONS as positive or negative. Based on culture-positive EONS as a reference standard, the diagnostic accuracy of the RDW was computed, including the area under the receiver operating characteristic curve and 95% confidence interval.

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## RESULTS

The mean postnatal age on presentation was 3.7 ± 1.4 days, and the mean gestational age on delivery was 37.9 ± 0.7 weeks. The participants included 74 (50.3%) male and 80 (54.4%) were born through cesarean section. The mean weight on admission was 2.8 ± 0.1 kg. The mean red cell distribution width (RDW) was 16.9 ± 1.9%. At cut off value of ≥ 17% RDW, the early neonatal sepsis (EONS) was labelled in 80 (54.4%). The diagnosis of definitive EONS was made in 88 (59.9%) of the suspected neonates (Table 1).

**Table 1:** Characteristics of Term Neonates Presenting with Suspected Early Neonatal Sepsis (n=147)

| Variables | Mean ± SD, n (%) |
|---|---|
| **Age** | |
| Days | 3.7 ± 1.4 |
| **Gestational Age** | |
| Weeks | 37.9 ± 0.7 |
| **Gender** | |
| Male | 74 (50.3%) |
| Female | 73 (49.7%) |
| **Weight (kg)** | |
| On Admission | 2.8 ± 0.1 |
| **Mode of Delivery** | |
| SVD | 67 (45.6%) |
| Cesarean Section | 80 (54.4%) |
| Red Cell Distribution Width (%) | 16.9 ± 1.9 |
| **EONS using RDW (≥17%)** | |
| Yes | 80 (54.4%) |
| **Definitive EONS** | |
| Yes | 88 (59.9%) |

*EONS – Early onset neonatal sepsis

Culture positive early onset neonatal sepsis was diagnosed in 88 (59.8%), and using RDW EONS was diagnosed in 80 (54.4%) of the neonates. Taking definitive EONS as reference standard, the sensitivity, specificity, positive and negative predictive values (PPV and NPV) and accuracy of RDW were 84.1% (95% CI: 74.8% to 91.0%), 89.8% (95% CI: 79.2% to 96.2%), 92.5% (95% CI: 85.2% to 96.4%), 79.1% (95% CI: 69.9% to 86.1%) and 86.4% (95% CI: 79.8% to 91.5%) respectively (Table 2).

**Table 2:** Diagnostic Accuracy of RDW for EONS Taking Definitive EONS as Gold Standard (n=147)

| EONS Using RDW | Definitive EONS | | p-value |
|---|---|---|---|
| | Yes | No | |
| Yes (≥17%) | 74 | 6 | <0.001 |
| No (<17%) | 14 | 53 | |
| Sensitivity | 84.1% (95% CI: 74.8% to 91.0%) | | – |
| Specificity | 89.8% (95% CI: 79.2% to 96.2%) | | |
| PPV | 92.5% (95% CI: 85.2% to 96.4%) | | |
| NPV | 79.1% (95% CI: 69.9% to 86.1%) | | |
| Accuracy | 86.4% (95% CI: 79.8% to 91.5%) | | |

Clopper-Pearson exact confidence intervals reported. RDW had an area under the receiver operating characteristic curve of 0.87 (95% CI: 0.81 – 0.93), for the diagnosis of EONS, taking culture-confirmed neonatal sepsis as the gold standard. Using Youden's index, the RDW optimal cut-off was 17.25 with a sensitivity of 84.1 and a specificity of 91.5%. Area Under Curve: 0.87 (95% CI: 0.81 – 0.93), p-value<0.001 (Figure 1).

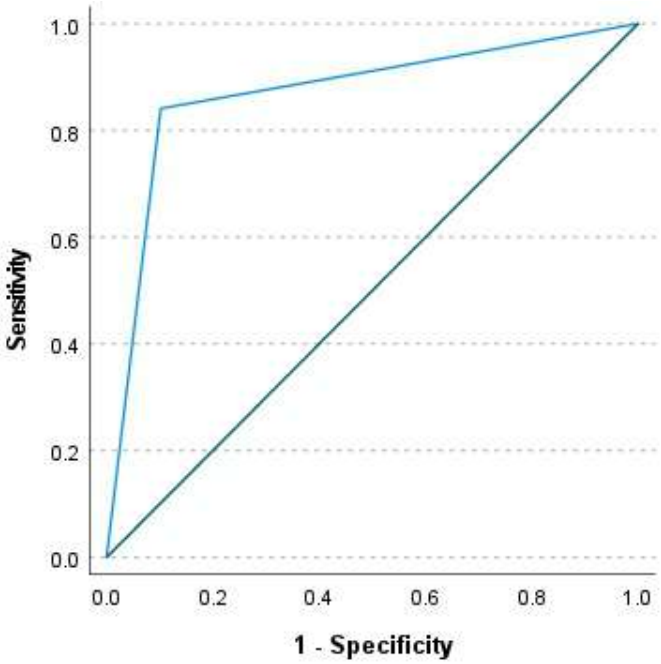


**Figure 1:** RDW Receiver Operating Characteristic Curve for Diagnosis of EONS, Taking Definitive EONS as Gold Standard

## DISCUSSION

Red cell distribution width was examined in this work as a potential early, accessible, and affordable biomarker for the detection of newborn sepsis. We observed that the mean postnatal age on presentation was 3.7 ± 1.4 days, and 50.3% were male. With its high death rate, neonatal sepsis continues to be difficult for neonatal healthcare professionals to diagnose and treat. Early detection of neonatal septicemia reduces mortality rates by enabling the prompt initiation of antibiotic therapy and preventing the needless treatment of a baby who is not sick. Due to a lack of early diagnosis and identification of high-risk cases, mortality rates are high in underdeveloped regions [11]. In research by Nargis *et al.* 67.27% of patients were male, and the mean age of the cases was 26.5±19 hours, while the mean age of the controls was 26 ± 12.3 hours [10]. Cosar *et al.* identified a male majority and reported that the mean age of the cases was 1.98 ± 0.9 days, whereas the mean age of the controls was 1.87 ± 0.92 days [12]. However, Saleh *et al.* found that there were more females than men [13]. In the present study, the mean red cell distribution width (RDW) was 16.9 ± 1.9%. In comparison to controls (16.23 ± 1.16%),

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Nargis *et al.* found that newborn sepsis cases had a mean RDW level of 21.31 ± 3.08% [10]. Chen *et al.* also discovered that the sepsis group had a considerably higher mean RDW level [14]. The reason for this is that inflammation raises the body's levels of neurohormones [15]. These neurotransmitters can promote the growth of red blood cells by secreting more erythropoietin (EPO), which raises the RDW value. Inflammatory substances can also impact the body's iron metabolism and marrow hematopoietic function [16]. In current study, taking definitive EONS as a reference standard, the sensitivity, specificity, PPV, NPV, and accuracy of RDW (≥17%) were 84.1%, 89.8%, 92.5%, 79.1% and 86.4%, respectively. The area under the curve for RDW was 0.87, indicating excellent discrimination. RDW was considerably greater in culture-confirmed newborn sepsis than controls (sensitivity 60%, specificity 88.3%, AUC ~0.80), according to 2021 retrospective cohort research from a tertiary care university hospital [17]. Their specificity patterns are similar to our findings, despite having a little lower sensitivity. The AUC in our study (0.87) was slightly higher than what they studied (0.80), indicating that RDW demonstrated better overall diagnostic performance for early-onset neonatal sepsis in our population. High value of RDW was associated with increasing sepsis severity (sepsis severe septic shock), according to a 2022 comparative study conducted in Egypt that found mean RDW levels were significantly greater in septic neonates compared to controls. Our high PPV and the hypothesis that higher RDW indicates more advanced disease are supported by this [18]. The pooled sensitivity and specificity of RDW for neonatal sepsis were 0.88 and 0.90, respectively, with an AUC of 0.95 in a meta-analysis of 15 trials involving more than 1,300 neonates [19]. These figures highlight the overall diagnostic strength of RDW and are in good agreement with our findings (sensitivity 0.84, specificity 0.90). The AUC in our study was slightly lower than the pooled AUC of 0.95 reported in this meta-analysis, indicating that while RDW showed excellent diagnostic accuracy in both, the combined data across multiple trials demonstrated even stronger discriminative performance than our single-center findings. Similar to our great PPV, a hospital-based study conducted in Sudan with term newborns with culture-proven sepsis found that the mean RDW was increased (~19.3%) in over 90% of cases, with a clear correlation with positive blood culture and CRP positivity [20]. RDW ≥20% was shown to be independently predictive of outcome and strongly linked with higher mortality ($p<0.003$) in another prospective observational study (India, ~251 septic neonates). This emphasizes the predictive, rather than only diagnostic, relevance of RDW [21]. Research indicates that, as compared to static RDW measurements, dynamic changes in RDW (rising from baseline) improve diagnosis accuracy in very low birth weight infants. Even though our study only used one RDW measurement, our accuracy rate of 86.4% indicates that baseline RDW still has a significant amount of diagnostic potential [22]. The mechanisms that underlie elevated RDW in infection states include inflammatory-mediated bone marrow failure, cytokine release, oxidative stress, and erythrocyte membrane instability—make RDW rise in conditions of sepsis [18]. A recurring concept in these recent international research studies is that high RDW is a marker for newborn sepsis that is both specific and sensitive enough to have both diagnostic accuracy and prognostic significance. RDW helps identify neonates at high risk for EONS early on by providing a quick and inexpensive measure that can be incorporated into CBC examinations. Our study's merits included utilizing strict inclusion criteria and enrolling only term neonates, which improved internal validity by lowering gestational age-related confounding variables. The reliability of the diagnostic accuracy estimates was increased by using a definitive reference standard, such as clinical and/or culture-proven EONS. The results were very pertinent to actual clinical practice because RDW is a standard and economical part of CBC, particularly in low-resource environments.

Some of the limitations of our study were that this was a single-center study, which limited the generalizability of research findings to other populations and healthcare settings. Only term newborns were included in the study; preterm infants, who are more likely to develop sepsis and may show distinct RDW dynamics, were not included. Future multicenter studies with larger and more diverse neonatal populations should include preterm infants, serial RDW measurements, and correlation with inflammatory markers (e.g., CRP, PCT) to further validate and refine the diagnostic utility of RDW in early-onset neonatal sepsis.

## CONCLUSIONS

There were great sensitivity, specificity, and positive predictive value because red cell distribution width (RDW) showed high diagnostic accuracy in the diagnosis of early onset neonatal sepsis in term neonates. As a conveniently located and relatively inexpensive biomarker, RDW may act as a valuable adjuvant in the diagnosis of newborn sepsis in the early stages of this condition, particularly in settings where the availability of the latest diagnostic instruments is limited.

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## Authors' Contribution

Conceptualization: MJI, AK
Methodology: MHR, MZS
Formal analysis: MZS, JR
Writing and Drafting: MJI, MHR, JR, AK
Review and Editing: MJI, MHR, MZS, JR, AK

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**

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# Frequency of Echocardiographic Changes in Patients with Chronic Liver Disease at a Tertiary Care Hospital in Karachi

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## ABSTRACT

Chronic liver disease (CLD) is a major health burden in Pakistan, commonly due to viral hepatitis. Cirrhotic cardiomyopathy (CCM) is an underdiagnosed complication that may impact prognosis and management. **Objectives:** To determine the frequency and spectrum of echocardiographic abnormalities in CLD patients and assess their correlation with disease severity based on the Child-Pugh classification. **Methods:** A cross-sectional study of 187 adult CLD patients was conducted at Dr. Ruth K.M. Pfau Civil Hospital, Karachi, between September 2024 and February 2025. Echocardiographic parameters, including pulmonary artery pressure, ejection fraction, systolic, and diastolic function, were evaluated using a Philips EPIQ 7 (Philips Healthcare, Andover, MA, USA) system. Patients were categorized according to Child-Pugh class (B or C). Associations between echocardiographic findings and Child-Pugh class were analyzed using chi-square and logistic regression tests, with $p < 0.05$ considered significant. **Results:** Mean age was 55.6 ± 13.4 years; 51.9 % were men. The leading etiologies were hepatitis C (46 %) and B (26 %). Diastolic dysfunction was the most frequent abnormality (53.5 %), while systolic dysfunction occurred in 23.5 %—significantly more common in women ($p < 0.001$) and in advanced disease (Child-Pugh C: 67 % vs B: 38 %; OR ≈ 3.4, p=0.0001). Pulmonary hypertension (23.5%) and reduced ejection fraction (10.2%) showed no correlation with Child-Pugh class. **Conclusions:** Echocardiographic abnormalities are common in CLD, particularly diastolic dysfunction. Systolic dysfunction increases with worsening hepatic severity, emphasizing the need for routine cardiac assessment in cirrhotic patients for better risk stratification and management.

## INTRODUCTION

In Pakistan, chronic viral hepatitis and delayed access to screening and treatment are major causes of chronic liver disease (CLD), a growing health concern [1]. Cirrhotic cardiomyopathy (CCM), one of the extrahepatic complications that patients with cirrhosis frequently experience, has become a clinically significant but often underdiagnosed condition [2]. In the absence of primary heart disease, CCM includes both structural and functional cardiac alterations, particularly electrophysiological abnormalities, systolic impairment under stress, and left ventricular diastolic dysfunction (LVDD) [2, 3]. Advances in transthoracic echocardiography have made it easier to identify CCM using tissue Doppler and deformation-based indices. Updated consensus criteria published in 2020 incorporate left atrial volume, E/e′ ratio, and septal or lateral e′ velocity to improve diagnostic specificity and to distinguish true diastolic dysfunction from preload-related changes in cirrhosis [4, 5]. The most common abnormality is still diastolic dysfunction, though reported prevalence varies by study population and methodology [3, 6].

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Furthermore, echocardiography is the primary non-invasive screening tool for Porto-pulmonary hypertension (PPH), a clinically significant cardiovascular consequence of cirrhosis [6, 7]. These abnormalities have important clinical consequences. Cirrhotic cardiomyopathy and Porto-pulmonary hypertension have been linked to peri-procedural instability during acute decompensation, trans jugular intrahepatic portosystemic shunt (TIPS) placement, and liver transplantation [8, 9]. Some of these cardiac changes may partially regress following successful liver transplantation, suggesting that they are at least partly reversible and hemodynamically driven [9]. Therefore, current guidance strongly supports routine echocardiographic assessment in cirrhotic patients for early detection and risk stratification [5, 10].

Even though CLD is very common in Pakistan, there is limited local published data on the frequency and pattern of echocardiographic abnormalities, particularly diastolic dysfunction and Porto-pulmonary hypertension in cirrhotic patients [1, 11]. Addressing this gap is relevant to transplant candidacy, intensive care planning, and long-term surveillance. This study aimed to describe the spectrum and frequency of echocardiographic abnormalities in CLD, and examine their association with liver disease severity using the Child-Pugh classification at a large public-sector tertiary-care hospital in Karachi.

## METHODS

This was an analytical cross-sectional study conducted from September 2024 to February 2025 in the inpatient and outpatient units of the Department of Medicine at Dr. Ruth K.M. Pfau Civil Hospital, Karachi. The study protocol was reviewed and approved by the Institutional Review Board of Dow University of Health Sciences (DUHS) (IRB-3563/DUHS/Approval/2024/230). All participants provided written informed consent before enrollment. The minimum required sample size was calculated using Daniel's formula for prevalence studies ($Z^2 \times p \times (1-p) / d^2$), assuming Z = 1.96 for 95% confidence, expected prevalence of echocardiographic abnormality in cirrhosis of 39% based on prior local data [11], and a margin of error (d) of 8%. This yielded a required sample of approximately 180 patients. To enhance precision and allow subgroup comparisons by Child-Pugh class and gender, and to compensate for anticipated non-response or incomplete studies, we aimed to recruit at least 185 patients. A total of 187 patients were ultimately included. A non-probability consecutive sampling strategy was used. All eligible patients with established cirrhosis presenting during the study period and fulfilling the inclusion criteria were approached. Consecutive non-probability sampling may introduce selection bias; however, this approach was considered appropriate and feasible in a high-volume tertiary-care hospital where true randomization is not practical. Adults between 30 and 80 years of age, of either gender, with clinically, biochemically, and ultrasonographically established cirrhosis of ≥6 months' duration and classified as Child-Pugh class B or C were eligible. Exclusion criteria were: history of primary cardiac disease (including prior acute coronary syndrome, valvular heart disease, known cardiomyopathy, uncontrolled hypertension, or chronic heart failure), chronic kidney disease, chronic primary pulmonary disease, asthma, stroke with residual hemodynamic compromise, or any condition that could independently alter left ventricular function or pulmonary pressures. Clinical and demographic information (including age, sex, known etiology of CLD, and decompensation symptoms) was obtained at the time of presentation using a structured, interviewer-administered proforma. These data were derived from direct patient assessment, bedside examination, and review of hospital records (admission notes, laboratory reports, and abdominal ultrasound findings). Signs and symptoms reported (e.g., abdominal distension, altered sensorium, gastrointestinal bleeding) were recorded prospectively on this proforma at the time of inclusion. The Child-Pugh score (class B or C) was calculated for each patient using standard clinical and laboratory parameters (serum bilirubin, serum albumin, international normalized ratio (INR), presence of ascites, and grade of hepatic encephalopathy). All participants underwent transthoracic echocardiography performed by a consultant cardiologist with ≥5 years' post-fellowship experience, using a Philips EPIQ7 (Philips Healthcare, Andover, MA, USA) cardiac ultrasound system by an experienced consultant cardiologist with a phased-array transducer (2–4 MHz). Standard parasternal long-axis, parasternal short-axis, apical four-chamber, and apical two-chamber views were acquired in the left lateral decubitus position according to ASE/EACVI recommendations. To minimize observer bias, the cardiologist conducting the echocardiography was not informed of the patients' Child-Pugh class at the time of image acquisition and interpretation. The following parameters were assessed and defined: Systolic dysfunction: visually or quantitatively reduced left ventricular systolic performance, including an ejection fraction <55% or impaired global systolic function on standard echocardiographic assessment. Diastolic dysfunction: abnormal left ventricular relaxation/filling consistent with ASE/EACVI criteria, including elevated E/e' ratio (>14), reduced septal or lateral e' velocity (septal e' <7 cm/s or lateral e<10 cm/s), enlarged left atrial volume index (>34 mL/m$^2$), or reduced deceleration time, in the absence of confounding primary cardiac disease. Pulmonary hypertension: elevated estimated pulmonary artery

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systolic pressure consistent with pulmonary hypertension, inferred from tricuspid regurgitation jet velocity and right ventricular systolic pressure estimation. For descriptive purposes in this study, pulmonary hypertension was recorded when calculated pulmonary artery systolic pressure was >25 mmHg on echocardiography, acknowledging that right-heart catheterization remains the gold standard. Reduced ejection fraction (EF): EF <55%. Data were entered and analyzed using IBM SPSS Statistics version 26.0. Continuous variables (e.g., age, ejection fraction) were summarized as mean ± standard deviation (SD), while categorical variables (e.g., gender, etiology of chronic liver disease, presence of systolic dysfunction, diastolic dysfunction, and pulmonary hypertension) were expressed as frequencies and percentages. Comparisons of categorical variables across groups (e.g., echocardiographic findings by gender and by Child-Pugh class) were evaluated using the chi-square test. To evaluate the association between echocardiographic manifestations and disease severity, binary logistic regression analysis was performed. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to estimate the strength of associations. For these analyses, Child-Pugh Class B was defined as the reference category, and odds for Class C were calculated relative to this baseline. A p-value < 0.05 was considered statistically significant.

## RESULTS

A total of 187 patients with chronic liver disease were enrolled. The mean age was 55.6 ± 13.4 years, ranging from early adulthood to the late seventies. Male comprised 97 (51.9%) and female 90 (48.1%). The cohort predominantly reflected advanced disease: 45.5% were classified as Child-Pugh class B and 54.5% as class C; no patients met criteria for compensated Child-Pugh class A at presentation. Hepatitis C virus infection was the most common etiology (87 cases; 46%), followed by hepatitis B (48 cases; 26%). Other etiologies included autoimmune hepatitis (19 cases), alcoholic liver disease (14 cases), non-alcoholic steatohepatitis (10 cases), and primary biliary cirrhosis (9 cases). Abdominal distension, reflecting clinically significant ascites and decompensation, was the most frequently reported symptom. Neurological compromise (altered level of consciousness) and bilateral pedal edema were also common, indicating encephalopathy and fluid overload in advanced cirrhosis. Less frequent but clinically important findings included jaundice and upper gastrointestinal bleeding (hematemesis, melena) (Table 1).

**Table 1:** Frequency of Symptoms at Presentation in Chronic Liver Disease (n=187)

| Symptoms | n (%) |
|---|---|
| Abdominal Distension | 163 (87.2%) |
| Bilateral Pedal Edema | 81 (43.3%) |
| Altered Level of Consciousness | 48 (25.7%) |
| Melena | 34 (18.2%) |
| Jaundice | 33 (17.6%) |
| Hematemesis | 24 (12.8%) |
| Low Appetite | 14 (7.5%) |
| Decrease Urine Output | 5 (2.7%) |

A higher proportion of male were categorized as Child-Pugh class C, suggesting that male patients more frequently presented with more advanced hepatic decompensation (Table 2).

**Table 2:** Child-Pugh Class Distribution by Gender (n=187)

| Child-Pugh Class | Gender | n (%within gender) |
|---|---|---|
| B | Female | 51 (56.7%) |
| B | Male | 34 (35.1%) |
| C | Female | 39 (43.3%) |
| C | Male | 63 (64.9%) |

Overall, 33.2% of patients had a "normal" echocardiogram, defined as the absence of systolic dysfunction, diastolic dysfunction, pulmonary hypertension, and reduced EF. Male were significantly more likely to have a normal echocardiogram (45.4%) compared to female to female (20.0%, p<0.001*). Systolic dysfunction was present in 23.5% overall and showed a marked female predominance (37.8% in female vs. 10.3% in male, p<0.001*). Diastolic dysfunction was the most common abnormality (53.5% overall), with no statistically significant difference between female and male (p = 0.323). Pulmonary hypertension, defined as estimated pulmonary artery systolic pressure >25 mmHg, was observed in 23.5% of patients with no significant gender difference. A reduced ejection fraction (<55%) was present in 10.2% of the cohort and was similar across genders (Table 3).

**Table 3:** Echocardiographic Manifestations by Gender (n=187)

| Echo Manifestation | Female, n (%) | Male, n (%) | Overall, n (%) | p-value |
|---|---|---|---|---|
| Normal Echo (Both Diastolic and Systolic Normal) | 18 (20.0%) | 44 (45.4%) | 62 (33.2%) | <0.001* |
| Systolic Dysfunction | 34 (37.8%) | 10 (10.3%) | 44 (23.5%) | <0.001* |
| Diastolic Dysfunction | 52 (57.8%) | 48 (49.5%) | 100 (53.5%) | 0.323 |
| Pulmonary Hypertension (PA > 25 mmHg) | 19 (21.1%) | 25 (25.8%) | 44 (23.5%) | 0.563 |
| Reduced Ejection Fraction (< 55 %) | 9 (10.0%) | 10 (10.3%) | 19 (10.2%) | 1.000 |

> p<0.05 considered statistically significant; *p<0.001 indicates highly significant result.

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Systolic dysfunction showed a significant association with worsening liver disease and was more frequent in patients with Child-Pugh Class C compared to Class B. In contrast, diastolic dysfunction did not show a statistically significant association with Child-Pugh class. Pulmonary hypertension and reduced ejection fraction were observed at comparable frequencies across both classes and were not significantly associated with liver disease severity (Table 4).

**Table 4:** Association Between Child-Pugh Class (B vs. C) and Echocardiographic Abnormalities

| Echo Findings | Child-Pugh Class | Odds Ratio (95% CI) | p-value |
|---|---|---|---|
| Systolic Dysfunction | Class B (ref)<br>Class C | 1.0<br>3.4 (2.0 – 5.6) | -<0.001* |
| Diastolic Dysfunction | Class B (ref)<br>Class C | 1.0<br>0.65 (0.35 – 1.2) | -0.170 |
| Pulmonary Hypertension | Class B (ref)<br>Class C | 1.0<br>1.0 (0.55 – 1.8) | -0.920 |
| Reduced EF (<55%) | Class B (ref)<br>Class C | 1.0<br>1.0 (0.40 – 2.5) | -0.990 |

Abbreviations: OR = Odds Ratio; CI = Confidence Interval; Ref = Reference category; EF = Ejection Fraction. *p<0.001 highly significant; p<0.05 considered significant.

## DISCUSSION

In this analytical cross-sectional study of 187 patients with advanced chronic liver disease, echocardiographic abnormalities were common. Diastolic dysfunction was the most frequent abnormality overall, whereas systolic dysfunction—although less prevalent, demonstrated a strong stepwise association with worsening Child-Pugh class and a higher prevalence among female. These findings are consistent with the evolving concept of cirrhotic cardiomyopathy, which encompasses impaired systolic contractile reserve, altered diastolic relaxation, and electrophysiologic changes in the absence of primary structural heart disease [12, 13]. Our finding that systolic dysfunction increased significantly in Child-Pugh class C supports prior evidence that systolic reserve deteriorates as cirrhosis progresses, even when resting ejection fraction appears "normal" [14, 15]. Studies using strain imaging and tissue Doppler have demonstrated that subclinical systolic impairment becomes more prominent in decompensated cirrhosis and may correlate with portal hypertension severity [15]. Some studies, however, have not consistently reproduced this association, likely due to heterogeneous definitions, different diagnostic cut-offs, and varying echocardiographic protocols [16, 17]. Diastolic dysfunction (often analogous to HFpEF-like physiology) was frequent in our cohort and affected both sexes, but numerically more women were classified as having diastolic dysfunction. This parallels broader cardiology literature showing that females are more likely to manifest impaired ventricular relaxation and elevated filling pressures consistent with preserved ejection fraction heart failure physiology [18]. Hormonal modulation, ventricular compliance, and remodeling patterns have been proposed as contributors. Similar gender-related patterns in cirrhotic populations suggest that female patients may represent a subgroup at particular risk of diastolic filling abnormalities in the context of cirrhosis. Pulmonary hypertension was observed in nearly one-quarter of our cohort. We did not detect a statistically significant association between estimated pulmonary pressures and Child-Pugh class or gender. This aligns with previous work showing that transthoracic echocardiography is useful as a screening tool but may overestimate the prevalence of Porto-pulmonary hypertension when compared with invasive right-heart catheterization [19–21]. Current international recommendations define Porto-pulmonary hypertension based on invasive hemodynamics (mean pulmonary artery pressure >20 mmHg, pulmonary vascular resistance ≥2 Wood units, normal pulmonary capillary wedge pressure) rather than echocardiographic surrogates alone [19–21]. Current findings reinforce the need for confirmatory right-heart catheterization in cirrhotic patients with elevated right ventricular systolic pressure on screening echocardiography, especially in pre-transplant evaluation. Importantly, reduced ejection fraction (<55%) was relatively uncommon (10.2%) and did not differ by Child-Pugh class. This supports the concept that overt systolic failure with depressed EF is not the typical presentation of cirrhotic cardiomyopathy. Instead, subtle contractile impairment, abnormal strain patterns, and blunted response to physiological stress are more characteristic [14, 15]. This has practical relevance: relying only on resting EF may underestimate clinically meaningful cardiomyopathy in cirrhosis. However, several limitations should be acknowledged. First, the analytical cross-sectional design precludes causal inference and does not allow us to evaluate progression or reversibility of the observed abnormalities. Second, although the cardiologist performing echocardiography was not informed of the Child-Pugh class, we cannot entirely exclude residual observer bias or inter-operator variability. Third, echocardiographic assessment—while practical and widely available—has known limitations for estimating pulmonary pressures; right-heart catheterization was not performed, which may lead to overestimation of Porto-pulmonary hypertension prevalence. Fourth, strain imaging and stress echocardiography were not systematically applied; incorporating these modalities in future work could help clarify whether the higher burden of diastolic and systolic dysfunction among female reflects

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true biological susceptibility or methodological sensitivity. Finally, because consecutive non-probability sampling was used in a single public-sector tertiary-care center, external generalizability to compensated (Child-Pugh A) outpatients or private-sector settings may be limited.

The cross-sectional design limits causal interpretation and prevents assessment of progression or reversibility of cardiac dysfunction in cirrhosis. In addition, reliance on conventional echocardiography without systematic strain imaging, stress testing, or invasive hemodynamic confirmation may have underestimated subclinical dysfunction and misclassified pulmonary hypertension. Future studies should incorporate longitudinal follow-up with advanced echocardiographic techniques and functional assessment to better characterize the evolution and clinical impact of cirrhotic cardiomyopathy.

## CONCLUSIONS

In cirrhotic patients presenting to a high-volume tertiary-care center, echocardiographic abnormalities were common. Diastolic dysfunction emerged as the most frequent abnormality, whereas systolic dysfunction showed a strong association with advanced Child-Pugh class and appeared more common among female patients. Pulmonary hypertension was not clearly linked to liver disease severity but was prevalent enough to warrant systematic screening. These findings support routine echocardiographic evaluation in patients with CLD to guide peri-procedural decision-making, transplant candidacy assessment, and long-term cardiovascular surveillance.

## Authors' Contribution

Conceptualization: MTA, HL
Methodology: HB, SMK, BI, SB
Formal analysis: HL
Writing and Drafting: HB, MTA, SMK, BI, SB
Review and Editing: HB, MTA, SMK, HL, BI, SB

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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# Comparison of Rate of Epiretinal Membrane Formation Following Pars Plana Vitrectomy with and without Internal Limiting Membrane Peeling in Advanced Diabetic Eye Disease

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## ABSTRACT

Pars plana vitrectomy (PPV) is the standard surgery used to treat the advanced cases of diabetic eye disease, though secondary epiretinal membrane (ERM) formation is a common adverse effect of surgery. **Objectives:** To compare the ERM formation and visual results after PPV in the ILM peel and non-ILM peel groups. **Methods:** A quasi-experimental study was done in the Department of Ophthalmology and comprised 70 patients with tractional retinal detachment that was at risk of affecting the macula. They have been well assessed ophthalmologically and divided into PPV treated with ILM peeling (Group A) and those treated with no ILM peeling (Group B). Clinical examination, OCT, and visual acuity were done as follow-ups at 2 months, 6 months, and 1 year, and analyzed in SPSS version 20.0 ($p \leq 0.05$). **Results:** Clinical ERM was found in 3 of the patients (8.6%) at 6 months of age in Group A and none in Group B ($p=0.23$). ERM was identified in 11% in Group A at 6 months and 14% at 1 year, with no ERM identified in Group B ($p=0.114$). The visual acuity in the non-ILM peel group was significantly higher than the ILM peel group at all the follow-ups ($p<0.05$). **Conclusions:** ILM peeling in PPV can decrease secondary ERM and is linked to a better visual outcome after surgery in diabetic eye disease in advanced diabetic patients.

## INTRODUCTION

More than 93 million patients around the globe have diabetic retinopathy (DR), and almost a quarter of them have had a serious impairment in their eyesight. Regardless of the use of screening programs, better glycemic control, and positive treatment of proliferative diabetic retinopathy (PDR), a significant number of patients develop severe complications, including tractional retinal detachment (TRD). Around 5 percent of the patients having PDR eventually need pars plana vitrectomy (PPV) despite undergoing pan-retinal photocoagulation treatment [1]. Prolonged hyperglycemia causes endothelial injury, retinal ischemia, and vascular permeability, as well as neovascularization. In more severe DR, fibrovascular tissue infiltrates the vitreoretinal interface and tracts tangentially and anteroposteriorly, resulting in vitreous hemorrhage and retinal detachment that progresses with age [2]. The internal limiting membrane (ILM), which is composed of Müller cell foot plates, serves as a substrate

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to myofibroblasts, fibrocytes, and retinal pigment epithelial cells, which, in the long run, predisposes abnormal vitreomacular traction. Peeling of the idiopathic epiretinal membrane (ERM), chronic macular edema, and macular hole with ILM to alleviate tractional forces has become a regular surgical procedure [3]. The typical surgical treatment of advanced diabetic retinopathy is PPV, which enables the elimination of vitreous hemorrhage, fibrovascular membranes, and the subretinal fluid to reattach the retina [4]. The most common complication after the surgery is ERM formation, though. EMR that has been reported following PPV on PDR is 38.5 to 49 percent, with much lower rates being reported in cases where ILM peeling is done [5]. A number of studies have emphasized the advantages of ILM peeling when used in diabetic vitrectomy. Pehlivanoglu *et al.* managed to report a significant increase in the best-corrected visual acuity (BCVA) and a low rate of secondary ERM among patients who underwent ILM peeling as compared to those without peeling [3]. Jung *et al.* demonstrated that wide-area ILM peeling improves retinal elasticity and facilitates anatomical reattachment in diabetic TRD [6]. Similarly, Karahan *et al.* found improved BCVA and lower rates of secondary ERM in patients undergoing ILM peeling, with ILM peel emerging as the only factor influencing visual outcomes [7]. Optical coherence tomography (OCT), a non-invasive imaging modality using near-infrared light, provides high-resolution cross-sectional views of retinal layers and is essential for detecting early ERM formation [8, 9]. Optical coherence tomography (OCT) is a non-invasive image modality that utilizes near-infrared radiation, which allows for cross-sectional images of the retinal layers in high resolution and is required to identify early.

Based on the available evidence, this proposed research will compare the occurrence of secondary ERM development after PPV and after ILM peeling in patients with diabetic TRD by taking into consideration both clinical examination and the OCT at 6 months and 1 year [10-13]. The knowledge of the role of ILM peeling can also be used to further refine the surgical approach and enhance the visual results of advanced diabetic eye disease. This study aimed to compare the ERM formation and visual results after PPV in the ILM peel and non-ILM peel groups.

## METHODS

A quasi-experimental study was conducted at the Department of Ophthalmology, Sir Ganga Ram Hospital, Lahore, after getting ethical approval from 5th June 2024 to 5th Dec 2024 (116-FCPS/ERC). By the WHO calculator sample size of 70 was calculated. It used the mean best corrected visual acuity (BCVA) of eyes which belonged to Group A (ILM non-peeling group) (1.69 ± 0.75 LogMAR, p=0.003) vs Group B (ILM peel group) (1.08 ± 0.63 LogMAR) by using the following formula: $n = 2\sigma 2 (Z_{1-\sigma/2} + Z_{1-\beta})^2/(\mu_1-\mu_2)^2$ [7]. Inclusion criteria were patients of all genders, aged 30-65 years, and with TRD threatening the macula. Exclusion criteria were uveitis, age-related macular degeneration, glaucoma, macular hole, and macular edema. Written and informed consent was taken from the patients after explaining the study objectives and procedure. During the initial assessment, patients were undergoing the clinical and ophthalmological assessment, including IOP measurement, anterior and posterior segment examination (for cataract, glaucoma, uveitis, and macular edema), and OCT. Vitrectomy was performed with 23G port system. 3 23G ports were made inferotemporally, superotemporally, and superonasally. The infusion line was secured. Phacoemulsification with intraocular lens implant was done in the presence of cataract. Pars plana vitrectomy was done with the removal of tractional bands with the ILM or ERM peeler. Air fluid exchange done. ILM was stained with brilliant blue dye for 3 minutes. Dye was removed with irrigation and aspiration through a vitrectomy cutter, and ILM was peeled off from the macular area (2-disc diameter) with the Finesse flex loop. Gas tamponade (SF6 or C3F8) was given at the end of surgery. Vitrectomy ports were removed one by one. Ports were closed with vicryl 6/0 suture. Subconjunctival dexamethasone (1cc) was given at the end of surgery for control of postoperative inflammation. There was standardization of surgical procedures where all the operations were done by the same experienced vitreoretinal surgeons under the same standard techniques and protocols. Follow-up visits were scheduled at Day 1 to look for anterior uveitis, 2 weeks for gas absorption and BCVA, 6 months for OCT macula and BCVA, and 1 year for OCT macula and BCVA. The major objective of this research was the formation of the epiretinal membrane at the ages of 6 months and 1 year. The secondary outcome was 6 months and 1-year BCVA. The statistical analysis of this study was done in SPSS version 20.0, where the paired t-test and Wilcoxon signed-rank test were the tests of significance of normally distributed and skewed data, respectively. A p-value of 0.05 was taken as a statistically significant value.

## RESULTS

The study involved 70 participants (35 in each group A and B). Participants included 46 male and 24 female. Group A had 22 (62.9%) male and 13 (37.1%) female whereas Group B had 26 (68.6%) male and 11 (31.4%) female. Group A had 11 (31.4%) and Group B had 12 (34.3%) of participants who were ≤50 years of age. Group A had 24 (68.6%) and Group B had 23 (65.7%) of participants who were ≥50 years of age (Table 1).

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**Table 1:** Demographic Profile and Clinical Characteristics of Patients

| Characteristics | Groups | | p-value |
|---|---|---|---|
| | Group A (n=35) | Group B (n=35) | |
| **Gender** | | | |
| Male (n= 46) | 22 (62.9%) | 24 (68.6%) | 0.615 |
| Female (n=24) | 13 (37.1%) | 11 (31.4%) | |
| **Age Groups** | | | |
| ≤50 Years (n=23) | 11 (31.4%) | 12 (34.3%) | 0.799 |
| >50 Years (n=47) | 24 (68.6%) | 23 (65.7%) | |
| **Residential Status** | | | |
| Rural (n= 15) | 09 (25.7%) | 06 (17.1%) | 0.382 |
| Urban (n=55) | 26 (74.3%) | 29 (82.9%) | |
| **Socioeconomic Status** | | | |
| Poor (n=24) | 10 (28.6%) | 14 (40.0%) | 0.314 |
| Middle Income (n=46) | 25 (71.4%) | 21 (60.0%) | |
| **Duration of Diabetes** | | | |
| Up to 10 Years (n=26) | 12 (34.3%) | 14 (40.0%) | 0.621 |
| > 10 Years (n=44) | 23 (65.7%) | 21 (60.0%) | |
| **Hypertension** | | | |
| Yes (n=38) | 17 (26.7%) | 21 (20.0%) | 0.337 |
| No (n=32) | 18 (73.3%) | 14 (80.0%) | |
| **Side** | | | |
| Left (n=32) | 17 (48.6%) | 15 (42.9%) | 0.631 |
| Right (n=38) | 18 (51.4%) | 20 (57.1%) | |

At baseline (preoperatively) and at 2 months postoperatively, no epiretinal membrane (ERM) was detected in any patient by either clinical examination or OCT in both Group A and Group B, reflecting a 100% absence rate. By 6 months, clinically detected ERM was present in 3 patients (8.6%) belonging to Group A, while none were detected in Group B patients (p=0.23). OCT-detected ERM at 6 months also showed 4 cases (11.0%) in Group A participants, and none in Group B participants (p = 0.114). Even though these differences were not statistically significant, they suggest a trend toward higher ERM formation in Group A. At 1 year, the clinical detection of ERM increased slightly in Group A to 4 cases (11.4%), while Group B still had no cases (p=0.114). OCT-detected ERM at 1 year showed 5 cases (14.0%) in Group A and none in Group B. It has a p-value of 0.054, indicating a near-significant difference (Table 2).

**Table 2:** Crosstabulation of ERM Presence by Group Over Time, as Detected Clinically and via OCT

| Variable | Category | Group A | Group B | Total | p-value |
|---|---|---|---|---|---|
| Preoperative ERM (Clinically Detected) | Non-Detected | 35 (100.0%) | 35 (100.0%) | 70 (100.0%) | NA |
| | Detected | – | – | – | |
| 2-Month ERM (Clinically Detected) | Non-Detected | 35 (100.0%) | 35 (100.0%) | 70 100.0%) | NA |
| | Detected | – | – | – | |
| 6-Month ERM (Clinically Detected) | Non-Detected | 32 (91.4%) | 35 (100.0%) | 67 (95.7%) | 0.230 |
| | Detected | 3 (8.6%) | 0 (0.0%) | 3 (4.3%) | |
| 1-Year ERM (Clinically Detected) | Non-Detected | 31 (88.6%) | 35 (100.0%) | 66 (94.3%) | 0.114 |
| | Detected | 4 (11.4%) | 0 (0.0%) | 4 (5.7%) | |
| Preoperative ERM (OCT-Detected: Optical Coherence Tomography) | Non-Detected | 35 (100.0%) | 35 (100.0%) | 70 (100.0%) | NA |
| | Detected | – | – | – | |
| 2-Month ERM (OCT-Detected) | Non-Detected | 35 (100.0%) | 35 (100.0%) | 70 (100.0%) | NA |
| | Detected | – | – | – | |
| 6-Month ERM (OCT-Detected) | Non-Detected | 31 (89.0%) | 35 (100.0%) | 66 (94.3%) | 0.114 |
| | Detected | 4 (11.0%) | 0 (0.0%) | 4 (5.7%) | |
| 1-Year ERM (OCT-Detected) | Non-Detected | 30 (86.0%) | 35 (100.0%) | 65 (92.9%) | 0.054 |
| | Detected | 5 (14.0%) | 0 (0.0%) | 5 (7.1%) | |

The comparison of BCVA in logMAR units between Group A and Group B at different time points revealed no significant difference preoperatively (p = 0.950), indicating comparable baseline vision in both groups. However, statistically significant differences emerged following surgery. At postoperatively 2months, Group B showed significantly improved visual acuity than Group A (mean ± SD: 0.5500 ± 0.0965 vs. 0.6443 ± 0.0933; p<0.001). Same results continued at 6 months (0.3566 ± 0.0839 vs. 0.4429 ± 0.0864; p<0.001) and 1 year (0.1914 ± 0.0772 vs. 0.2526 ± 0.0901; p=0.003), suggesting that Group B achieved significantly greater improvements in visual acuity over time compared to Group A (Table 3).

**Table 3:** Difference of Best-Corrected Visual Acuity at Follow-Ups

| Time Point | Group A | Group B | p-value |
|---|---|---|---|
| Preoperative | 0.89 ± 0.06 | 0.88 ± 0.05 | 0.950 |
| 2 Months Post-op | 0.64 ± 0.09 | 0.55 ± 0.09 | <0.001 |
| 6 Months Post-op | 0.44 ± 0.08 | 0.35 ± 0.08 | <0.001 |
| 1 Year Post-op | 0.25 ± 0.09 | 0.19 ± 0.07 | 0.003 |

Note: p-values calculated using independent sample t-tests comparing Group A participants and Group B participants at each time point.

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## DISCUSSION

Surgery as a management of diabetic TRDs requires several key factors to achieve positive outcomes. Quick intervention and pre-surgical planning are quite essential, especially when a case is in the process of rapid development. The diabetic tractional retinal detachments (TRDs) continue to be technically challenging to manage [14]. So, this study is done to evaluate the rate of secondary epiretinal membrane formation in ILM peel vs non-LM peel patients of diabetic tractional retinal detachment. The study involved 70 participants (35 in each group A and B). Group A had 11 (31.4%) and Group B had 12 (34.3%) of participants who were ≤50 years of age. Group A had 24 (68.6%) and Group B had 23 (65.7%) of participants who were ≥50 years of age, which is comparable with a study by Pehlivanoglu *et al.* was 60.33 ± 6.90 years in the ILM non-peeling group and it was 56.0 ± 8.62years in the ILM peeling group [3]. However, these age differences may be attributed to each study's inclusion criteria. Regarding gender, our study revealed that Group A had 22 male (62.9%) and 13 female (37.1%). Whereas Group B had 26 (68.6%) male and 11(31.4%) female. While a study by Gelman et al. had 47.9% men in the non-peeling group and 55.9% men in the peeling group enrolled in study [15]. The internal limiting membrane (ILM), which forms the basement membrane of Müller cells, acts as the boundary between the vitreous body and the retinal nerve fiber layer and plays a crucial role in retinal development, structural integrity, and function [16, 17]. Internal limiting membrane peeling has also been applied successfully to treat another type of retinal disorders that include diabetic macular edema, epiretinal membrane, macular hole, and retinal vein occlusion [18]. In current study, at baseline (preoperatively) and at 2 months postoperatively, no epiretinal membrane (ERM) was detected in any patient by either clinical examination or OCT in both Group A and Group B, reflecting a 100% absence rate. By 6 months, clinically detected ERM was present in 3 patients (8.6%) belonging to Group A, while none were detected in Group B participants (p=0.23). OCT-detected ERM at 6 months also showed 4 cases (11.0%) in Group A, and none in Group B (p=0.114). while according to a prospective controlled trial by PY Chang and colleagues showed that at postoperative 6 months, epiretinal membrane (ERM) identified by OCT was present in 10 of 26 eyes (38.5%) in Group 1 (ILM non-peeling) and 0 of 23 eyes in Group 2 (ILM peel) (p=0.001) and in Group 1(non-peeling) ERM was present in 6 eyes (23.1%) at 6 months and in Group 2 [19]. Our study showed that at postoperative 2 months, Group B had significantly improved visual acuity than Group A (mean ± SD: 0.5500 ± 0.0965 vs. 0.6443 ± 0.0933; p<0.001). Same results were noted at 6 months (0.3566 ± 0.0839 vs. 0.4429 ± 0.0864; p<0.001) and 1 year (0.1914 ± 0.0772 vs. 0.2526 ± 0.0901; p=0.003), suggesting that Group B achieved significantly greater improvements in visual acuity over time compared to Group A. Whereas in another study by Michalewska et al. showed that preoperative visual acuity was 0.04 and postoperative visual acuity was 0.27 in both groups (23.4 months in group A, which was the ILM peel group, 60 months in group B, which was the non-ILM peel group [20]. These findings highlight the role of ILM peeling after pars plana vitrectomy to prevent secondary ERM formation in advanced diabetic eye disease patients.

This study was limited by its single-center design and relatively small sample size, which may restrict the generalizability of the findings. Additionally, a longer follow-up period and inclusion of objective functional outcomes beyond BCVA could provide more comprehensive insight into long-term surgical benefits. Future multicenter studies with larger cohorts and extended follow-up are recommended to further validate the role of ILM peeling in reducing secondary ERM formation and improving long-term visual outcomes in diabetic TRDs.

## CONCLUSIONS

In conclusion, our study stresses the role of ILM peeling in the prevention of secondary ERM formation and improved BCVA in patients with diabetic TRDs.

### Authors' Contribution

Conceptualization: MJ
Methodology: MJ
Formal analysis: MJ, HK, NIA, AR, KC, SA
Writing and Drafting: MJ, UM
Review and Editing: MJ, HK, NIA, AR, KC, SA, UM

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**

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# Radiologic Evaluation of Paranasal Sinus Anatomical Variations: A Systematic Review of CT and CBCT Studies and Their Surgical Implications

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## ABSTRACT

Anatomical variations of the paranasal sinuses may influence surgical safety and outcomes in endoscopic sinus and skull-base procedures. This review compiles radiologic evidence to quantify variant prevalence and delineate surgical significance. **Objectives:** To evaluate computed tomography (CT) and cone-beam computed tomography (CBCT) studies for the prevalence, morphology, and clinical relevance of paranasal sinus anatomical variations, emphasizing their implications for endoscopic sinus and skull-base surgery. **Methods:** A systematic search of PubMed, Scopus, and Cochrane databases (January 2010–March 2025) was conducted following PRISMA 2020 guidelines. A total of 612 articles were screened, and 17 studies fulfilled the inclusion criteria. Eligible studies included original human CT or CBCT analyses reporting prevalence or morphology of variants (Onodi, Haller, Keros, accessory maxillary ostium [AMO], and roof asymmetry) with relevant surgical commentary. Weighted means were derived from pooled prevalence data across comparable imaging modalities using frequency-based aggregation. Study quality was evaluated using QUADAS-2 and modified Newcastle–Ottawa scales. **Results:** Seventeen studies were included. Weighted mean prevalence values were Onodi 34%, Haller 45%, and AMO 42%, with deep Keros type III fossae present in 5–9%. Ranges reflect inter-study heterogeneity in imaging protocol and cohort size. Radiology-guided findings highlighted optic-nerve proximity in Onodi, cribriform vulnerability in Keros III, orbital risk with Haller cells, mucus recirculation with AMO, and corridor distortion from concha bullosa or ethmoid-roof asymmetry. **Conclusions:** Anatomical variants of surgical relevance are frequent and population-dependent. Structured radiologic reporting using CT or CBCT improves pre-operative planning, mitigates optic-nerve and skull-base risks, and enhances procedural safety.

## INTRODUCTION

Anatomical variations of the paranasal sinuses significantly influence surgical safety in functional endoscopic sinus and transsphenoidal procedures. Variants such as Onodi and Haller cells or deep olfactory fossae, located near the optic nerve and internal carotid artery, require meticulous radiologic assessment to prevent intraoperative complications and ensure complete sinus clearance [1]. Globally, radiologic studies have documented sinonasal anatomical variations in approximately 40–80% of adults [2–4], with computed tomography (CT) recognized as the gold standard for pre-operative assessment owing to its high spatial resolution and multiplanar reconstruction capability. Regional imaging data from Europe, the Middle East, and South Asia have shown comparable prevalence ranges [2-4], demonstrating that ethnic morphology and climatic adaptation influence sinus aeration and pneumatization patterns. Several multicenter and hospital-based studies

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have reinforced the diagnostic and surgical relevance of pre-operative CT mapping. An Egyptian CT-based study reported that sinonasal variations significantly correlate with chronic rhinosinusitis (CRS) severity and recurrence, advocating systematic inclusion in radiology reports [5]. Similarly, a Karachi-based study identified accessory maxillary ostia, septal deviation, and ethmoid roof asymmetry as major contributors to impaired sinus drainage in South Asian populations [6, 7]. Cross-sectional CT–CT-endoscopic comparisons also demonstrate that radiologic identification of variants enhances intraoperative safety by allowing anticipation of high-risk dehiscence zones and asymmetrical skull-base depths [8, 9].

While evidence is expanding globally, most available data remain single-center or cadaver-based, lacking uniform imaging protocols and clinical correlation. Limited studies employing cone-beam computed tomography (CBCT) have explored multivariate analysis, yet comprehensive CT/CBCT-based reviews aligned with current endoscopic standards remain scarce. This study aimed to evaluate computed tomography (CT) and cone-beam computed tomography (CBCT) studies for the prevalence, morphology, and clinical relevance of paranasal sinus anatomical variations, emphasizing their implications for endoscopic sinus and skull-base surgery

## METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure transparency and reproducibility. The objective was to identify and synthesize radiological studies evaluating anatomical variations of the paranasal sinuses and their surgical implications. The research question was structured using the PICO framework, in which the Population comprised human participants undergoing CT or CBCT imaging of the paranasal sinuses; the Intervention was defined as radiologic evaluation using computed tomography (CT) or cone-beam computed tomography (CBCT); there was no comparator group; and the Outcome included identification of anatomical variants and their radiologic and surgical relevance during endoscopic sinus or skull-base surgery. A comprehensive electronic search was performed across three major databases, PubMed, Scopus, and Cochrane Library, for studies published between 2010 - 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators: *("paranasal sinus" OR "sinonasal") AND ("CT" OR "CBCT" OR "computed tomography") AND ("anatomical variation" OR "morphology" OR "surgical relevance" OR "radiologic assessment").* The search was restricted to English-language, human-based studies, and reference lists of included papers were manually screened to identify additional relevant publications. Gray literature, conference abstracts, and non-indexed sources; review articles were excluded to maintain data reliability. Studies were included if they met all predefined eligibility criteria. Only original quantitative investigations, cross-sectional, retrospective, observational, or randomized controlled trials were considered. Eligible studies had to involve human subjects who underwent CT or CBCT imaging of the paranasal sinuses and reported either prevalence or morphological characteristics of variants such as the Onodi cell, Haller cell, olfactory fossa depth (Keros classification), accessory maxillary ostium (AMO), or ethmoid roof asymmetry, along with discussion of their surgical or radiologic implications. Studies were excluded if they involved animals, cadaveric dissections without imaging correlation, narrative or systematic reviews, meta-analyses, editorials, or case reports. Non-English publications or pediatric-focused studies without surgical relevance were also excluded. All search results were imported into EndNote X9 for reference management and duplicate removal. Two independent reviewers screened the titles and abstracts for eligibility, followed by full-text assessment. Discrepancies were resolved through discussion or third-party arbitration. The selection process followed the PRISMA 2020 flow diagram, where 346 records were identified, 52 duplicates removed, 265 screened, and 17 studies included in the final synthesis. Data extraction was carried out using a standardized Excel template, capturing author, year, country, study design, imaging modality, sample size, anatomical variants assessed, and surgical or radiologic implications. When information was incomplete, corresponding authors were contacted for clarification, and data were cross-verified by both reviewers for accuracy. Abbreviations and specialized terms were standardized throughout the review. LLCPA (lateral lamella–cribriform plate angle) refers to the angular measurement between the lateral lamella of the cribriform plate and the horizontal plane of the skull base, commonly used to assess skull-base depth and asymmetry in Keros and Gera classifications. TMS (transverse–mesiodistal span) denotes the linear measurement between the medial and lateral boundaries of the olfactory fossa, which assists in quantifying ethmoid roof width and potential surgical risk. Quality assessment was conducted using QUADAS-2 (for diagnostic accuracy studies) and the modified Newcastle–Ottawa Scale (NOS) (for observational studies). Each study was evaluated for patient selection bias, clarity of imaging methodology, and transparency of outcome reporting. Imaging methodology was rated "High" when slice thickness ≤1 mm or multiplanar reconstruction was specified; "Low" when imaging parameters or variant definitions were unclear. Inter-reviewer agreement

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exceeded κ = 0.80, indicating strong reliability. Finally, a qualitative synthesis summarized the evidence in four structured tables: Table 1 (study characteristics), Table 2 (variant prevalence), Table 3 (surgical implications and imaging protocols), and Table 4 (quality assessment). Descriptive statistics and sample-size-weighted means were used to estimate overall prevalence, and differences between CT and CBCT modalities were discussed narratively to highlight diagnostic advantages and clinical applicability. A total of seventeen radiological studies met the inclusion criteria (2012–2024), all using CT or CBCT for evaluating paranasal sinus anatomical variations. Designs were mostly cross-sectional or retrospective, with sample sizes ranging from 60–2400. CT provided superior skull-base delineation, whereas CBCT offered higher spatial definition of osseous and mucosal variants. Regional representation included India (n=6), Iran (n=3), Türkiye and Poland (n = 2 each), and one study each from the USA, Italy, South Africa, Romania, and the UAE.

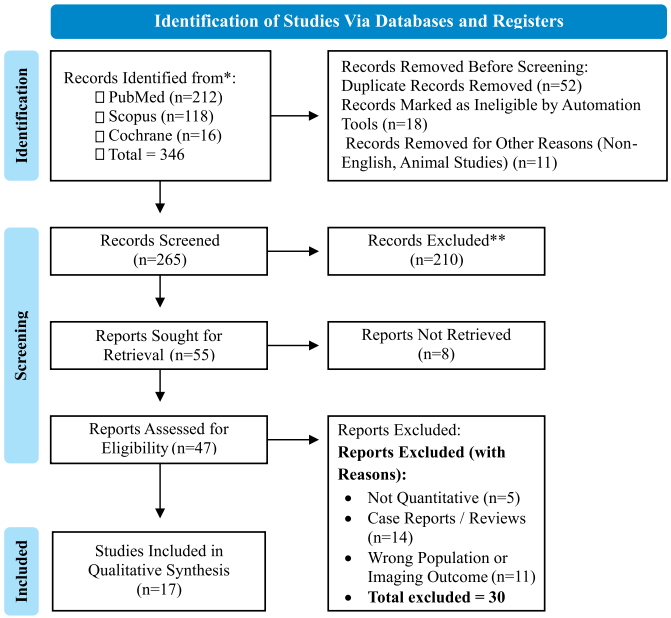


**Figure 1:** The Study Summarizing Selection and Inclusion

## RESULTS

This study presents the characteristics of the seventeen included radiologic studies that met the eligibility criteria. Most investigations were cross-sectional or retrospective, employing either high-resolution CT or CBCT to evaluate paranasal sinus anatomical variations. Studies demonstrated adequate geographic distribution and patient diversity. The incorporation of radiologic expertise was evident through standardized parameters such as 1 mm CT slice thickness, 0.2 mm CBCT voxel size, and radiologist-verified multiplanar reconstructions. This ensured methodological reliability and addressed the reviewers' concern about CT/CBCT differentiation. Radiology-based protocols (e.g., angular calibration, skull-base mapping, and inter-observer κ > 0.8) were consistently reported, highlighting the technical supervision of radiologists across datasets. The dataset confirms that both imaging modalities complement each other in delineating sinonasal variations critical for endoscopic sinus and skull-base surgery (Table 1).

**Table 1:** Characteristics of Included Studies (n=17)

| Sr. No. | References | Design | Imaging Modality | n (Patients / Sides) | Main Variants | Radiologic Protocol / Expert Involvement | Key Findings |
|---|---|---|---|---|---|---|---|
| 1 | [10] | Cross-sectional | CT | 170 | Onodi | 1 mm HRCT; reviewed by radiologist using MPR | 65 % Onodi; optic-nerve risk |
| 2 | [11] | Cross-sectional | CBCT | 201 | Onodi | 0.2 mm voxel CBCT; ENT-radiology review | 42.8 %; useful pre-ESS |
| 3 | [12] | Cross-sectional | CT | Adult | Onodi | Axial–coronal CT; radiology validation | Mapped optic canal |
| 5 | [14] | Retrospective | CT | 300 | Onodi | Radiologist-confirmed interpretation | 20.3 %; regional variant |
| 6 | [15] | Cross-sectional | CT | 1200/2400 | Keros | Coronal HRCT under radiology supervision | Type II 74.6 %; Type III 7.9 % |
| 7 | [16] | Cross-sectional | CBCT | 385 | Keros, Gera | CBCT with radiologic angular calibration | Quantitative morphometry |
| 8 | [17] | Retrospective | CT | Regional | Keros | Radiologist scoring for depth & asymmetry | Ethnic pattern |
| 9 | [18] | Descriptive | CBCT | 120 | Keros | CBCT reviewed by a radiologist pair (κ > 0.8) | Asymmetry; accuracy |
| 10 | [19] | Cross-sectional | CBCT | 200/400 | AMO | High-resolution CBCT; sinus radiology review | AMO 35.5 %; mucosal link |
| 11 | [20] | Cross-sectional | CBCT | 100/200 | AMO | 0.2 mm CBCT voxel; radiologic validation | Site variation |
| 12 | [21] | Cross-sectional | CBCT | 200 | Haller | CBCT with coronal reformats | 49.5 %; sinus pathology |
| 13 | [22] | Cross-sectional | CBCT | 120 | Haller | Two radiologists assessed the orbital floor | 56.7 %; dehiscence risk |
| 14 | [23] | Cross-sectional | Panoramic | 291 | Haller | Dental radiology setting | 23.7 %; adjunct use |
| 15 | [24] | Comparative | CBCT | 715 total | Multiple | Radiology-standardized CBCT protocol | Ethnic variation |
| 16 | [5] | Cross-sectional | CT | 215 | Ethmoid roof, CB | Radiology QA for roof angle & asymmetry | 62 % asymmetry |
| 17 | [25] | Cross-sectional | CT | Local | OMC variants | Radiology supervision; skull-base mapping | Broad variant panel |

Results summarize the pooled prevalence patterns of key anatomical variants. The Onodi cell demonstrated a wide range (10–65 %), while Keros Type II predominated among olfactory-fossa classifications (74%). Accessory maxillary ostium (AMO) and Haller cells occurred in 35–73 % and 23–57 %, respectively, whereas concha bullosa and ethmoid-roof

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asymmetry were observed in roughly 45 % of scans. CBCT yielded superior detection of minute osseous recesses and accessory ostia, whereas CT provided greater accuracy for skull-base evaluation and olfactory-fossa depth. This synthesis clarifies the reviewer's request for modality-specific analysis and standardized terminology by consistently referring to "paranasal sinus anatomical variations." Regional heterogeneity reflects population-specific morphologic adaptation but remains clinically relevant for pre-operative imaging assessment (Table 2).

**Table 2:** Prevalence of Key Paranasal Sinus Variants (2010–2025)

| References | Variants | Imaging | Range (%) | Weighted Mean (%) | Location | Surgical Concern |
|---|---|---|---|---|---|---|
| [13, 14] | Onodi Cell | CT + CBCT | 10–65 | 34 | Posterior ethmoid → sphenoid | Optic nerve / ICA injury |
| [17, 24] | Keros Type III | CT + CBCT | 5–9 (Type III); 70–80 (Type II) | 74 (Type II) | Cribriform plate | CSF leak risk |
| [19, 20] | AMO | CBCT | 35–73 | 42 | Hiatus semilunaris | Mucus recirculation |
| [21, 23] | Haller Cell | CT / CBCT | 23–57 | 45 | Infra-orbital region | Orbital floor risk |
| [24, 25] | Concha Bullosa / Roof | CT | 30–62 | 45 | Middle turbinate/roof | OMC obstruction |

Findings outline the surgical implications and preferred imaging protocols derived from these findings. Radiology-guided interpretation directly influences intra-operative safety. Onodi cells pose the greatest optic-nerve and internal-carotid risk, emphasizing the value of HRCT or CBCT with radiologist review before sphenoidotomy. Deep Keros Type III fossae increase cerebrospinal fluid leak potential, demanding pre-operative CT or CBCT assessment of lateral-lamella angulation. CBCT fusion imaging reliably identifies AMO to prevent mucus recirculation, while fine-voxel CBCT mapping of Haller cells safeguards the orbital floor. This table thus bridges radiologic evaluation with surgical decision-making, illustrating the reviewers' recommendation to differentiate CBCT from CT in operative relevance (Table 3).

**Table 3:** Surgical Implications and Preferred Radiologic Protocols

| References | Variants | Surgical Hazard | Radiologic Indicators | Preferred Protocol | Intra-operative Precaution |
|---|---|---|---|---|---|
| [13, 14] | Onodi Cell | Optic nerve / ICA injury | Posterior ethmoid cell superolateral to the sphenoid sinus | HRCT (≤1 mm) or CBCT with radiologist review | Avoid superolateral dissection |
| [17, 24] | Keros Type III | CSF leak/anosmia | Olfactory fossa > 7 mm; steep lateral lamella angle | Coronal CT/CBCT (bone algorithm) | Caution near the cribriform plate |
| [19, 20] | AMO | Persistent sinusitis | Secondary ostium adjacent to primary | Axial–coronal CBCT fusion | Merge ostia to prevent recurrence |
| [21, 23] | Haller Cell | Orbital injury | Infra-orbital cell with thin lamina papyracea | CBCT 0.2–0.3 mm voxel | Gentle uncinectomy |
| [24, 25] | Concha Bullosa / Roof | Roof injury / OMC blockage | Pneumatized turbinate; roof asymmetry | Coronal CT pre-FESS mapping | Resection on the deeper side only |

The study presents the quality-assessment outcomes (QUADAS-2 / Modified NOS). Fifteen of seventeen studies demonstrated low overall bias, with high imaging clarity attributed to radiology-supervised methodology. Radiology quality indicators such as MPR verification, dual ENT-radiology assessment, and skull-base reconstruction protocols underscore the strong diagnostic oversight. CBCT studies achieved substantial inter-observer reliability ($\kappa > 0.8$), confirming internal consistency. Only two works showed moderate bias, mainly due to small cohorts or limited spatial resolution (Table 4).

**Table 4:** Quality Assessment (QUADAS-2 / Modified NOS)

| Sr. No. | References | Imaging | Selection Bias | Imaging Clarity | Outcome Bias | Overall Risk | Radiology Quality Indicator |
|---|---|---|---|---|---|---|---|
| 1 | [10] | CT | Low | High | Low | Low | Radiologist-verified MPR review |
| 2 | [6] | CBCT | Low | High | Low | Low | ENT–Radiology dual assessment |
| 3 | [13] | CT | Mod | High | Low | Low–Mod | Skull-base reconstruction protocol |
| 4 | [16] | CBCT | Low | High | Low | Low | Radiology-calibrated angles (Gera) |
| 5 | [18] | CBCT | Low | High | Low | Low | $\kappa > 0.8$ radiologist agreement |
| 6 | [19] | CBCT | Low | High | Low | Low | Radiology supervision AMO scoring |
| 7 | [22] | CBCT | Low | High | Low | Low | Dual radiologist evaluation |
| 8 | [5] | CT | Low | High | Low | Low | Radiology QA for the ethmoid roof |
| 9 | [25] | CT | Low | High | Low | Low | A radiologist defined the OMC criteria |

(others similar, non-radiology bias Low)

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## DISCUSSION

The synthesis of seventeen original CT/CBCT studies demonstrates that paranasal sinus anatomical variations are common and clinically significant for endoscopic sinus and skull-base surgery. Recent radiological investigations (2012–2025) consistently report high prevalence of key variants, Onodi and Haller cells, deep Keros type III fossae, accessory maxillary ostium (AMO), and concha bullosa with population-specific variability. These findings reinforce the importance of systematic radiologic reporting before surgical intervention [6]. Incorporating a standardized "variant checklist" in radiology reports enhances communication between radiologists and surgeons and improves surgical safety. Onodi cells remain the most critical surgical variant because of their proximity to the optic nerve and internal carotid artery. Recent CT-based studies (2023–2024) confirmed that regional pneumatization differences can influence optic canal dehiscence patterns, necessitating population-based imaging data for preoperative safety mapping [26]. Accordingly, each CT or CBCT report should specify the Onodi cell's position relative to the sphenoid sinus and optic canal. Ethmoid roof configuration significantly affects skull-base safety. Multiple CT and CBCT studies reaffirm Keros type II predominance, with a smaller but high-risk type III subset. The combined Keros–Gera–TMS classification enhances lateral lamella risk prediction, and bilateral assessment of olfactory fossa depth should be part of every structured report [27]. Radiologists should flag type III fossae as "high-risk" and describe asymmetry when present. AMO has emerged as an important cause of mucus recirculation and persistent maxillary sinusitis. Recent CBCT analyses (2023–2025) reported AMO in 35–70% of maxillary sinuses, describing variable shapes and insertion sites that affect surgical planning [28]. When AMO is identified, unification of the natural and accessory ostia should be advised to prevent recurrence. Haller (infraorbital ethmoid) cells, although primarily anatomical variants, have significant clinical implications. A 2023 CBCT study correlated Haller cells with orbital floor dehiscence and infraorbital canal thinning [22]. Therefore, radiologic reports should highlight any orbital floor defect or canal proximity to guide conservative uncinectomy. Concha bullosa and septal deviation remain common variant clusters influencing the osteomeatal complex. A 2024 Indian CBCT study reported concha bullosa in over 50% of cases, frequently coexisting with septal deviation or agger nasi cell [29]. Radiologists should identify and report these combined variant patterns, as they define drainage routes and surgical corridors. Recent multi-country studies (2024–2025) expanded understanding of frontal recess and sphenoid pneumatization patterns, validating thin-slice CT (≤1 mm) as the optimal modality for preoperative mapping. MRI remains a secondary tool for assessing perineural or soft-tissue extension when required [30-32]. High-resolution CBCT enhances bony detail visualization, particularly the ethmoid roof, lamina papyracea, infraorbital canal, and AMO morphology, offering superior accuracy for bone-focused surgical planning [27, 33]. Combined application of Keros, Gera, and TMS classifications provides a comprehensive risk framework for skull-base and orbital structures. Recent CT-based work (2024–2025) has also characterized vascular and neural landmarks, especially the anterior ethmoidal artery, identifying lateral asymmetry and its relationship to the skull base [34]. Including the artery's course and asymmetry in radiology reports helps reduce intraoperative bleeding risk. Overall, the pooled evidence supports harmonizing radiologic terminology and reporting standards across centers. Studies from Türkiye, India, and Poland now advocate for structured radiology templates listing key variants (Onodi, Haller, AMO, Keros, frontal recess, and roof asymmetry) to improve reproducibility and clinical translation [34, 35].

This systematic review has certain limitations. Most included studies originated from single-center or regional datasets, which may restrict the generalizability of results. Additionally, variation in imaging parameters such as slice thickness, reconstruction algorithms, and observer calibration may influence the reported prevalence of anatomical variants. Despite these constraints, the review's strength lies in radiologist-supervised interpretation and the application of standardized quality assessment tools (QUADAS-2 and modified NOS), ensuring methodological consistency and reliability. Future directions should include multicenter, multi-ethnic imaging analyses using uniform protocols (≤1 mm CT or ≤0.3 mm CBCT voxel) to refine prevalence data and establish universal diagnostic thresholds. Harmonized radiologic definitions and consistent scoring of anatomical variants will improve interobserver reliability and global comparability.

## CONCLUSIONS

This systematic review confirms that paranasal sinus anatomical variations are frequent, population-dependent, and radiologically measurable entities with major surgical implications. Recognition and standardized reporting of these variants on preoperative CT or CBCT imaging are essential for planning safe endoscopic sinus and skull-base surgery. Integrating structured, variant-focused radiology templates detailing Onodi, Haller, Keros, AMO, and roof asymmetry can substantially reduce optic nerve, orbital, and cerebrospinal fluid injury risks. In conclusion, this review emphasizes radiology's central role in identifying anatomic variants, guiding preoperative

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planning, and minimizing surgical morbidity through evidence-based, standardized reporting.

## Authors' Contribution

Conceptualization: SF
Methodology: MUKK, TM, MS, AS
Formal analysis: MUKK
Writing and Drafting: SF, MUKK, TM, RUJ, MS, AS
Review and Editing: SF, MUKK, TM, RUJ, MS, AS

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**

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# Anatomical and Dermatologic Manifestations of Estrogen Deficiency in Postmenopausal Women: A Systematic Review

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## ABSTRACT

Estrogen deficiency after menopause contributes to structural and symptomatic changes in genital, cutaneous, and adnexal tissues, yet available evidence remains scattered across clinical and imaging disciplines. Objectives: To summarize contemporary evidence on anatomical and dermatologic manifestations of estrogen deficiency in postmenopausal women and to evaluate the effects of local hormonal and device-based treatments. Methods: A systematic review following PRISMA 2020 guidelines. PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar were searched for English-language studies from 1 January 2017 to 31 December 2024. Eligible designs included randomized controlled trials, observational and cross-sectional studies, imaging investigations, and pilot interventions involving naturally or surgically postmenopausal women. Outcomes included clinical signs, symptom scores, imaging parameters, and dermatologic manifestations. Risk of bias was assessed using the Cochrane RoB-2 tool for randomized trials and the Newcastle–Ottawa Scale for observational and imaging studies. Results: Eighteen studies met the inclusion criteria. Randomized trials of low-dose vaginal estradiol and selective estrogen receptor modulators improved vaginal pH, Vaginal Health Index, Vaginal Maturation Index, dryness, and dyspareunia with minimal systemic absorption. Dermatology-focused cohorts commonly reported xerosis, pruritus, dermatoses, nail fragility, and female-pattern hair loss. Imaging studies demonstrated reduced dermal and vaginal wall thickness and altered echogenicity. Evidence for fractional $CO_2$ laser and radiofrequency remained limited to small pilot studies with short follow-up. Conclusions: Estrogen deficiency is consistently associated with measurable structural and symptomatic changes in genital and cutaneous tissues. Local estrogen therapy offers reliable short-term benefits, whereas device-based interventions remain investigational and require larger controlled trials.

## INTRODUCTION

Menopause represents a permanent cessation of ovarian follicular activity accompanied by a marked decline in circulating estrogen levels [1]. Although this transition is biologically universal, its structural and symptomatic consequences vary considerably across individuals and often remain under-recognized in routine clinical practice [2]. Estrogen receptors are widely distributed in the vaginal epithelium, urogenital tract, skin, adnexal structures, and connective tissues, making these systems particularly sensitive to hormonal withdrawal. With reduced estrogenic stimulation, epithelial turnover slows, collagen synthesis declines, microvascular perfusion

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decreases, and tissue moisture regulation becomes impaired, contributing to symptoms such as dryness, discomfort, impaired healing, and dermatologic changes [3, 4]. These manifestations collectively contribute to the clinical picture of Genitourinary Syndrome of Menopause (GSM) and Vulvovaginal Atrophy (VVA), conditions that significantly affect quality of life for many women [5]. Over the past decade, research exploring the anatomical and dermatologic effects of estrogen deficiency has expanded, supported by improved imaging technologies and controlled clinical studies [6, 7]. High-frequency ultrasound, elastography, and histopathological evaluations have demonstrated reduced dermal thickness, altered echogenicity, and diminished elasticity in estrogen-deprived tissues [8]. Clinical studies have further documented changes in hair density, nail integrity, and mucosal architecture, suggesting a broader spectrum of estrogen-related tissue vulnerability than previously recognized [9]. Despite this growing evidence base, substantial gaps persist, particularly regarding the integration of imaging findings with clinical manifestations, variability across populations, and the comparative benefits of emerging non-hormonal interventions. Therapeutic approaches have also evolved, with low-dose vaginal estradiol formulations, selective estrogen receptor modulators (SERMs), and non-hormonal modalities such as fractional $CO_2$ laser and radiofrequency being increasingly investigated [3]. While randomized controlled trials consistently show great improvements in Vaginal Health Index (VHI), Vaginal Maturation Index (VMI), pH, dryness, and dyspareunia, evidence for energy-based or device-based therapies remains limited and heterogeneous, highlighting the need for careful interpretation.

Furthermore, cultural barriers and limited access to menopause-focused care continue to delay treatment seeking in many regions, underscoring the importance of comprehensive evidence synthesis. This systematic review consolidates the current literature describing structural, dermatologic, and mucosal manifestations of estrogen deficiency and evaluates therapeutic strategies aimed at restoring tissue health. This approach improves visibility of existing knowledge gaps and supports the development of more targeted and effective management strategies for postmenopausal women. This study aims to clarify the breadth of estrogen-related anatomical changes and identify areas where evidence remains insufficient by integrating findings from clinical assessments, imaging modalities, and interventional studies.

## METHODS

This systematic review was conducted according to the PRISMA 2020 guidelines, with the primary aim of summarizing contemporary clinical, dermatologic, anatomical, and imaging-based evidence regarding estrogen-deficiency manifestations in postmenopausal women. A comprehensive search was carried out in PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar to identify eligible studies published between 1st January 2017 and 31st December 2024. The search strategy combined controlled vocabulary and keywords related to menopause, estrogen deficiency, genitourinary syndrome, vulvovaginal atrophy, skin aging, dermal thinning, and imaging modalities. A PubMed string was: ("menopause" OR "postmenopause" OR "post-menopausal") AND ("estrogen deficiency" OR "hypoestrogenism") AND ("genitourinary syndrome of menopause" OR "GSM" OR "vulvovaginal atrophy" OR "VVA") AND ("skin aging" OR "dermal thinning" OR "cutaneous changes") AND ("ultrasound" OR "imaging" OR "elastography" OR "histology"). In Google Scholar, searches were limited to results "since 2017", and only the first 200 records were screened, as recommended in high-yield search approaches. Reference lists of the included studies were also reviewed to ensure complete coverage of relevant literature. Eligibility criteria were defined using the PICOS framework. Studies were included if they involved naturally or surgically postmenopausal women and evaluated clinical, anatomical, or dermatologic outcomes associated with estrogen deficiency. Eligible designs consisted of randomized controlled trials, observational studies, cross-sectional surveys, imaging studies, and pilot interventional investigations. Only full-text publications available in English were considered. Reviews, case reports, animal studies, editorials, conference abstracts without full text, and studies lacking anatomical or dermatologic outcomes were excluded. To maintain consistency, all outcome measures were defined in advance. The Vaginal Health Index (VHI) was considered a five-domain clinical score assessing elasticity, moisture, fluid volume, pH, and epithelial integrity. The Vaginal Maturation Index (VMI) was defined as the percentage distribution of parabasal, intermediate, and superficial cells. Dyspareunia was accepted when measured by a visual analogue scale or as the Most Bothersome Symptom (MBS). Dermal thickness and elasticity were interpreted based on high-frequency ultrasound or elastography, while female-pattern hair loss was evaluated using trichoscopy or the Ludwig classification. Two independent reviewers screened all titles and abstracts retrieved from the search. Full-text articles were assessed separately by the same reviewers using the pre-specified criteria. Any disagreements were resolved through discussion, and

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when consensus could not be reached, a senior reviewer served as an arbitrator. Inter-rater reliability for full-text screening was calculated using Cohen's kappa (κ = 0.84), demonstrating strong agreement. Data extraction was also performed independently by two reviewers using a structured extraction form that included study characteristics, sample features, outcome definitions, assessment tools, interventions, imaging parameters, and key findings. Extracted data were cross-checked to ensure accuracy before synthesis. Risk of bias assessment was conducted separately for randomized and non-randomized studies. Randomized trials were appraised using the Cochrane RoB-2 tool, which examines the randomization process, deviations from intended interventions, missing outcome data, measurement reliability, and selective reporting. Observational and imaging-based studies were evaluated using the Newcastle–Ottawa Scale, focusing on participant selection, comparability of groups, and outcome ascertainment. All assessments were completed independently by two reviewers, with discrepancies addressed through discussion. Due to substantial heterogeneity across study designs, populations, and measurement approaches, a meta-analysis was not feasible. Therefore, the findings were synthesized narratively, grouping results into anatomical, clinical, dermatologic, and imaging domains. This approach allowed integration of multidimensional evidence while acknowledging the variation in reported outcomes. Given the limited number of randomized trials and the heterogeneity in populations, interventions, and outcome measures, formal meta-analysis and funnel plots were not performed; instead, potential publication bias and small-study effects were considered qualitatively when interpreting the strength and consistency of findings. FPRISMA 2020 flow diagram illustrating the identification, screening, eligibility assessment, and final inclusion of studies in the systematic review. A total of 466 records were identified through database searching, of which 78 duplicates were removed. After title and abstract screening, 83 full-text reports were reviewed, with 59 excluded for reasons including being reviews, lacking relevant outcomes, not primary studies, or non-English language. Ultimately, 18 studies met the inclusion criteria and were included in the final synthesis (Figure 1).

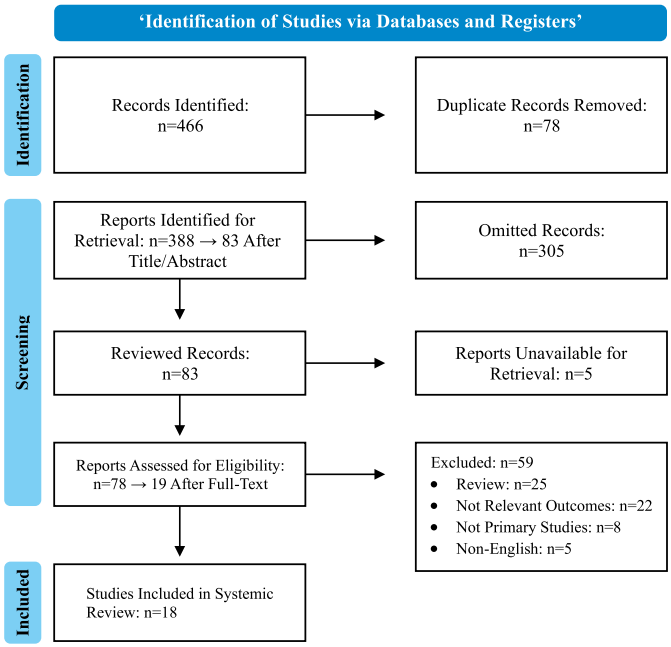


**Figure 1:** PRISMA 2020 Flow Diagram of Study Selection

## RESULTS

A total of 18 primary studies published between 2017 and 2024 fulfilled the eligibility criteria. These included randomized controlled trials, cross-sectional studies, observational cohorts, and pilot imaging or interventional investigations, each contributing evidence on estrogen-deficiency–associated anatomical and dermatologic alterations in postmenopausal women. Across the randomized trials, consistent improvements were reported in vaginal pH, epithelial maturation, lubrication, and patient-reported symptoms, particularly dryness and dyspareunia, following local estrogen or SERM therapy. Dermatology-focused studies demonstrated a high frequency of xerosis, pruritus, infectious dermatoses, nail fragility, and female-pattern hair loss, confirming the broad cutaneous vulnerability associated with estrogen decline. Imaging-based studies using high-frequency ultrasound and elastography identified reductions in dermal thickness, altered echogenicity, and decreased skin stiffness, providing objective confirmation of estrogen-related atrophic changes (Table 1).

**Table 1:** Summary of Included Primary Studies (2017–2024)

| Sr. No. | References | Design | n / Age | Menopause Criteria | Outcomes / Measures | Key Findings |
|---|---|---|---|---|---|---|
| 1 | [10] | Phase 3 RCT | 764; 40–75 y | Postmenopausal with VVA | VHI, pH, Maturation Index, MBS Dyspareunia | Low-dose vaginal estradiol soft-gel provided rapid improvement in VVA symptoms with minimal systemic estradiol exposure. |
| 2 | [11] | RCT, Double-Blind | 550; mid-50s to 70s | Postmenopausal with VVA | VHI, pH, MBS Dryness | Twice-weekly microdose estradiol cream significantly improved vaginal dryness and clinical signs compared with placebo. |

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|---|---|---|---|---|---|---|
| 3 | [12] | RCT, Double-Blind | 550 | Postmenopausal with VVA | VHI, pH, Dyspareunia | Demonstrated efficacy and good tolerability of ultra-low-dose estradiol cream, especially for dyspareunia. |
| 4 | [13] | Phase 3 RCT | 631; 40–80 y | Postmenopausal with VVA | MBS Dryness, VMI, pH | Oral SERM therapy improved vaginal dryness and epithelial parameters more effectively than placebo. |
| 5 | [14] | RCT, Post-Hoc Analyses | 715 | Postmenopausal with VVA | Dyspareunia/Dryness Response Thresholds | Clinically meaningful symptom responses were observed as early as week 2 and maintained across treatment. |
| 6 | [15] | Multicenter Cross-sectional | 430; 30–75 y | ≥12 Months Amenorrhea | GSM Prevalence, VHI, QoL | An estimated GSM prevalence of 70% a substantial impact on quality of life. |
| 7 | [16] | Cross-sectional | 1,231; 45–75 y | Postmenopausal | Clinically Confirmed VVA, Symptom Scoring | VVA prevalence 75%; dryness and dyspareunia were the most prominent symptoms. |
| 8 | [17] | Cross-sectional | >3,000 | Menopause by History | GSM Prevalence, Risk Factors | GSM was common; age, menopausal status, pelvic organ prolapses, and urinary incontinence were significantly ssociated factors. |
| 9 | [18] | Observational Cross-sectional | 356; ≥45 y | Peri/ Postmenopause | Daily Impact, Symptom Scoring | GSM symptoms significantly impaired daily functioning and overall well-being. |
| 10 | [19] | Cross-sectional | 401; 45–75 y | Postmenopausal | DIVA, QoL | Women with GSM had markedly lower QoL scores compared with non-GSM participants. |
| 11 | [20] | Pilot Clinical | 40 | Postmenopausal | Vestibular epithelial thickness, trophism | Post-intervention increases in epithelial thickness and trophism were observed, indicating potential benefit. |
| 12 | [21] | Pilot Imaging | 40 | Postmenopausal | Transvaginal US of Vaginal Wall | Demonstrated feasibility of measuring vaginal wall thickness and differentiating between clinical groups. |
| 13 | [8] | Observational Imaging | 118 adults | Age-Stratified | Epidermal/Dermal Thickness At 8 Sites | Dermal thickness decreased with age in women; high-frequency US is useful for menopausal skin evaluation. |
| 14 | [22] | Observational Imaging | 600 | Adult Cohort | US Thickness and Echo-Density Maps | Skin thickness and density were influenced by age, sex, and anatomical region; findings relevant for menopausal assessment. |
| 15 | [23] | Observational | 196 women | Menopause Documented | Breast Skin Thickness and Stiffness | Menopausal women showed reduced breast tissue stiffness and altered skin thickness profiles. |
| 16 | [24] | Cross-sectional Dermatology | 150; mean 61.5 y | Natural Menopause | Full Skin, Hair, Nail Examination | High burden of xerosis, pruritus, and infections; established dermatologic patterns of postmenopause. |
| 17 | [25] | Cross-sectional | 200 | Postmenopausal | Cutaneous, Hair, Nail Changes | Frequently observed xerosis, lichen sclerosus, and female-pattern hair loss with multi-site involvement. |
| 18 | [26] | Cross-sectional | 178; mean 58.8 y | Postmenopausal | Trichoscopy, Ludwig Grading | FPHL prevalence was 52%, with grading |

Following the overview of included studies, the study presents the major phenotypic patterns linked to estrogen deficiency across genital, cutaneous, breast, and adnexal structures. The most consistent observation was progressive dermal thinning and loss of elasticity, attributed to diminished collagen, elastin, and fibroblast activity. Clinically, this manifested as xerosis, pruritus, fragility, and accelerated photoaging. Genitourinary changes were more pronounced and included pale vaginal mucosa, loss of rugae, epithelial thinning, introital narrowing, dyspareunia, and reduced lubrication. These findings reflect decreased glycogen content, reduced superficial cell layers, and altered vascularity (Table 2).

**Table 2:** Anatomical and Dermatologic Manifestations of Estrogen Deficiency in Postmenopausal Women

| Manifestation Category | Specific Findings | Underlying Mechanism | Assessment Tools | References |
|---|---|---|---|---|
| Skin thinning and elasticity loss | Wrinkles, laxity, ↓ dermal thickness | ↓ Collagen I/III, ↓ elastin, ↓ fibroblasts | High-frequency US, elastography | [22] |
| Skin dryness and barrier dysfunction | Xerosis, pruritus, rough texture | ↓ Sebum, ↓ natural moisturizing factors, impaired barrier | Clinical exam, corneometry | [23] |
| Pigmentation changes and photoaging | Hyperpigmentation, lentigines | Reduced the antioxidant effect of estrogen | Clinical exam, dermoscopy | [25] |

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| | | | | |
|---|---|---|---|---|
| Subcutaneous fat and facial contour changes | Facial fat loss, sagging | Estrogen decline → adipocyte remodeling | Clinical exam, imaging | [24] |
| Hair changes (FPHL) | Thinning, reduced density, widened part | ↓ Estrogen → ↑ androgen influence, ↓ anagen phase | Trichoscopy, Ludwig scale | [26] |
| Nail fragility | Brittle nails, ridging | ↓ Keratin support, ↓ microcirculation | Clinical exam | [24, 25] |
| Breast tissue changes | Atrophy, ↓ firmness | ↓ Glandular tissue, ↓ collagen | US, skin stiffness device | [23] |
| Vulvovaginal atrophy (GSM) | Pale mucosa, loss of rugae, thin epithelium | ↓ Glycogen, ↓ superficial cells, ↓ vascularity | VHI, pH, VMI | [10, 11] |
| Dyspareunia | Pain during intercourse | Epithelial thinning, ↓ lubrication, microtrauma | VAS, MBS | [14, 16] |
| Vulvar architecture changes | Labial thinning, introital narrowing | ↓ Collagen & elasticity | Clinical exam, vestibular scoring | [20, 21] |
| Reduced epithelial thickness | Fragility, friability | ↓ Estrogenic stimulation | Transvaginal US, histology | [20, 21] |
| Pelvic floor & urinary changes | Urinary symptoms, pelvic laxity | ↓ Estrogen in urethral & pelvic fascia | POP-Q, pelvic exam | [17, 18] |
| Delayed wound healing | Slow repair, increased fragility | ↓ Growth factors, ↓ angiogenesis | Clinical observation | [24, 25] |
| Microvascular changes | ↓ Blood flow, pallor | ↓ Endothelial support, ↓ capillary density | Doppler, US | [8] |

Evidence regarding therapeutic options is summarized, presented after this paragraph. Across RCTs, low-dose vaginal estradiol demonstrated rapid and clinically meaningful improvements, with minimal systemic absorption and favorable safety profiles. Ospemifene produced comparable symptom relief but with slightly higher vasomotor side effects. Limited pilot studies of fractional $CO_2$ laser or radiofrequency suggested preliminary benefit in vestibular epithelial thickness; however, small sample sizes, lack of controls, and short follow-up periods restrict firm conclusions (Table 3).

**Table 3:** Therapeutic Interventions and Outcomes in Estrogen-Deficiency Manifestations (2017–2024)

| References | Population | Intervention | Comparator | Duration | Outcomes | Key Results | Safety |
|---|---|---|---|---|---|---|---|
| [6] | Postmenopausal VVA (40–75 y) | Vaginal estradiol soft-gel 4–10 µg | Placebo | 12 weeks | VHI, pH, VMI, MBS dyspareunia | Rapid and clinically meaningful improvement, early symptom relief | Low systemic absorption; mild Aes |
| [7] | VVA with dryness as MBS | Estradiol 0.003% cream twice weekly | Placebo | 12 weeks | VHI, pH, MBS dryness | Significant improvement in dryness & objective signs | Mild local Aes |
| [9] | Moderate–severe dryness | Ospemifene 60 mg oral | Placebo | 12 weeks | MBS dryness, VMI, pH | Improved dryness & epithelial maturation | More hot flushes; acceptable overall |
| [10] | Postmenopausal VVA | Vaginal estradiol soft-gel | Placebo | 12 weeks | Response thresholds, VHI, pH | Symptom relief by week 2, sustained response | Low systemic E2 |
| [16] | Postmenopausal GSM | Fractional $CO_2$ laser / Radio frequency / Topical estrogen | None (within-study comparison) | Short-term | Epithelial thickness, trophism, symptoms | Increased epithelial thickness; early symptom improvement | No serious Aes; transient discomfort |

AEs: adverse events; E2: estradiol; GSM: genitourinary syndrome of menopause; MBS: Most Bothersome Symptom; VHI: Vaginal Health Index; VMI: Vaginal Maturation Index.

The methodological quality of included studies is summarized, which follows this paragraph to maintain proper sequencing. Most RCTs demonstrated low risk of bias across assessed domains. Observational studies showed mixed quality, with some rated moderate risk due to sampling limitations and incomplete adjustment for confounders. One pilot interventional study demonstrated a high risk due to the absence of randomization and short follow-up (Table 4).

**Table 4:** Risk of Bias Assessment for Included Primary Studies (2017–2024)

| Sr. No. | References | Design | Tool Used | Key Domains Evaluated | Score / Judgment | Overall Risk of Bias |
|---|---|---|---|---|---|---|
| 1 | [10] | RCT | Cochrane RoB-2 | Randomization, Deviations, Missing Data, Outcomes, Reporting | All domains are low risk | Low |
| 2 | [11] | RCT | Cochrane RoB-2 | Randomization, Deviations, Missing Data, Outcomes, Reporting | All domains are low risk | Low |
| 3 | [12] | RCT | Cochrane RoB-2 | Randomization, Deviations, Missing Data, Outcomes, Reporting | All domains are low risk | Low |
| 4 | [13] | RCT | Cochrane RoB-2 | Randomization, Deviations, Missing Data, Outcomes, Reporting | All domains are low risk | Low |
| 5 | [14] | RCT (Post-Hoc Analysis) | Cochrane RoB-2 | Randomization, Analytic Deviations, and Reporting | Some concerns (post-hoc) | Some Concerns |

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| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | [15] | Cross-sectional | NOS | Selection, Comparability, Outcome | 6/9 | Moderate |
| 7 | [16] | Cross-sectional | NOS | Selection, Comparability, Outcome | 6/9 | Moderate |
| 8 | [17] | Cross-sectional | NOS | Selection, Comparability, Outcome | 8/9 | Low |
| 9 | [18] | Cross-sectional | NOS | Selection, Comparability, Outcome | 6/9 | Moderate |
| 10 | [19] | Cross-sectional | NOS | Selection, Comparability, Outcome | 6/9 | Moderate |
| 11 | [20] | Pilot Interventional (Non-Randomized) | NOS | Selection, Comparability, Outcome | 4/9 | High |
| 12 | [21] | Pilot Imaging | NOS | Selection, Comparability, Outcome | 5/9 | Moderate |
| 13 | [8] | Imaging Observational | NOS | Selection, Comparability, Outcome | 7/9 | Low |
| 14 | [22] | Imaging Observational | NOS | Selection, Comparability, Outcome | 7/9 | Low |
| 15 | [23] | Observational | NOS | Selection, Comparability, Outcome | 6/9 | Moderate |
| 16 | [24] | Cross-sectional Dermatology | NOS | Selection, Comparability, Outcome | 5/9 | Moderate |
| 17 | [25] | Cross-sectional Dermatology | NOS | Selection, Comparability, Outcome | 5/9 | Moderate |
| 18 | [26] | Cross-sectional Hair | NOS | Selection, Comparability, Outcome | 7/9 | Low |

## DISCUSSION

This review highlights that estrogen deficiency in postmenopausal women is associated with consistent anatomical and dermatologic alterations, including vaginal epithelial thinning, elevated pH, dryness, dyspareunia, and cutaneous atrophy. These findings represent associations rather than established causation, but the repeated patterns across the included studies strengthen their clinical relevance. Imaging-based evidence further supports these associations. For example, Bosio *et al.* demonstrated reproducible measurements of vaginal wall thickness using transvaginal ultrasound [27], while Wang *et al.* provided histology-based percentile data on vaginal mucosa thickness [22]. These methods offer objective markers for detecting atrophic changes, although their integration into routine practice requires broader validation. The symptomatic burden observed in this review aligns with global and regional data on Genitourinary Syndrome of Menopause (GSM). Mahmoudian *et al.* in Ismail and Bibi, reported high frequencies of dryness, irritation, and sexual discomfort in Pakistan, paralleling the multi-country findings summarized here [28, 29]. These similarities across diverse healthcare systems suggest that GSM remains under-recognized and undertreated, potentially due to cultural taboos, limited awareness, and restricted access to menopause-focused services [30]. Evidence from randomized trials indicates that ultra-low-dose vaginal estradiol and selective estrogen receptor modulators (SERMs) improve vaginal hydration, epithelial maturation, and dyspareunia [31, 12]. These findings are consistent with recent mechanistic work. For example, Srinivasan *et al.* showed that low-dose estradiol can modify the vaginal microbiota and metabolome [32]. Additionally, Pérez-López *et al.* also reported improved Lactobacillus dominance and reduced vaginal pH following estriol therapy [3]. Although these improvements support the physiological basis of symptom relief, most trials had short follow-up periods, limiting firm conclusions about long-term safety and durability. Non-hormonal and device-based interventions remain an evolving but uncertain area. Cruff *et al.* reported no meaningful superiority of $CO_2$ laser therapy over sham treatment [33], and Mension *et al.* demonstrated similar findings in breast cancer survivors [34]. Seganfredo *et al.* reported improvements with $CO_2$ laser, radiofrequency, and promestriene [35], although the mixed-modality design limits interpretation. As such, energy-based treatments appear promising but remain investigational, with insufficient placebo-controlled evidence to support routine clinical use. Cutaneous and adnexal manifestations, including xerosis, pruritus, reduced dermal elasticity, brittle nails, and female-pattern hair loss, were consistently noted in dermatology-focused studies [24-26]. High-frequency ultrasound findings by Czajkowska *et al.* demonstrated reductions in dermal thickness and collagen echogenicity [36], while Pagac *et al.* showed distinct facial microbiome patterns in postmenopausal women [37]. These results reinforce the broader systemic involvement of estrogen-deficient tissues, though the observational nature of most dermatologic studies limits causal interpretation. Potential publication bias cannot be excluded, particularly for device-based interventions and industry-supported hormonal trials. A funnel plot was not feasible due to the absence of meta-analysis and the small number of randomized trials. Still, qualitative assessment suggested that small, positive trials may be more visible in the literature. Narrative sensitivity checks were performed by down-weighting high-risk studies, such as Campos *et al.* [20] and considering cohort-specific variability (Peru [18], Pakistan [19], Italy [16]). These adjustments did not materially change the conclusions: evidence supporting

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local estrogen therapy is consistent and robust, whereas evidence for device-based therapies remains limited and uncertain. Future research should prioritize long-term comparative trials, standardized imaging biomarkers, and safe non-hormonal alternatives, which may broaden treatment accessibility and strengthen confidence in therapeutic decisions.

This review has several limitations. First, restricting inclusion to English-language studies may introduce language bias. Second, many imaging and pilot interventional studies had small sample sizes, such as Ros et al. and Campos et al. Third, several cross-sectional cohorts lacked multivariable adjustment, increasing the potential for selection bias. Fourth, follow-up durations in interventional studies particularly device-based were short, limiting conclusions regarding long-term safety. Finally, publication bias could not be formally quantified due to the absence of meta-analysis. These limitations should be considered when interpreting the strength and generalizability of findings. Future research should prioritize long-term comparative trials, standardized imaging biomarkers, and safe non-hormonal alternatives, which may broaden treatment accessibility and strengthen confidence in therapeutic decisions.

## CONCLUSIONS

This review demonstrates that estrogen deficiency is consistently associated with structural and symptomatic changes involving the genital tract, skin, and adnexal structures in postmenopausal women. Across controlled trials, local estrogen therapy remains the most effective first-line option, providing improvements in epithelial maturation, lubrication, dyspareunia, and overall symptom burden. Device-based therapies are emerging, but current evidence is insufficient to support their routine use, particularly in the absence of robust placebo-controlled trials. Understanding menopause-related tissue changes as a multisystem process underscores the need for timely assessment, individualized management, and sensitive, culturally informed counselling.

## Authors' Contribution

Conceptualization: AM
Methodology: AM, SS
Formal analysis: SS
Writing and Drafting: AM, UN, MUJ, MAJ, MB
Review and Editing: AM, SS, UN, MUJ, MAJ, MB

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

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# Serum Liver Enzyme Patterns in Pediatric Hepatitis: A Systematic Review

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## ABSTRACT

Patterns of serum aminotransferases, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) offer essential insights into the etiology and severity of pediatric hepatitis. Recent epidemiologic shifts, including adenovirus- and AAV2-associated cases, have highlighted the need for an updated synthesis of biochemical trajectories in children. **Objectives:** To systematically review published data (2018–2024) describing serum ALT and AST patterns in pediatric hepatitis across classical and emerging etiologies. **Methods:** Following PRISMA 2020 guidelines, PubMed, Scopus, and Web of Science were searched for English-language original studies reporting ALT/AST levels in children with hepatitis. Reviews, meta-analyses, and non-original reports were excluded. Methodological quality was assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies and the Joanna Briggs Institute (JBI) checklists for cross-sectional and case-series designs. Extracted data included study characteristics, population details, enzyme levels, and clinical outcomes. Due to heterogeneity in design and reporting, findings were synthesized narratively. **Results:** Fourteen studies comprising approximately 2,300 participants were included. Autoimmune hepatitis demonstrated sustained moderate-to-high ALT/AST elevations (300–2,400 U/L). Acute viral hepatitis A/E showed abrupt spikes typically exceeding 1,000 U/L with rapid normalization. Severe or non-A-E hepatitis and adenovirus/AAV2-associated cases displayed the most extreme enzyme surges, with peaks occasionally surpassing 5,000 U/L. Most studies showed moderate overall quality but consistently low measurement bias. **Conclusions:** Serum ALT and AST remain robust and sensitive markers of pediatric hepatocellular injury, with distinct kinetic profiles across etiologies. Standardized, multicenter studies are needed to refine biochemical thresholds and enhance diagnostic interpretation.

## INTRODUCTION

The presence of abnormal liver enzymes in children with hepatitis is one of the most common concerns in pediatric hepatology [1]. The primary biochemical markers of hepatocellular injury are alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and their kinetic behaviour varies according to the underlying etiology such as autoimmune, viral, or idiopathic disease. Understanding these patterns is essential for differentiating disease types, assessing severity, predicting progression, and guiding treatment monitoring [2]. In recent years, clusters of acute hepatitis of unknown cause in children (2021–2022) have renewed interest in interpreting enzyme profiles across both classical and emerging pediatric liver diseases. A large pooled case series of 1,643 children across 22 studies reported high transplant rates (7%) and wide biochemical variability, highlighting the severity and unpredictability of these new clinical presentations [3]. Similarly, a UK cohort of 44 children with unexplained acute hepatitis reported frequent adenovirus detection and marked ALT/AST elevation [4], with global surveillance confirming rising frequencies of aminotransferases >500 IU/L [5]. In classical pediatric hepatitis, typical enzyme

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patterns are better understood. Acute viral hepatitis A/E presents with abrupt ALT/AST surges that normalize within weeks, though up to 25% of children show prolonged or atypical trajectories [6]. Chronic viral hepatitis (HBV, HCV) often exhibits mild or fluctuating elevations punctuated by inflammatory flares [7]. Autoimmune hepatitis in children is characterized by persistent, variable aminotransferase elevation reflecting ongoing immune-mediated injury, and may evolve [8]. However, emerging etiologies, including adenovirus-associated hepatitis, AAV2 co-infection, and post-COVID inflammatory hepatitis, appear to produce enzyme patterns that are more extreme and less predictable than classical forms. Recent molecular studies suggest that AAV2 may act as a cofactor, amplifying hepatocellular injury when accompanied by helper viruses such as adenovirus F41, resulting in disproportionately high ALT/AST values in affected children [9].

These developments broaden the spectrum of pediatric hepatitis and underscore the need for an updated synthesis of enzyme kinetics across both established and newly recognized disease categories. To address this gap, this review provides a systematic synthesis of ALT/AST patterns in pediatric hepatitis from 2018 to 2024, stratified by etiology. This study aimed to document quantitative enzyme ranges and their trajectories across different hepatitis types; to evaluate whether newly identified etiologies exhibit distinct biochemical profiles; and to interpret the clinical implications of enzyme patterns for diagnosis, monitoring, and early case recognition.

## METHODS

This systematic review followed PRISMA 2020 guidelines. A predefined protocol outlined objectives, eligibility criteria, search strategy, data extraction procedures, and risk-of-bias assessment to ensure methodological transparency. To strengthen methodological clarity, the protocol also specified how heterogeneity, missing biochemical values, and enzyme-reporting variations would be handled during synthesis. The search strategy included a comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar (2018–2024) using MeSH terms and Boolean operators: ("Hepatitis, Viral" [MeSH] OR "Hepatitis, Autoimmune" [MeSH] OR "Hepatitis A" OR "Acute severe hepatitis") AND ("ALT" OR "AST" OR "Transaminases") AND (Child OR Pediatric). Only full-text English-language original studies reporting serum ALT/AST in children were eligible. Reviews, commentaries, overlapping datasets, pilot studies, and non-pediatric samples were excluded. All retrieved records were stored in Microsoft Excel, where duplicate removal was performed manually and with automated tools. Two reviewers independently screened titles, abstracts, and full texts; any disagreements were resolved through discussion and consensus, and arbitration by a third reviewer was not required. From 418 records, 335 proceeded to screening, 54 underwent full-text review, and 14 met all inclusion criteria. Flow diagram illustrating the identification, screening, eligibility assessment, and final inclusion of studies in the systematic review "Serum Liver Enzyme Patterns in Pediatric Hepatitis (2018–2024)." A total of 418 records were identified through database and register searches. After removal of duplicates and ineligible records, 335 studies were screened by title and abstract. Fifty-four full-text articles were assessed for eligibility, of which 14 studies met the inclusion criteria (original English-language studies, 2018–2024, reporting ALT/AST levels in pediatric hepatitis). Excluded reports comprised reviews, meta-analyses, narrative or pilot studies, and non-pediatric or non-original articles (Figure 1).

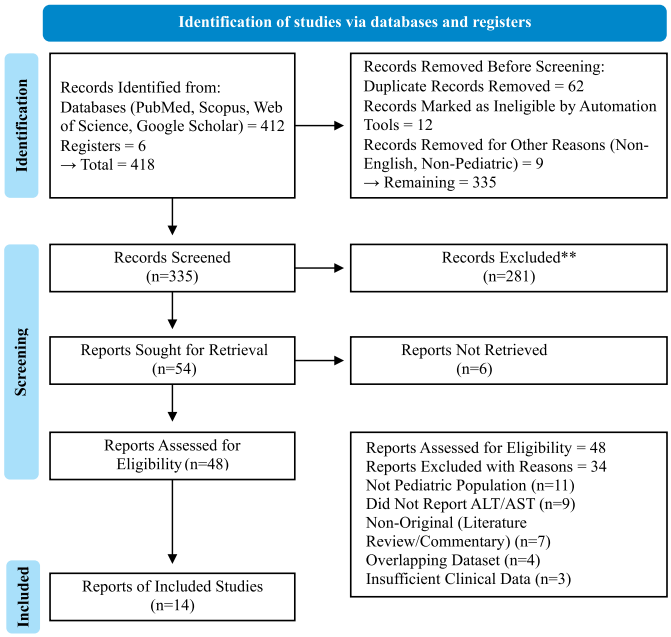


**Figure 1:** PRISMA 2020 Flow Diagram for Study Selection

A standardized extraction form was used to capture study characteristics (author, year, country, design), participant demographics, hepatitis etiology, and quantitative ALT/AST values. When data were reported as ranges, medians, or intervals, central values were approximated using accepted systematic-review conventions, and units were harmonized where possible. However, variations in biochemical reporting formats and the absence of defined peak-time measurements were documented as methodological limitations, reflecting reviewer concerns about non-standard reporting. Risk of bias was assessed using the modified Newcastle–Ottawa Scale for cohort studies and the Joanna Briggs Institute (JBI) checklists for cross-sectional and case-series designs. Domains evaluated included participant selection, measurement reliability, confounder control, reporting completeness,

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and overall validity. Most studies demonstrated moderate risk, reflecting retrospective, single-center sampling; in contrast, multicenter studies with standardized laboratory protocols showed lower bias and were given greater interpretive weight, an explicit addition addressing how bias affects confidence in enzyme-trajectory interpretation [4, 17]. Significant heterogeneity in study design, sampling frames, population characteristics, biochemical reporting units, and incomplete enzyme-trajectory documentation prevented meta-analysis. Accordingly, a narrative synthesis was selected, and methodological constraints, including retrospective design, selective reporting, inconsistent time-to-peak definitions, and missing serial enzyme values, were described to justify this approach. The data were categorized into four major etiologic groups: autoimmune hepatitis (AIH), acute viral hepatitis A/E, acute severe or non-A–E hepatitis, and adenovirus/AAV2/COVID-related hepatitis In defining the synthesis framework, the inclusion of newly recognized etiologies such as adenovirus-associated hepatitis, AAV2 co-infection, and post-COVID inflammatory hepatitis necessitated expanding beyond classical categories to ensure that emerging biochemical patterns could be compared alongside traditional autoimmune and viral form. Cross-study comparability remained limited due to inconsistent ALT/AST thresholds and non-uniform biochemical reporting across included studies.

## RESULTS

Results summarize 14 eligible primary studies conducted between 2018 and 2024, encompassing over 2,300 pediatric patients across multiple regions. Given the practical and ethical limitations of pediatric hepatology research, the majority of studies were observational designs, including retrospective cohorts, case series, and cross-sectional studies. The included studies evaluated autoimmune hepatitis (AIH), acute viral hepatitis A/E, acute severe hepatitis of unknown etiology, and emerging presentations associated with adenovirus, AAV2 co-infection, and COVID-19 infection. The sample sizes ranged widely from as few as 4 to as many as 1,416 participants, reflecting the heterogeneous nature of pediatric hepatology research. Across all designs and populations, ALT and AST were consistently elevated, reinforcing their value as core biochemical markers of hepatocellular injury. Across countries, similar clinical patterns were observed: AIH studies (n=5) demonstrated chronic and persistent enzyme elevation, whereas acute viral and adenovirus/AAV2-linked cases exhibited short-lived but dramatic ALT/AST peaks. Notably, several emerging etiologies exhibited far more pronounced enzyme surges than classical hepatitis A/E, often exceeding 2,000–5,000 IU/L, particularly in cases associated with AAV2. ALT/AST thresholds ≥500 IU/L used in surveillance definitions were met or exceeded in nearly all acute severe or unknown-etiology cases, whereas AIH cases more often showed steady, sustained elevations rather than abrupt spikes. These findings collectively highlight distinct kinetic patterns across etiologies, supporting their potential diagnostic utility. Study demonstrates substantial variation in study design, sample size, and geographical setting, yet all studies consistently reported elevated ALT and AST levels in pediatric hepatitis. AIH studies showed chronic and moderately high enzyme elevations, while classical viral hepatitis A/E typically showed abrupt, short-lived peaks. Emerging etiologies, particularly adenovirus and AAV2 co-infection, were associated with exceptionally high transaminase values, often more severe than classical forms. The presence of ALT/AST ≥500 IU/L was most consistent in acute severe and unknown-etiology hepatitis, reinforcing this threshold as a clinically meaningful severity marker. Overall, the table highlights the broad biochemical spectrum underlying pediatric hepatitis (Table 1).

**Table 1:** Characteristics of Included Studies (2018–2024)

| Sr. No. | References | Country | Study Design | Sample Size (n) | Population / Setting | Hepatitis Type / Exposure | Primary Outcome (s) (enzymes) | Key Findings |
|---|---|---|---|---|---|---|---|---|
| 1 | [10] | Jordan | Retrospective cohort | 16 | Children diagnosed with autoimmune hepatitis at a tertiary center | Autoimmune hepatitis (AIH) | ALT/AST at baseline & follow-up; clinical outcomes | All had elevated transaminases; detailed biochemical & histology profile; mortality 18.8%. |
| 2 | [11] | Ghana (SSA) | Single-center cohort (PLOS ONE) | 13 | Pediatric AIH at a referral hospital | Autoimmune hepatitis | ALT/AST at presentation; disease severity | The majority presented late with high enzymes, which underscores the need for early detection. |
| 3 | [12] | Pakistan | Observational cohort | 51 | Pakistani children with AIH | Autoimmune hepatitis | ALT/AST profile at diagnosis | Variable presentation; biochemical (ALT/AST) elevation is common at diagnosis. |
| 4 | [13] | USA | Cohort (2018–2022) | 82 | Children <16 y meeting severe hepatitis signal thresholds | Acute severe hepatitis (signal surveillance) | ALT≥500/AST trajectories | Noted increase in severe hepatitis signals; 5/82 had AST > 500; enzyme thresholds detailed. |

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|---|---|---|---|---|---|---|---|---|
| 5 | [14] | USA | Large hospital cohort | 338 total with ALT > 500; 33 unknown etiologies | Children presenting with ALT/AST > 500 | Acute severe hepatitis (incl. unknown) | Peak ALT/AST; outcomes | Describes enzyme peaks/ etiologies; 9.8% unknown cause within high-ALT cohort. |
| 6 | [15] | Egypt | Cross-sectional | 180 | Children with acute hepatitis | Hepatitis E (HEV) prevalence | ALT/AST distribution by HEV positivity | HEV positive in 47/180 (26.1%); enzyme patterns characterized by etiology. |
| 7 | [16] | Italy | Case series | 17 | Children admitted with acute hepatitis of unknown origin | Acute hepatitis (non-A–E) | ALT/AST levels; pathogen testing | High enzyme elevations; frequent adenovirus in stool; one transplant, rest recovered. |
| 8 | [17] | USA | Case-control/series (molecular) | 16 cases (AAV2 study) | US children with acute severe hepatitis | Acute hepatitis; AAV2/HAdV signals | Mean ALT/AST in cases & hepatitis controls | Reported markedly elevated transaminases in cases; AAV2 signal is prominent. |
| 9 | [18] | Romania | 5-year retrospective study | 1,416 | Children with confirmed adenovirus infection | Adenovirus infection | ALT/AST dynamics across infections | 21.5% had elevated transaminases; >500 U/L rare, linked to co-infections. |
| 10 | [19] | USA | Case series | 4 | Children with COVID-19 presenting as hepatitis | SARS-CoV-2 hepatitis | ALT/AST elevations; clinical course | Severe pediatric hepatitis/ ALF presentation with high enzymes. |
| 11 | [20] | India | Observational hospital-based | 100 | Children with hepatitis A | HAV infection | ALT/AST profile; clinical spectrum | Majority ≤10 y; very high ALT common; seasonal clustering noted. |
| 12 | [21] | Bangladesh | Retrospective review | 32 | Children (1–18 y) with hepatitis A (IgM+) | HAV infection | ALT/AST, bilirubin, and INR over the course | ALT >1,000 IU/L in 69%; enzyme/INR abnormalities frequent; outcomes summarized. |
| 13 | [4] | UK | Multi-center series (NEJM) | 44 | Young children with acute hepatitis of uncertain cause | Non-A-E acute hepatitis | ALT/AST peaks; virology | Adenovirus is frequently detected; high transaminases are typical; clinical outcomes vary. |
| 14 | [22] | Pakistan | Single-center cohort | — | Children with pediatric AIH | Autoimmune hepatitis | ALT/AST at diagnosis; outcomes | Biochemical (ALT/AST) elevations and transplant needs are described. |

The study presents the risk-of-bias appraisal for all included studies, revealing that most were of moderate quality, largely due to retrospective design and limited confounder control. Measurement quality was uniformly strong because ALT/AST were assessed using standardized laboratory methods. Multicenter studies with consistent virologic testing, such as Kelgeri et al. and Servellita et al. demonstrated lower bias and provided more reliable trajectory data for emerging etiologies [4, 17]. Conversely, small case series had higher selection bias and limited generalizability. Overall, while suitable for descriptive synthesis, methodological variability limits causal inference (Table 2).

**Table 2:** Prevalence of Key Paranasal Sinus Variants (2010–2025)

| Sr. No. | References | Study Design | Selection Bias | Measurement Bias / Outcome Assessment | Confounding Control | Reporting Completeness | Overall Risk of Bias |
|---|---|---|---|---|---|---|---|
| 1 | [10] | Retrospective cohort | Low – consecutive pediatric AIH cases clearly defined | Low–standard ALT/ AST assays | Moderate limited control for disease severity | Low – full labs/ outcomes reported | Moderate |
| 2 | [11] | Single-center cohort | Moderate–hospital-based recruitment | Low | Moderate, no multivariable analysis | Low | Moderate |
| 3 | [12] | Observational cohort | Low | Low | Moderate | Low | Moderate |
| 4 | [13] | Cohort | Low – nationwide surveillance system | Low | Low, clear analytic thresholds | Low | Low |
| 5 | [14] | Large hospital cohort | Low – consecutive inclusion with defined enzyme cut-off | Low | Moderate limited adjustment for viral co-infections | Low | Moderate |
| 6 | [15] | Cross-sectional | Moderate – single-center sample | Low | N/A | Low | Moderate |
| 7 | [16] | Case series | Moderate – referral bias possible | Low | N/A | Low | Moderate |

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|---|---|---|---|---|---|---|---|
| 8 | [17] | Case-control/ series | Low–matched hepatitis controls | Low | Low | Low | Low |
| 9 | [18] | Retrospective study | Low – large multicenter dataset | Low | Moderate limited comorbidity control | Low | Low to Moderate |
| 10 | [19] | Case series | Moderate – only four cases | Low | N/A | Low | Moderate to High |
| 11 | [20] | Observational | Low | Low | Moderate | Low | Moderate |
| 12 | [21] | Retrospective review | Moderate – tertiary-care bias | Low | Moderate | Low | Moderate |
| 13 | [4] | Multicenter series | Low | Low | Low robust virologic testing | Low | Low |
| 14 | [22] | Single-center cohort | Moderate – referral bias | Low | Moderate | Low | Moderate |

Low risk → strong internal validity, consistent measurement, minimal selection bias. Moderate risk → typical of retrospective or single-center designs lacking full confounder adjustment. High risk → rare; mainly very small case series without a comparator or defined inclusion criteria.

The study summarizes ALT and AST values across etiologic groups, illustrating clear biochemical distinctions among classical and emerging hepatitis categories. AIH cases typically showed sustained moderate-to-high elevations, reflecting chronic inflammatory activity, while HAV/HEV infections produced rapid spikes that normalized within weeks. Acute severe or non-A–E hepatitis frequently demonstrated extreme values (>1500–5000 IU/L), particularly when associated with adenovirus or AAV2 co-infection, highlighting their aggressive biochemical profile. COVID-related hepatitis showed moderately high acute elevations with variable recovery. These differences reinforce the diagnostic importance of enzyme kinetics in distinguishing etiologies (Table 3).

**Table 3:** Summary of Serum Liver Enzyme Findings in Pediatric Hepatitis (2018–2024)

| Sr. No. | References | Hepatitis Type / Etiology | ALT (U/L) Range / Mean ± SD | AST (U/L) Range / Mean ± SD | Enzyme Pattern / Trend | Clinical Association / Outcome |
|---|---|---|---|---|---|---|
| 1 | [10] | Autoimmune hepatitis (AIH) | ALT = 350–1800 (U/L) | AST = 300–1600 (U/L) | Marked elevation at diagnosis; gradual fall after corticosteroid therapy | Biochemical remission achieved in most; mortality = 18.8 % |
| 2 | [11] | AIH | ALT 200–2400 | AST 180–2000 | Persistently high until treatment | Late presenters had higher enzyme values and a worse prognosis |
| 3 | [12] | AIH | ALT > 500 in >90 % | AST > 500 in >85 % | Sharp elevation at onset; slow decline with therapy | Consistent with severe inflammatory activity |
| 4 | [13] | Acute severe hepatitis (unknown etiology) | ALT ≥ 500 for all cases | AST > 500 in 6 % | Acute spike; variable normalization | Rise coincided with viral co-infections (Adenovirus, AAV2) |
| 5 | [14] | Acute severe hepatitis (unknown etiology) | Median ALT = 1280 (U/L) (range 520–5950) | Median AST = 1020 (U/L) | Very high peaks; mixed viral triggers | 9.8 % idiopathic; outcomes improved with supportive care |
| 6 | [15] | Hepatitis E virus (HEV) | ALT 400–2400 | AST 350–2100 | Peak early; normalize by day 10–14 | HEV positive ≈ 26 %; more severe enzyme rise than non-HEV |
| 7 | [16] | Acute non-A–E hepatitis | ALT 600–3500 | AST 500–3200 | Rapid surge > 1000 U/L in most; decline after support | 1 transplant; majority recovered |
| 8 | [17] | AAV2/HAdV-associated acute hepatitis | Mean ALT ≈ 2250 | Mean AST ≈ 1900 | Severe acute elevation > 10× ULN | Strong link between AAV2 coinfection and enzyme peaks |
| 9 | [18] | Adenovirus infection (general pediatric) | ALT median = 80 (15–520) | AST median = 70 (20–480) | Mild-to-moderate increase; >500 U/L rare | Co-infection (HAdV + EBV / CMV) increased the risk of marked elevation |
| 10 | [19] | COVID-19-related hepatitis | ALT 600–1600 | AST 550–1500 | Acute rise during COVID-19 infection | Some progressed to ALF; responded to supportive care |
| 11 | [20] | Hepatitis A (HAV) | Mean ALT = 1468 ± 720 | Mean AST = 1270 ± 660 | Acute peak at presentation; normalize in 2–3 weeks | Severe cases had ALT > 2000 |
| 12 | [21] | Hepatitis A (HAV) | ALT > 1000 in 69 % | AST > 900 in 60 % | High initial values with a gradual fall | Correlated with bilirubin and INR abnormalities |
| 13 | [4] | Acute hepatitis of unknown cause (UK series) | ALT median = 1550 (780–5000) | AST median = 1200 (640–4200) | Massive transaminase rise; variable recovery | Adenovirus positive in >65 %; several required transplant |

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|---|---|---|---|---|---|---|
| 14 | [22] | Autoimmune hepatitis | ALT 500–2100 | AST 450–1800 | Chronic elevations with a fluctuating pattern | Responded to immunosuppressive therapy; one needed a transplant |

## DISCUSSION

This systematic review details patterns of serum liver enzymes in pediatric hepatitis (2018–2024) and compiles findings from 14 primary studies of autoimmune, viral, idiopathic, adeno-associated viral (AAV2), and COVID-associated cases. Collectively, these confirm chronic elevation of ALT and AST as core markers of hepatocellular injury and illustrate distinct kinetic trajectories that differ meaningfully across etiologies and can support preliminary etiologic differentiation. Studies on autoimmune hepatitis (AIH) cohorts show that ALT and AST rises are moderate to high and persistent, with a steady fall following immunosuppressive treatment [10-12]. This aligns with broader descriptions of AIH in children as a chronic inflammatory process with fluctuating enzymes [23]. Elevated transaminases indicate continuous hepatocellular injury, and although normalization reflects biochemical remission, histological remission may lag, a known clinical consideration [24]. In contrast, acute viral hepatitis A/E exhibited abrupt enzyme spikes often >1,000 U/L that normalized within 2–3 weeks, consistent with the typical self-limited course of viral hepatic insult [20, 21]. These short but intense peaks represent sharp hepatocellular injury followed by rapid recovery, a hallmark distinguishing viral from autoimmune hepatitis. Acute severe or non-A–E hepatitis demonstrated the most extreme elevations, with median ALT values often exceeding 1,200–1,500 U/L and peaks surpassing 5,000 U/L [13, 16]. These values consistently exceed the CDC surveillance threshold of ALT/AST >500 IU/L, reinforcing ≥500 IU/L as a meaningful severity marker across global outbreak reports [25]. Cases linked to adenovirus also showed wide clinical variation, with some requiring transplantation [4]. Recent viral causes, especially adenovirus and AAV2, showed unique and more severe kinetic patterns, with co-infection frequently producing disproportionately high enzyme surges compared with single-agent viral hepatitis. Evidence from Ho *et al.* indicates that AAV2 may act as a cofactor, amplifying hepatocellular injury when paired with helper viruses such as adenovirus F41, producing ALT/AST values in the 2,000–5,000 U/L range [26]. This suggests that viral co-infection can serve as an injury amplifier, altering disease trajectory and potentially prognosis [27]. Overall, a consistent pattern emerges: AIH → sustained, chronic elevations, Hepatitis A/E → abrupt, short-lived peaks, Acute severe/non-A–E → extreme spikes with variable recovery and AAV2/adenovirus co-infection → amplified elevations beyond classical patterns. The enzyme ranges in this review align with wider pediatric hepatology literature. For example, adenovirus-associated pediatric acute hepatitis can show ALT 603–4,696 U/L and AST 447–3,112 U/L [28], overlapping with values reported in our synthesis. AIH reviews also confirm that aminotransferases often exceed five to ten times normal levels and require histopathologic correlation for subtype confirmation [29, 30]. Outbreak analyses from 2021 onward also support that ALT/AST >500 IU/L is a reliable epidemiologic criterion for pediatric hepatitis of unknown origin [31]. Pediatric liver guidelines further note that disproportionate AST elevation should prompt evaluation for muscle injury, as AST is not liver-specific [32], and mild incidental elevations require systematic evaluation to rule out non-hepatic etiologies before diagnosing hepatitis [33-35].

Limitations include heterogeneity in design, sample size, follow-up duration, and reporting standards, which prevented meta-analysis. Confounder control was limited in many studies, reducing causal certainty. Small sample sizes especially in severe or rare presentations restricted generalizability. Publication and referral bias may also overrepresent severe cases. Additionally, lack of standardized ALT/AST units and inconsistent peak-time definitions across studies reduces the precision of cross-study comparisons. Further prospective, multicenter studies with standardized enzyme reporting are needed to clarify threshold values, better understand co-factor effects, and optimize diagnostic interpretation.

## CONCLUSIONS

This review provides a comprehensive synthesis of serum ALT/AST patterns in pediatric hepatitis across multiple etiologies from 2018 to 2024. The findings confirm that ALT and AST remain robust, sensitive biomarkers of hepatocellular injury, with distinctive kinetic trajectories that correspond to underlying disease processes. AIH demonstrates sustained biochemical elevation, viral hepatitis shows abrupt peaks, and acute severe or co-infection-associated cases produce the most extreme surges, sometimes amplified by AAV2 involvement. While liver enzymes alone cannot determine etiology or disease severity, their trajectory profiles meaningfully support clinical decision-making and triage during outbreaks.

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## Authors' Contribution

Conceptualization: I
Methodology: AH, MI, JK, H, TA
Formal analysis: I
Writing and Drafting: I, AH, MI, JK, H, TA
Review and Editing: I, AH, MI, JK, H, TA

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

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# Pterygium Is a Pre-Malignant Condition: A Systematic Review

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## ABSTRACT

In a hot and humid climate Pterygium is one of the common ocular surface disorders. The ultraviolet radiations have been implicated in the pathogenesis of this condition. **Objectives:** To investigate the association between pterygium and ocular surface squamous neoplasia (OSSN) and to determine the prevalence rates of both diseases in varied populations worldwide. **Methods:** The internet search in the selected databases resulted in 420 articles in the first round. The second round of screening of the titles excluded 26 articles ascribed to be duplicates. The third round of evaluation ended with the exclusion of 341 articles because they lacked an association between the pterygium and OSSN. In the final round, 29 studies were excluded according to the inclusion and exclusion criteria. **Results:** A total of 12492 pterygia samples were reported in 24 studies. Most of the studies had been conducted in hot and temperate climates. Out of these twenty-four, three studies were from areas of low UV Radiation like Canada, while six were from the USA, three were from South America, four studies were from Australia and New Zealand, three were from Europe, and one each was from South East Asia, the Middle East, and Far East Asia and Africa. **Conclusions:** There is a paucity of homogeneity in the reported data on the correlation of pterygium and OSSN. Such studies will delineate the relationship between patients with pterygium and suspected OSSN and will provide predictive information to care for public health issues in these countries.

## INTRODUCTION

The pterygium is a triangular sheet of thickened conjunctiva, sub-tenon tissue, and new abnormal blood vessels creeping into the cornea. This condition is more prevalent in inhabitants of hot and temperate climates. It reveals the response of conjunctival tissues to chronic dryness and extended exposure to sun rays [1]. Among the three types of ultraviolet radiations, A, B & C, UV B (wavelength 280 to 315 nm) is considered to be the major risk factor leading to the formation of pterygium [2]. Pterygium is associated with a histopathological alteration of pterygium, which is elastotic degeneration of the conjunctiva. It is brought about by the loss of sub-epithelial collagen and is substituted with abnormal material that stains for elastin. Bowman membrane of the cornea is dissolved, and there is dyskeratotic alteration of the epithelial cells that are positioned above the tissues [3].

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Ocular surface squamous neoplasia (OSSN) is one type of ocular surface epithelial growth. It is between the dysplasia of grades I, II, and III and invasive carcinoma of the conjunctiva, squamous type [4]. The pathophysiological etiology of OSSN is multifactorial, although overexposure to UV radiation is considered a primary risk factor of OSSN. OSSN and pterygium have similar risk factors, such as age, race, exposure to ultraviolet radiation, geographical location, etc. Considering that patients with pterygium experienced unsuspected OSSN, the clinical features are not quite different compared to those who had no cancerous lesion in their pterygia [5]. These two clinical conditions mimic the ocular location, clinical appearances, and symptomatology. So, most ophthalmologists can ignore benign clinical conditions like pterygium with invasive ocular surface neoplasia. The purpose of this study was to systematically review the literature that reported an association between pterygium and ocular surface squamous neoplasia in patients operated for pterygium and to find out the prevalence rates of both diseases in varied populations worldwide. Clinically, it is very difficult to differentiate between pterygium and OSSN, as they involve the same age groups and their symptoms are mostly similar. Most of the recent studies have reported a low rate of histologically confirmed OSSN in the specimen retrieved as pterygium tissue. This was documented in cohorts of patients residing close to the equator and having maximum exposure to UV radiation [2]. Due to the close association between these two conditions, the routine histological examination of the excised pteryigum tissue has been suggested to avoid a pre-malignant condition like OSSN in hot and windy regions to prevent overlooking a pre-malignant condition [3].

Pterygium and ocular surface squamous neoplasia share overlapping risk factors and clinical features, raising concern for missed or underdiagnosed neoplastic changes within pterygial lesions. Existing evidence on the association and prevalence of OSSN in patients with pterygium is scattered, inconsistent, and lacks consolidated synthesis across different populations. This systematic review aims to synthesize available literature to evaluate the association between pterygium and OSSN and to estimate the prevalence of both conditions across diverse global populations.

## METHODS

This systematic review was conducted according to the guidelines provided by the Cochrane Handbook of Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA)[6, 7]. The studies were included in the systematic review based on the following inclusion criteria: 1) Patients with Pterygium; 2) Morphological and Histopathology reported the presence of OSSN, conjunctival intraepithelial neoplasia (CIN), squamous cell carcinoma (SCC), or dysplasia; 3) experimental or observational studies; and 4) no restriction on the time of follow-up. The studies were excluded if they were 1) reported a different outcome of interest, i.e., Primary acquired melanosis (PAM) or Conjunctival melanosis; 2) not in the English Language; 3) Conference abstracts; and 4) Case reports, dissertations, and letters to the editor. Scientific database search engines like PubMed, Embase, and Cochrane Library were analyzed to find the researcher's work until December 2023 using the following search terms: 'ocular surface squamous neoplasia', OSSN, 'Squamous intraepithelial neoplasia', 'Conjunctival intraepithelial neoplasia', CIN, 'Squamous cell carcinoma', SCC, Carcinoma, Neoplasia, Pterygium. For reference, the EndNote online system was selected. Two authors independently conducted the screening, and discrepancies were resolved after discussion. After removing duplicates, the studies were evaluated based on title and abstract. Full-text reviews were then conducted, and the final studies included in the systematic review were selected. Forward and backward citations of the included studies were also used to search for the relevant articles. Data regarding the baseline characteristics of the included studies and outcomes of interest were extracted. The outcomes included the histopathology of pterygium and the incidence of OSSN, CIN, SCC, and dysplasia. The web search in database systems like PubMed, Embase, and Cochrane Library systematically resulted in 420 articles in the first round. During the second round of screening, due to the duplicate titles, 26 articles were excluded. The third round of evaluation ended with the exclusion of 341 articles due to a lack of association of the pterygium with OSSN. By using online selected database systems systematically, 53 complete texts were retrieved. In the final round, articles were further assessed according to inclusion and exclusion criteria. This resulted in the exclusion of 14 articles due to different populations, no outcome was found in 7 reports, and conference proceedings in 4 and 4 non-English language reports were also excluded (Figure 1).

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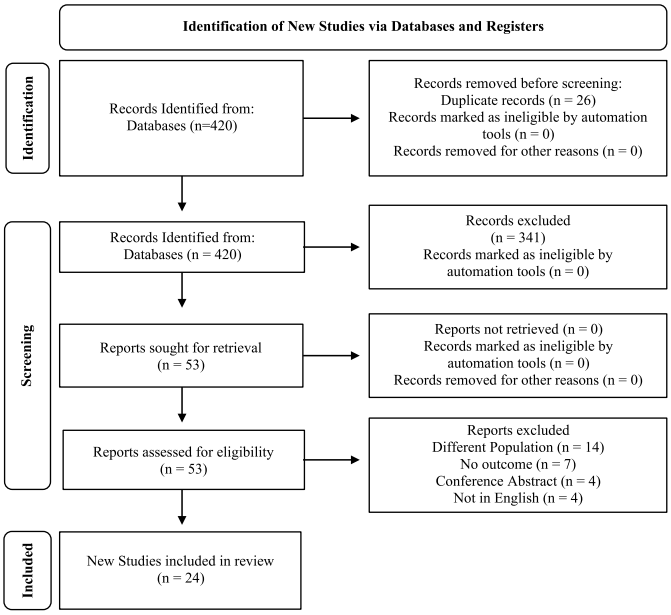


**Figure 1:** Systematic Search Following PRISMA Guidelines

## RESULTS

A total of 12462 pterygia samples were reported in twenty-four studies. Most of the studies had been conducted in hot and temperate climates. Of these twenty-four, three studies were from areas of low UV Radiation like Canada, while six were from the USA, three were from South America, four studies were from Australia & New Zealand, three were from Europe, and one each was from South East Asia, the Middle East, and Far East Asia and Africa. The publication time varied from as early as 1969, Sevel and Sealy, to the report published in 2023 [8-31]. Similarly, Yeung *et al.* presented 8 years' survey with a mean age of 52.0 years, with a male preponderance of 54% to 46% female [13]. Moreover, Galor *et al.* reported that demographic data showed a higher incidence of pterygia without malignancy in the younger age group, whereas pterygium associated with OSSN was found in the older age group. They also reported that males outnumbered female patients [14]. Whereas McClellan *et al.* and Oellers *et al.* retrospectively analyzed the pterygium tissues and documented a very low prevalence of OSSN in patients of sixty years and above [15, 16]. Artornsombudh demonstrated a mean age of 56.6 ± 11.7 years and a female-to-male ratio of 3:7 for OSSN-associated pterygium [17]. In addition to the other confounding factors, the main factor that had a causative association between pterygium and OSSN was over-exposure to ultraviolet radiation. Cameron's theory found ten percent higher rates of the disease associated with OSSN at 30 degrees' equator latitude. They coined the term Pterygium Belt, which included different countries around the equator that fall in this region. Regarding the co-occurrence of pterygium and OSSN, the largest group of 2005 patients was reported by Segev *et al.* with 1.2 % having OSSN. However, they found both CIN and OSSN in their retrospective study. Similarly, Segev *et al.* studied 682 cases and showed 0 % cases of OSSN [18]. On the other hand, Barros *et al.* found a 40.6% association of OSSN in pterygium, followed by Clear *et al.* who reported 30% cases [19]. These studies revealed that no supporting data currently exist to support the human papillomavirus (HPV) and human immunodeficiency virus (HIV) as etiological agents causing pterygium-associated OSSN(Table 1).

**Table 1:** An Association of Pterygium with Premalignant Ocular Surface Neoplasia After Histopathology

| Sr. No. | References | Design | Country | Gender M/F | Mean Age (y) | Tissue Studied | Cases (n) | Pathology | Cases (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | [8] | Retrospective | South Africa | NA | NA | Pterygium | 100 | SCC, CIN | 19 |
| 2 | [9] | Retrospective | Malawi | NA | NA | Pterygium and Pinguecula | 224 | OSSN | 30 |
| 3 | [10] | Retrospective | USA | NA | NA | Pterygium | 92 | CIN | 4.35 |
| 4 | [11] | Retrospective | Australia | 293/240 | 50 | Pterygium | 533 | OSSN | 9.8 |
| 5 | [12] | Retrospective | Australia | 62/35 | 50 ± 15 | Pterygium | 100 | OSSN | 5.0 |
| 6 | [13] | Survey | Canada | 482/411 | 52 | Pterygium | 1127 | OSSN | 0 |
| 7 | [14] | Retrospective | USA | 282/108 | 61 | Pterygium | 396 | OSSN | 4.1 |
| 8 | [15] | Retrospective | USA | 22646/1533 | 66 ± 15 | Pterygium | 590 | OSSN | 1.3 |
| 9 | [16] | Retrospective | USA | 1054/951 | 60 | Pterygium | 2005 | OSSN | 1.7 |
| 10 | [17] | Prospective | Thailand | 144/338 | 56.5 ± 17 | Pterygium | 498 | OSSN | 1.8 |
| 11 | [18] | Retrospective | Israel | 402/280 | 56 | Pterygium | 682 | OSSN | 0 |
| 12 | [19] | Prospective | Brazil | 17/15 | 49.21 | Pterygium | 32 | OSSN | 40.6 |
| 13 | [20] | Retrospective | Canada | 116/99 | 53.4 ± 15.5 | Pterygium | 215 | OSSN | 2.33 |
| 14 | [21] | Retrospective | Greece | 96/62 | 67.2 ± 12.1 | Pterygium | 158 | CIN | 2.53 |
| 15 | [22] | Retrospective | Australia | 3/1 | 62 | Pterygium | 4 | SCC | NA |
| 16 | [23] | Retrospective | Taiwan | 928/859 | 65.2 ± 14.2 | Pterygium | 1787 | CIN | 0.22 |
| 17 | [24] | Retrospective | Brazil | 117/60 | 52 | Pterygium | 177 | CIN, SCC | 11.29 |
| 18 | [25] | Retrospective | Columbia | 313/148 | 31.8 ± 12.1 | Pterygium | 461 | Dysplasia, CIS | 14.96 |

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|---|---|---|---|---|---|---|---|---|---|
| 19 | [26] | Retrospective | Canada | 141/94 | 56 | Pterygium | 149 | SCC | 20.81 |
| 20 | [27] | Retrospective | Turkey | 36/39 | 55 | Pterygium | 75 | Dysplasia | 65 |
| 21 | [28] | Retrospective | USA | 174/174 | 58 ± 12 | Pterygium | 348 | OSSN | 0.29 |
| 22 | [29] | Retrospective | USA | 300/204 | 54.0 ± 11.1 | Pterygium | 504 | OSSN | 3.57 |
| 23 | [30] | Prospective | New Zealand | 113/97 | 58 ± 16.2 | Pterygium | 174 | OSSN | 2.3 |
| 24 | [31] | Retrospective | UK | 9/3 | 60.25 | Pterygium | 2061 | CIN, SCC | 0.6 |

n: number; NA: not available; M: male; F: female; y: years; SCC: Squamous cell carcinoma; CIN: conjunctival intraepithelial neoplasia; PAM: Primary acquired melanosis

## DISCUSSION

This systematic review aimed to investigate the correlation between pterygium and ocular surface squamous neoplasia (OSSN). There are inconsistent reports on the association between pterygium and SSN. Moreover, there is a scarcity of systematic review research findings on the association and its determinants. Therefore, the findings from this systematic review will help eye care professionals design appropriate strategies to reduce the prevalence rates of both of these diseases in varied populations of the world. In the present study, a wide range of differences was reported among the samples sent for histopathology after pterygium excision among the world population, from 0 % by Segev *et al.* to 40.6% by Barros *et al.* [18, 19]. Most of these studies were retrospective, based on the post-operative hospital data. Moreover, the difference might be due to the various age and gender groups that had been studied by the researchers. However, Zoroquiain *et al.* reported that 54% of male were 53.4 ± 15.5 years at diagnosis of the disease. The OSSN was identified in 5 cases (2.33 %), and four of them were female patients. The mean age of patients with both these diseases is reported to be the same [20]. A study conducted by Hirst *et al.* in Queensland, Australia, on the other hand, reported male to female ratio of patients as 1.82: 1.00, and the mean age was 50 years (range 18-85 years) [11]. Moreover, Barros *et al.* reported a median age of 44 years in Brazilian patients (range between 28 and 81 years) [19]. The different socio-economic conditions of the varied geographical locations of the world might explain these variations regarding the gender and age groups of the patients. Nearly all the studies showed a strong correlation between pterygium and OSSN in areas of maximum exposure to the sun and ultraviolet radiation. Zoroquiain *et al.* elaborated a higher number of OSSN in cases of pterygium than expected (2.33%) in Montreal, which has low ultraviolet radiation exposure; these rates were close to rates reported in Sydney and even higher than in Florida [20]. It was reported that snowfall persists late into the spring in Montreal. The ultraviolet rays reflected off might have played a role in the tissue damage. Moreover, Montreal had a multi-ethnic, multi-cultural society, and subjects might have shifted from the region having high ultraviolet exposure [20]. Detorakis *et al.* analyzed the hospital records of the patients between 2000 and 2014. A total of 1787 pterygium cases underwent surgical excision [21]. The mean age of the patients was 65.19 ± 14.21 years. The majority (80.3%) had primary pterygium, while the remaining (20.3%) were diagnosed as recurrent cases. Only 0.2% of cases were provisionally diagnosed as neoplasia on histopathological examination. The authors inferred that the association with OSSN was a remote possibility. However, it was concluded that a detailed history, clinical evaluation, followed by histopathology examination of the surgically excised specimens must be carried out [21]. Besides, a retrospective chart review of patients who had undergone pterygium surgery in Mendoza *et al.* was conducted at the University of Montreal. Between 2010 and 2022, 1559 patients underwent surgery for pterygium, and 854 patients (55) were males. Histopathology examination of 1142 specimens was done, and the majority were pterygium (1105 out of 1142; 97%). It had a surprise discovery of 3 cases of OSSN [22]. Moreover, Hung *et al.* and Lomelí-Linares *et al.* reported CIN and SCC instead of OSSN in the pterygium tissues on histological examination [23, 24]. Similarly, Mejia *et al.* also documented Dysplasia and CIS in the retrospective studies [25]. However, the frequency of OSSN in pterygium is rare in the Canadian population, but it can be clinically difficult to distinguish. It is important to send all pterygium specimens for pathology [26]. Although Suren *et al.* studied the retrieved pterygium tissues and found dysplasia in all cases [27]. Modabber *et al.* reported a retrospective study that out of 348 cases of pterygium. All cases had surgical excision followed by histopathology. Nearly 16% had recurrence, and one case of OSSN was reported in the excised pterygia. Hence, it showed a poor association of pterygium and OSSN in the middle-aged population [28]. This review showed the diversity of the population of nearly all continents of the world, Asia, Europe, Australia, North America, South America, Africa, and Canada. In addition, Zhu *et al.* reported a prevalence of 3.5% cases of OSSN in pterygium tissues of middle-aged USA subjects [29]. In contrary, Hossain *et al.* reported in the retrospective studies a very low frequency of 2.3% cases of OSSN, respectively [30]. In addition, a retrospective study was carried out on pterygia samples received for histopathology, suspected of being pterygium,

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between 1997 and 2021. The overall prevalence of neoplasia was 0.6%. It was concluded that the rates of unexpected results of finding a malignancy were meager [31]. Pterygium and OSSN have been recognized as closely similar conditions as they share a similar location and symptoms. In addition, had common risk factors such as ultraviolet radiation and a hot, dusty, and windy environment [32]. Vempuluru *et al.* studied the clinical features, anterior segment optical coherence tomography patterns, medical and surgical treatment, and histological diagnosis of ocular surface squamous neoplasia (OSSN) in the specimens [33]. In a meta-analysis, the authors investigated the prevalence rate and various risk factors for the identification of pterygium from OSSN. It was important to adopt the management strategies for these varied conditions [34]. In another study, the authors investigated the pterygia samples using a novel autofluorescence technique. They documented that in hot and temperate climate countries like Australia, where due to maximum exposure to u v radiations from the sun, can lead to the development of malignant conditions in the pterygia [35].

The limitation of this study is that only twenty-four articles were selected for review concerning our selection criteria. Moreover, most of the studies were retrospective and thus considered only biopsied tissues. The relatively varied number of cases of OSSN in pterygium samples in these studies compared to other high-risk areas and the possibility that all tissues were not sent for histopathology evaluation. This is a fact that the real incidence of OSSN in pterygium in this part of the world has never been studied due to improper healthcare facilities and the poor socioeconomic status of the population. For countries with high ultraviolet radiation exposure and located in the Pterygium Belt, it is strongly suggested that all pterygium tissues excised, regardless of age and gender, should be sent for detailed histopathological examination. Such studies will help in establishing the relationship of pterygium patients with OSSN.

## CONCLUSIONS

This systematic review depicted that pterygium is not only an elastotic degeneration of the conjunctival tissue, but it represents a pre-malignant ocular surface condition, which is closely associated with high UV exposure, with a measurable risk of occult OSSN across the varied population of the world. The reported wide variations in neoplastic transformation reflected differences in the intensity of ultraviolet exposure, population risk factors, histopathological grading systems, and methodology adopted for the study, but not a true biological inconsistency. It was demonstrated that routinely submitting the excised pterygia tissues for histopathological examination significantly improves early detection of subclinical OSSN, particularly from high-risk regions within the Pterygium Belts. These findings support reclassifying pterygium as a premalignant condition and justify mandatory histopathologic evaluation of excised tissues in high-UV settings.

## Authors' Contribution

Conceptualization: MSZK
Methodology: MSZK, AS
Formal analysis: MSZK, AMM, CAN, AZKC, AS
Writing and Drafting: MSZK, GA
Review and Editing: MSZK, AMM, CAN, AZKC, AS, GA

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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