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Twincretins and the Gut Microbiome: The Missing Link



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The novel treatment for type-II diabetes mellitus (T2DM), obesity, and associated metabolic dysfunctions is based on the insulinotropic actions of the two gut incretin hormones, glucagon-like peptide-1 (GLP-1) and the gastric inhibitory polypeptide (GIP), together known as twincretins. GLP-1 is primarily secreted by the small intestine and colon. While GIP is secreted from the duodenum and proximal jejunum. Both are secreted in response to a meal [1].

The human microbiome is composed of healthy bacteria, viruses, and microbes that boost metabolism and immunity and protect against pathogenic organisms. These also break down dietary fibers into metabolites that directly stimulate the endogenous release of incretins, which further regulate appetite and blood sugar [2].

Few studies demonstrate that twincretins promote a healthier microbial ecosystem. This results in an abundance of healthy gut bacteria like *Bifidobacterium*, *Akkermansia muciniphila*, and *Bacteroides*. This regulates appetite and blood sugar [3]. However, it is unclear how the gut microbiome may regulate insulin resistance, glucose control, and metabolic health. This is such an interesting and very beneficial link in many ways. Twincretins strengthen the gut lining, decreasing its permeability, which results in less penetration of harmful bacterial endotoxins into the body and hence lowers inflammation [4]. Twincretins also enhance gut microbiota and affect the adipokine pathway, altering fat metabolism [5]. Twincretins also alter bile acid metabolism, which helps reduce liver lipid deposition, thus helpful in managing Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) [6].

This bidirectional relationship between the gut microbiome and twincretins is far more beneficial in patients with obesity, diabetes, and metabolic dysfunctions. While twincretins suppress inflammation and alter bacterial diversity, gut microbes are responsible for drug metabolism and the release of endocrine hormones [1-3].

Recent limited studies correlate poor metabolism with a decrease in bacteria. The most missing healthy bacteria include *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, *Bacteroides*, and *Bifidobacterium* [1-5].

The dynamic triangular relationship among twincretins, microbial composition, and metabolism is the basis for future therapies on obesity, associated metabolic dysfunction, and diabetes. In the future, routine microbiome profiling could predict a patient's response to incretin drugs, allowing clinicians to tailor treatments using targeted prebiotics or probiotics. Your baseline microbial composition dictates how effectively your body responds to twincretins. The people with healthy bacteria will have improved insulin sensitivity as well as GLP-1 secretion. Individuals with fewer healthy bacteria may show "GLP-1 resistance". This severely affects weight-loss and glucose-lowering potential [1, 2].

The future of weight loss therapies lies in the emerging field of pharmacomicrobiomics. A personalized treatment approach will work for every patient rather than one approach for all patients, like microbiome profile, which should be checked in every patient to predict the exact response to twincretins. Secondly, twincretins should be combined with precise prebiotics or probiotics to potentiate the gut's healthy microbiome in advance. This will surely increase twincretin's effect and hence personalized metabolic dysfunction, diabetes, and weight management [1-5].

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Original Article



Comparison of Prolene Sutures Versus Skin Staples for Mesh Fixation in Lichtenstein Inguinal Hernioplasty: A Randomized Controlled Trial

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ABSTRACT

Chronic postoperative groin pain following Lichtenstein inguinal hernia repair is commonly attributed to nerve irritation during mesh fixation. Alternative fixation methods, such as skin staples, have been proposed to reduce postoperative pain. **Objectives:** To compare postoperative pain outcomes following mesh fixation with Prolene sutures versus skin staples in Lichtenstein inguinal hernioplasty. **Methods:** This randomized controlled trial was conducted at Mayo Hospital, Lahore. 132 adult male patients undergoing elective unilateral Lichtenstein inguinal hernioplasty were randomized to mesh fixation using either Prolene sutures or stainless-steel skin staples. Postoperative pain was assessed using the Visual Analogue Scale (VAS) on postoperative days 1, 14, 30, and 90. Statistical analysis included the Mann-Whitney U test, chi-square test, and logistic regression. **Results:** Baseline characteristics were comparable between groups. Median VAS on day 1 was higher in the Prolene group compared to the staple group, but pain scores declined significantly in both groups over time. By day 90, 37.9% of patients were pain-free, with no significant difference in pain-free rates between fixation methods ($p=0.858$). No independent predictors of persistent pain were identified. **Conclusions:** Mesh fixation with Prolene sutures and skin staples results in comparable postoperative pain outcomes. Fixation choice may therefore be guided by surgeon preference and operative considerations.

INTRODUCTION

Inguinal hernia repair is among the most frequently performed procedures in general surgery, with the Lichtenstein tension-free mesh technique widely regarded as the standard open approach due to its simplicity, reproducibility, and low recurrence rates [1]. Despite these advantages, chronic postoperative groin pain (inguinodynia) remains a significant complication. It continues to be a major cause of patient dissatisfaction and impaired quality of life following inguinal hernia repair

[2]. The aetiology of chronic post-herniorrhaphy pain is multifactorial, with nerve irritation, nerve entrapment, and excessive fibrosis during mesh fixation being the most commonly implicated mechanisms [3]. Traditionally, polypropylene mesh is secured using non-absorbable Prolene sutures. While effective, suture fixation has been associated with increased tissue handling and the potential for nerve involvement, which may contribute to early postoperative pain and the development of chronic



symptoms [4]. To address these concerns, alternative mesh fixation techniques have been explored, including absorbable sutures, tissue adhesives, self-gripping meshes, and skin staples. Skin staples offer potential advantages, including reduced operative time, standardized depth of fixation, and decreased tissue trauma. Several studies have reported lower early postoperative pain with staple fixation compared to suture fixation in open Lichtenstein repair; however, findings regarding long-term pain outcomes remain inconsistent [5,6].

Most existing evidence comparing fixation techniques originates from small trials or heterogeneous study populations, and regional data from low- and middle-income settings remain limited. Furthermore, while early postoperative pain has been evaluated in many studies, fewer have assessed pain trajectories over an extended follow-up period using standardized pain scales. The present randomized controlled trial was therefore conducted to compare postoperative pain outcomes following mesh fixation with Prolene sutures versus skin staples in Lichtenstein inguinal hernioplasty. In addition, this study aimed to evaluate the pattern and trajectory of postoperative pain reduction over a 90-day follow-up period to determine whether the choice of fixation technique influences both early and longer-term pain outcomes.

METHODS

This randomized controlled trial was conducted at the East Surgical Ward, Mayo Hospital, Lahore, over six months, following institutional ethical approval (IRB No. 511/RC/KEMU; dated 28th June 2025) and clinical trial registry number: NCT07210424. The study was conducted from July 2025 to December 2025. Although both sexes were eligible, only male patients presented to us with the condition during the study period. After obtaining informed consent, 132 adult male patients aged 18–65 years undergoing elective unilateral Lichtenstein inguinal hernia repair were included and randomly assigned to two groups. Patients were excluded if they had chronic obstructive pulmonary disease, were immunocompromised (including HIV, hepatitis B or C positivity, or diabetes mellitus), had obstructive uropathy, or suffered from chronic constipation. The study was conducted and reported in accordance with CONSORT guidelines. A CONSORT flow diagram illustrating participant enrolment, allocation, follow-up, and analysis is presented (Figure 1).

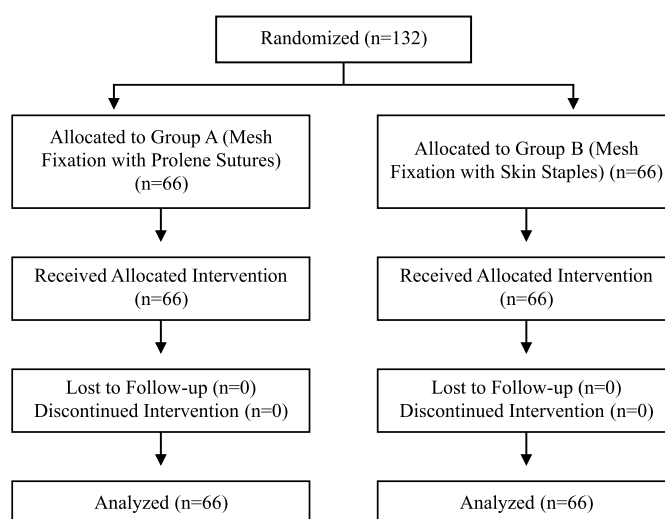


Figure 1: CONSORT Flow for Participant Enrolment, Allocation, Follow-Up, and Analysis

Patients were randomized using a lottery method into Group A: Mesh fixation with Prolene sutures and Group B: Mesh fixation with stainless-steel skin staples. Postoperative pain was assessed using a 10-point Visual Analogue Scale (VAS) on postoperative days 1, 14, 30, and 90 by a blinded assessor. A VAS score >3 was considered clinically significant pain. Data distribution for continuous variables (VAS pain scores at each postoperative time point, age, and BMI) was assessed using histograms, Q-Q plots, and the Shapiro-Wilk test. Because VAS scores demonstrated significant deviation from normality ($p < 0.050$), nonparametric statistical methods were used for continuous data analysis. Continuous variables are presented as median and interquartile range (IQR). Between-group comparisons of pain scores at each follow-up time point (postoperative days 1, 14, 30, and 90) were performed using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test or Fisher's exact test where appropriate. For long-term outcomes, pain at day 90 was analyzed both as a dichotomous variable (pain-free vs pain present; VAS = 0 vs >0) and as clinically significant pain (VAS >3). Associations between baseline variables and persistent pain at day 90 were explored using univariate and multivariable logistic regression models. Variables entered into the multivariable model included age, body mass index (BMI), treatment group, and baseline postoperative VAS score. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Longitudinal trends in pain reduction within each group were evaluated descriptively across follow-up intervals using serial non-parametric comparisons. A p -value ≤ 0.050 was considered statistically significant. Statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY).

RESULTS

A total of 132 male patients were included in the dataset. Participants were evenly distributed between Group A (Prolene Fixation) and Group B (Staples) (66 in each group). All individuals were male, so gender differences could not be evaluated. The pain outcomes were assessed using the Visual Analogue Scale (VAS). The study summarizes baseline demographic and clinical characteristics of both groups. The median age was 48 years in both groups, and BMI distributions were comparable. The median body mass index (BMI) of participants was 22.9 kg m^{-2} (IQR 3.3), with slightly higher values in Group B (median 23.15 kg m^{-2} , IQR 3.05) than in Group A (median 22.6 kg m^{-2} , IQR 3.48). Baseline pain level (VAS Day 1) was higher in Group A (median 3.55, IQR 2.40) compared with Group B (median 2.80, IQR 1.95), indicating that individuals in Group A reported more severe pain at the start of the study (Table 1).

Table 1: Baseline Characteristics of Study Population (Median [IQR])

Variable	Group A, (n = 66)	Group B, (n = 66)
Age (years)	48 (21.75)	48 (23.00)
BMI (kg m^{-2})	22.6 (3.48)	23.15 (3.05)
VAS day 1	3.55 (2.40)	2.80 (1.95)
VAS day 14	1.70 (1.08)	1.20 (0.98)
VAS day 30	0.40 (0.50)	0.40 (0.80)
VAS day 90	0.20 (0.40)	0.20 (0.50)

Median VAS scores declined in both groups. In Group A and Group B, respectively, median VAS scores were 3.55 and 2.80 on day 1, 1.70 and 1.20 on day 14, 0.40 and 0.40 on day 30, and 0.20 and 0.20 on day 90. By days 30 and 90, the median scores were similar between groups (Figure 2).

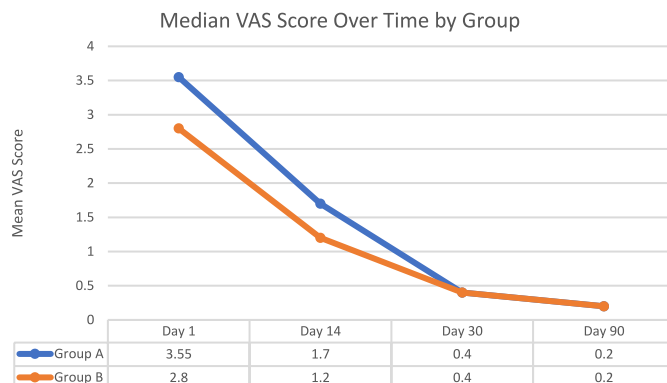


Figure 2: Median Visual Analogue Scale (VAS) Scores at Each Follow-Up for Group A and Group B

To explore long-term pain outcomes, VAS Day 90 scores were dichotomized into "no pain" (VAS = 0) and "pain present" (VAS > 0). At day 90, 50 patients (37.9%) were pain-free. Longitudinal trends were described using serial median comparisons. Pain-free rates did not differ significantly between groups ($p=0.858$). The median age

and BMI were similar between pain-free and pain-present patients. Baseline pain tended to be slightly lower among patients who were pain-free by day 90, but the difference did not reach statistical significance ($p=0.156$). Overall, there was no evidence that demographic factors, BMI, or baseline pain predicted pain-free status at three months. At day 90, clinically significant pain (VAS > 3) was uncommon and did not differ significantly between the Prolene and staple groups ($p>0.050$) (Table 2).

Table 2: Pain-Free Status at Day 90 by Baseline Variables

Variable (Categories)	Pain-Free	Pain Present	p-value
Group, n(%)	A: 26 (39.4%), B: 24 (36.4%)	A: 40 (60.6%), B: 42 (63.6%)	0.858
Age (Median [IQR])	45.0 (21.0)	49.0 (22.0)	0.184
BMI (Median [IQR])	23.0 (3.1)	22.8 (3.3)	0.341
VAS Day 1 (Median [IQR])	3.0 (2.2)	3.4 (2.1)	0.156

Mann-Whitney U test used for continuous variables. Chi-square test used for categorical variables

To identify factors associated with persistent pain at day 90, both univariate and multivariable logistic regression models were fitted with pain present as the dependent variable. Predictor variables included age, BMI, treatment group, and baseline VAS score. The univariate analysis showed that none of the variables was significantly associated with persistent pain. For example, the odds ratio (OR) for group (reference = Group A) was 1.14 (95 % CI 0.56 – 2.30; $p=0.720$), indicating that assignment to Group B did not significantly alter the odds of pain at day 90. In the multivariable model, which adjusted for all predictors simultaneously, the associations remained nonsignificant. The pseudo- R^2 of the multivariable model was 0.006, and the likelihood ratio test was not significant ($p=0.903$), suggesting that the model explained little of the variation in pain outcomes (Table 3).

Table 3: Logistic Regression Predicting Pain at Day 90

Predictor	OR (95 % CI)	p-value
Univariate Models		
Age (Per 1-Yr Increase)	1.01 (0.99 – 1.04)	0.390
BMI (per 1- kg m^{-2} Increase)	1.02 (0.88 – 1.17)	0.820
Group (B vs A)	1.14 (0.56 – 2.30)	0.720
Baseline VAS (Per 1-Unit Increase)	0.96 (0.79 – 1.18)	0.710
Multivariable Model†		
Age	1.01 (0.99 – 1.04)	0.370
BMI	1.01 (0.88 – 1.17)	0.860
Group (B vs A)	1.07 (0.51 – 2.24)	0.870
Baseline VAS	0.96 (0.77 – 1.18)	0.680

†The multivariable model simultaneously adjusted for age, BMI, group, and baseline VAS score

DISCUSSION

This randomized controlled trial compared postoperative pain outcomes following mesh fixation with Prolene sutures versus skin staples in open Lichtenstein inguinal hernia repair. The principal finding of our study is that although staple fixation was associated with lower pain scores in the immediate postoperative period, this early difference did not persist beyond the first few weeks. By 30 days and continuing through 90 days of follow-up, pain scores and pain-free rates were comparable between the two fixation techniques. These findings suggest that the choice of mesh fixation method does not significantly influence long-term postoperative pain outcomes. In the early postoperative period, patients in the Prolene suture group reported higher pain scores compared to those in the staple group. Wani *et al.* reported that staple fixation significantly reduced operative time while maintaining postoperative outcomes similar to those with polypropylene sutures [5]. Ali *et al.* observed a slightly lower incidence of postoperative pain in the stapler group, although the difference was not statistically significant [6]. In addition, the systematic review by Alabi *et al.* found no consistent superiority of one fixation technique over another regarding chronic pain outcomes [7]. These findings are broadly consistent with our observation of lower early pain with staple fixation. Suture fixation requires multiple needles passes through the inguinal tissues, which may increase tissue trauma and transient nerve irritation. In contrast, skin staples allow rapid fixation with less tissue handling, which may explain the lower early pain scores observed in our staple group. Alabi *et al.* in a systematic review of fixation techniques, reported no consistent superiority of mechanical fixation methods for chronic pain outcomes, although some techniques may influence postoperative pain profiles [7]. Khulique *et al.* reported lower surgical site infection rates with staple fixation while observing comparable rates of other postoperative complications [8]. Additionally, Hassan *et al.* demonstrated that variations in suture techniques can significantly influence postoperative pain following Lichtenstein repair [9]. The clinical importance of early postoperative pain has also been highlighted by Sultana *et al.* who showed that reductions in early pain significantly improve patient satisfaction during recovery [10]. Despite this early difference, pain trajectories in both groups showed a steady and parallel decline over time. By one month postoperatively, pain levels were low and no longer significantly different between the two groups. This convergence suggests that early postoperative pain related to fixation technique is largely transient and diminishes as tissue healing progresses. By the 90-day follow-up, approximately one-third of patients in both

groups were completely pain-free, and the proportion of patients reporting any residual pain did not differ significantly between fixation methods. The relatively high proportion of patients reporting some degree of pain at 90 days should be interpreted with caution. In our study, pain was dichotomized into “no pain” versus “any pain,” which may capture even mild or intermittent symptoms. Cirocchi *et al.* reported that the incidence of chronic postoperative inguinal pain varies widely across studies, reflecting differences in definitions, surgical techniques, and follow-up periods [11]. Similarly, Calderon *et al.* observed that chronic pain rates at three months after hernia repair are generally low and often associated with improved quality of life [12]. Earlier work by Poobalan *et al.* also showed that although many patients report some postoperative discomfort, clinically significant pain affecting daily activities occurs in a much smaller subset [13]. These observations suggest that the residual pain seen in our cohort likely represents mild symptoms during the late healing phase rather than disabling chronic pain. Importantly, our multivariable analysis identified no independent predictors of persistent pain at 90 days, including fixation method, age, body mass index, or baseline pain intensity. Aziz *et al.* reported differences in early postoperative pain between fixation techniques in laparoscopic TAPP repair, although other early complications were comparable between groups [14]. In contrast, Zhou *et al.* found that patient-related factors such as younger age, obesity, and smoking were associated with higher perioperative pain levels [15]. Similarly, Van Den Dop *et al.* identified several patient and surgical factors, including surgical technique and nerve handling, as contributors to chronic postoperative inguinal pain [16]. These variations across studies may reflect differences in study design, follow-up duration, and patient populations. From a clinical perspective, our results suggest that both Prolene sutures and skin staples are acceptable options for mesh fixation in open Lichtenstein hernioplasty. Matikainen *et al.* reported that different fixation techniques, including sutures and less-penetrating methods, showed no significant differences in long-term pain or recurrence rates after Lichtenstein repair [17]. Similarly, Matikainen *et al.* found that fixation type did not independently predict chronic postoperative groin pain [18]. In contrast, Sharma *et al.* demonstrated that modified fixation techniques may reduce operative time and postoperative discomfort [19]. Expert consensus recommendations have also highlighted the potential advantages of alternative fixation approaches while emphasizing the need for further evidence [20]. These findings support our observation that fixation choice can be guided by surgeon preference and operative considerations without compromising long-term patient

comfort.

This study has several limitations. First, the follow-up period was limited to 90 days, which captures the transition from acute to early chronic postoperative pain but does not allow assessment of longer-term pain persistence. Second, although both sexes were eligible, only male patients were enrolled during the study period, limiting generalizability to female patients. Third, formal longitudinal modelling and group-by-time interaction testing were not performed; pain trajectory comparisons were therefore based on serial assessments at predefined time points using non-parametric methods. Additionally, operative time, recurrence rates, nerve handling, and postoperative analgesic use were not analyzed, which may partly explain the regression model's limited explanatory power. Despite these limitations, the randomized design, standardized surgical technique, blinded pain assessment, and structured follow-up strengthen the study's internal validity. Within these constraints, our findings suggest that the mesh fixation technique, whether Prolene sutures or skin staples, does not significantly influence long-term postoperative pain following Lichtenstein inguinal hernia repair.

CONCLUSIONS

This study demonstrates that both Prolene sutures and skin staples are effective options for mesh fixation in Lichtenstein inguinal hernia repair, with comparable long-term pain outcomes. While staple fixation showed lower pain scores in the immediate postoperative period, this difference resolved by one month. By day 90, pain-free rates were comparable between groups, and no clinical predictors of chronic pain were identified. These findings suggest that the choice of fixation technique can be guided by surgeon preference and operative considerations without compromising long-term patient comfort.

Authors' Contribution

Conceptualization: AA

Methodology: AA, SM, AS

Formal analysis: SM, AS

Writing and Drafting: MHJ, FE, MZS

Review and Editing: AA, MHJ, SM, AS, FE, MZS, MYN

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



Patient Reported Symptoms and Quality of Life during Radiotherapy: Cross-Sectional Analytical Study in a Tertiary Care Setting

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ABSTRACT

Radiotherapy is integral to cancer care, yet its impact on patient-reported symptoms and health-related quality of life (HRQoL) remains understudied. **Objectives:** To assess the severity of patient-reported symptoms and HRQoL during active radiotherapy and examine associations between specific symptoms and QoL domains among adult cancer patients. **Methods:** This cross-sectional analytical study was conducted from July 2024 to June 2025 at Bahawal Victoria Hospital, Bahawalpur. A total of 85 adult patients undergoing external beam radiotherapy (without concurrent chemotherapy) completed validated PRO instruments, the EORTC QLQ-C30 and site-specific modules (e.g., QLQ-H&N35, QLQ-CR29), and the PRO-CTCAE at mid-treatment. Data were analyzed using SPSS Version 23.0; Spearman correlation and multiple linear regression identified symptom QoL relationships. **Results:** Mean global QoL score was 58.4 ± 18.3 . Fatigue (64.7 ± 24.1), pain (57.3 ± 26.8), and insomnia (52.9 ± 28.4) were the most severe symptoms. PRO-CTCAE revealed 71.8% reported moderate to severe fatigue. Fatigue ($r = -0.52$), pain ($r = -0.48$), and appetite loss ($r = -0.41$) strongly correlated with lower QoL (all $p < 0.001$). Regression confirmed fatigue ($\beta = -0.31$), pain ($\beta = -0.24$), and palliative intent ($\beta = -0.9$) as independent predictors of reduced global QoL (adjusted $R^2 = 0.486$). **Conclusions:** Fatigue, pain, and treatment intent significantly impair QoL during radiotherapy. Routine PRO integration and context-adapted supportive care are urgently needed to preserve patient well-being in resource-limited oncology services.

INTRODUCTION

Cancer is the leading cause of morbidity and mortality globally, with an estimated 20 million new cases in 2022 and a projected 77% increase in global cancer incidence by 2050, particularly higher in developing nations [1]. Radiotherapy (RT) is a cornerstone of cancer treatment, with approximately 50% of all cancer patients needing RT at some point during their care trajectory [2]. Despite its curative and palliative efficacy, RT is often associated with acute and late toxicities that can significantly impair patients' daily functioning and well-being [3]. In parallel with advances in radiation delivery techniques, there has

been a paradigm shift toward patient-centered care, emphasizing health-related quality of life (HRQoL) and symptom burden as critical treatment outcomes [4]. Patient-reported outcomes (PROs) are now recognized as essential metrics for evaluating treatment tolerability, guiding supportive care interventions, and informing shared decision making [5]. Regulatory bodies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), increasingly endorse the integration of PROs into clinical trials and routine oncology practice [6]. However, significant knowledge



gaps persist, especially in LMICs, where the majority of the cancer patients reside, but access to comprehensive supportive care and routine PRO collection remains limited [7]. Existing literature on RT related symptoms and HRQoL originates from high-income countries and often focuses on specific tumor sites (e.g., prostate, head and neck) or combines RT with systemic therapies, making it difficult to isolate the unique effects of radiotherapy alone [8]. Locally relevant evidence can help in the development of pragmatic, scalable interventions that prioritize patient experience without compromising oncologic outcomes [9-11]. The objective of the study was to assess the severity of patient-reported symptoms and health-related quality of life (HRQoL) among adult patients undergoing active radiotherapy and to examine the associations between specific symptom burdens and key HRQoL domains.

The cross-sectional data capturing real-time symptom experiences during active RT, particularly using standardized, validated PRO instruments like the EORTC QLQ-C30 or PRO-CTCAE, remain limited in diverse, resource-constrained settings. This gap is critical because symptom profiles and QoL impacts may differ substantially based on sociocultural factors, nutritional status, comorbidities, and healthcare infrastructure. Without context-specific evidence, supportive care strategies developed in high-resource environments may not be feasible or effective in LMIC, where patient volumes are high and multidisciplinary teams are often understaffed. Therefore, this study aimed to identify the spectrum and severity of patient-reported symptoms and their association with HRQoL among adults undergoing radiotherapy.

METHODS

This cross-sectional analytical study was conducted at the Department of Oncology, Bahawal Victoria Hospital, Bahawalpur, from July 2024 to June 2025. The study protocol was reviewed and approved by the Institutional Ethics Review Committee of Quaid-e-Azam Medical College (Ref: 2467/DME/QAMC Bahawalpur; dated 30th June 2024). All participants provided written informed consent. Confidentiality was maintained through anonymization, and participants were informed of their right to withdraw from the study at any time without affecting their clinical care. A sample size of 85 adult patients was calculated a priori using standard statistical formulas to provide adequate statistical power (80%) to detect a moderate correlation ($r=0.30$) between global health status (as measured by the EORTC QLQ-C30) and key symptom domains such as fatigue or pain. These parameters were based on effect sizes reported in similar radiotherapy populations [12, 13], assuming a significance level of $\alpha = 0.05$. Participants were selected using non-

probability consecutive sampling. Eligible patients were adults (≥ 18 years) receiving external beam radiotherapy either with curative or palliative intent who were capable of providing informed consent. Patients were excluded if they had cognitive or psychiatric impairments that would preclude reliable self-reporting, were receiving concurrent chemotherapy (to isolate the effects of radiotherapy alone), or were undergoing re-irradiation. Data were collected using a structured questionnaire comprising two sections. The first section was socio-demographic variables, including age, gender, cancer type, and stage (per AJCC/UICC 8th edition), treatment intent, radiation site, total prescribed dose and fractionation schedule. The second section incorporated validated patient-reported outcome (PRO) instruments: the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) to assess global HRQoL and functional/symptom domains; the relevant EORTC site-specific module (e.g., QLQ-H&N35 for head and neck cancers or QLQ-CR29 for colorectal cancers). Eligible patients were approached during their radiotherapy course, typically around the midpoint of treatment, to determine real-time symptom experiences. After obtaining written informed consent, participants completed the PRO instruments either independently or with minimal assistance from the researcher. Statistical analyses were performed using SPSS version 23.0. Descriptive statistics summarized participant characteristics and PRO scores with quantitative variables reported as means $\pm$ standard deviations or medians with interquartile ranges depending on distribution normality. EORTC QLQ-C30 and module scores were linearly transformed to a 0-100 scale according to the EORTC scoring manual. Higher scores represent better functioning (for functional/global scales) and worse symptoms (for symptom scales). Associations between symptom severity scores (from PRO-CTCAE and QLQ-C30/QLQ-modules) and HRQoL domains were evaluated using the Spearman rank correlation coefficient due to non-normal distributions of PRO data. Multiple linear regression models were constructed to identify independent predictors of global health status, adjusting for potential confounders such as age, gender, treatment intent, radiation dose, and tumor site. Before regression modeling, assumptions of normality (Shapiro-Wilk test), multicollinearity (Variance Inflation Factor < 5), and homoscedasticity were verified. Subgroup analyses were done to explore differences in symptom-QoL relationships by radiation field (e.g., head/neck vs. pelvis), treatment intent (curative vs. palliative), and key demographic factors. Statistical significance was defined as p -value < 0.050 .

RESULTS

A total of 85 adult patients receiving external beam radiotherapy completed the full set of patient-reported outcome (PRO) measures at midcourse radiotherapy (median treatment day: 15; interquartile range: 12–18). The majority of participants were male (n=52, 61.2%), with a mean age of 54.3 ± 12.7 years. The most common primary tumor sites were head and neck (38.8%), followed by pelvic malignancies (27.1%) and thoracic cancers (18.8%). Approximately two-thirds (68.2%) received radiotherapy with curative intent, while the remainder underwent palliative treatment (Table 1).

Table 1: Socio-demographic and Clinical Characteristics of Participants (n=85)

Characteristics	n (%) or Mean $\pm$ SD
Age (years)	54.3 $\pm$ 12.7
Gender	
Male	52 (61.2%)
Female	33 (38.8%)
Cancer Type	
Head and Neck	33 (38.8%)
Pelvic (Cervix, Prostate, Rectum)	23 (27.1%)
Thoracic (Lung, Esophagus)	16 (18.8%)
Breast	8 (9.4%)
Other	5 (5.9%)
Disease Stage (AJCC/UICC 8th)	
Stage I-II	28 (32.9%)
Stage III-IV	57 (67.1%)
Treatment Intent	
Curative	58 (68.2%)
Palliative	27 (31.8%)
Other	
Median Radiation Dose (Gy)	50.4 $\pm$ 10.2
Median Fractions	25 (IQR: 20–28)

Mean global health status score of 58.4 ± 18.3 (on a 0–100 scale, where higher scores indicate better QoL). The lowest scores were observed in physical functioning (mean = 62.1 ± 20.5) and role functioning (mean = 59.8 ± 22.6). The most prominent complaints on the QLQ-C30 were fatigue (mean 64.7 ± 24.1), pain (mean 57.3 ± 26.8), and sleep disturbance (mean 52.9 ± 28.4) (Table 2).

Table 2: EORTC QLQ-C30 Global Health Status and Functional/Symptom Domain Scores (n=85)

Domain	Mean Score $\pm$ SD
Global Health Status/QoL	58.4 $\pm$ 18.3
Functioning Scales	
Physical Functioning	62.1 $\pm$ 20.5
Role Functioning	59.8 $\pm$ 22.6
Emotional Functioning	67.3 $\pm$ 21.1
Cognitive Functioning	71.5 $\pm$ 19.8
Social Functioning	64.2 $\pm$ 23.0

Symptom Scales	
Fatigue	64.7 $\pm$ 24.1
Pain	57.3 $\pm$ 26.8
Nausea/Vomiting	32.4 $\pm$ 25.6
Dyspnea	38.1 $\pm$ 27.3
Insomnia	52.9 $\pm$ 28.4
Appetite Loss	49.6 $\pm$ 29.1
Constipation	36.2 $\pm$ 26.7
Diarrhea	41.3 $\pm$ 28.0
Financial Difficulties	50.8 $\pm$ 30.5

Scores range from 0–100; higher scores = better functioning (for functional/global scales) or worse symptoms (for symptom scales)

PRO-CTCAE outcomes indicated that nearly three-quarters of participants (71.8%) experienced fatigue at a moderate or severe level, and 63.5% reported pain that negatively affected their ability to perform everyday activities. Distinct symptom patterns emerged by disease site. Individuals with head and neck malignancies (n=33) commonly reported pronounced swallowing impairment (QLQ-H&N35 mean 68.2 ± 23.4) and problematic thick saliva (mean 70.1 ± 25.0). In contrast, patients with pelvic cancers (n=23) most frequently experienced gastrointestinal symptoms, particularly diarrhea, as reflected by elevated scores on the QLQ-CR29 diarrhea scale (mean 61.5 ± 27.2) (Table 3).

Table 3: Frequency and Severity of Key Symptoms Using PRO-CTCAE (n=85)

Symptoms	Any Severity, (%)	Moderate/Severe, (%)	Interference with Daily Life $\geq$ Moderate, (%)
Fatigue	89.4%	71.8%	68.2%
Pain	82.4%	63.5%	61.2%
Skin reaction	76.5%	45.9%	32.9%
Nausea	48.2%	22.4%	18.8%
Insomnia	74.1%	56.5%	50.6%
Appetite loss	65.9%	49.4%	44.7%

Correlation analyses using Spearman's method demonstrated that higher symptom severity was consistently associated with poorer overall quality of life. Fatigue ($r = -0.52$, $p < 0.001$), pain ($r = -0.48$, $p < 0.001$), and reduced appetite ($r = -0.41$, $p < 0.001$) showed inverse relationships with global health status. Additionally, nausea/vomiting and financial strain were significantly correlated with lower global QoL scores ($r = -0.34$ and $r = -0.36$, respectively; both $p < 0.001$) (Table 4).

Table 4: Spearman's Correlation Coefficients between Top 5 Symptoms and Global Health Status (n=85)

Symptom (PRO Source)	Correlation (r)	p-value
Fatigue (QLQ-C30)	-0.52	<0.001
Pain (QLQ-C30)	-0.48	<0.001
Appetite Loss (QLQ-C30)	-0.41	<0.001

Financial Difficulties (QLQ-C30)	-0.36	0.001
Nausea/Vomiting (QLQ-C30)	-0.34	0.002

In the multiple linear regression model (Table 5), fatigue ($\beta = -0.31$, $p=0.003$), pain ($\beta = -0.24$, $p=0.012$), and treatment intent (palliative vs. curative: $\beta = -8.9$, $p=0.021$) are independent predictors of lower global QoL (adjusted $R^2 = 0.486$, $p<0.001$). Age, gender, tumor site, and radiation dose were not statistically significant after adjustment. Subgroup analyses indicated that symptom QoL associations were stronger in the palliative group, where fatigue alone accounted for 39% of the variability in global QoL ($r = -0.62$, $p<0.001$). No significant differences were observed by gender.

Table 5: Multiple Linear Regression: Predictors of Global Health Status (EORTC QLQ-C30)

Predictors	Unstandardized β	SE	Standardized β	p-value
Fatigue	-0.24	0.08	-0.31	0.003
Pain	-0.20	0.08	-0.24	0.012
Treatment intent (Palliative)	-8.9	3.7	-0.22	0.021
Radiation Dose (Gy)	-0.05	0.04	-0.06	0.210
Tumor Site	1.2	2.1	0.05	0.564
Age	-0.08	0.09	-0.09	0.364
Sex (Male)	3.2	4.1	0.08	0.438
Model Summary				
- Adjusted R^2	—	—	0.486	<0.001

DISCUSSION

This cross-sectional study highlights a considerable symptom burden and reduced health-related quality of life among patients undergoing active radiotherapy in low-resource settings. Fatigue, pain, and insomnia were the most frequently reported symptoms, and overall QoL scores were markedly lower than population norms and reports from high-income countries [14, 15]. The mean global health score is consistent with findings from other developing countries but remains well below levels typically observed in Western populations. These differences likely reflect a combination of treatment-related toxicity, socio-economic challenges, limited supportive care, and delayed presentation, which are common in Pakistan within the oncology context [16]. The negative associations identified between fatigue, pain, and overall quality of life are consistent with findings from studies conducted in Pakistan; however, the magnitude of these relationships underscores their heightened clinical relevance in environments where symptom management resources are constrained [17]. Fatigue emerged as the predominant and most disabling symptom, a finding that was consistently demonstrated across both EORTC instruments and PRO-CTCAE assessments. Similar observations have been documented in multicenter investigations from India and Bangladesh, in which fatigue

was repeatedly reported as the most burdensome symptom during radiotherapy and was often associated with underlying anemia and compromised nutritional status [18]. Furthermore, the financial strain observed in this study reflects socioeconomic challenges faced by cancer patients, where healthcare expenditures are predominantly paid out of pocket, and financial support is limited [19]. This economic burden showed a strong relationship with reduced quality of life, highlighting the importance of integrating financial counseling and supportive care into oncology treatment [20]. Variation in symptom patterns according to disease sites support patient reported outcome. Individuals with head and neck cancers commonly experienced mucosal and salivary complications, in line with established radiobiological effects of treatment, whereas patients with pelvic tumors reported marked gastrointestinal disturbances. These patterns are consistent with findings of a study conducted in a public sector hospital of Pakistan [21]. An important finding was the heightened influence of symptom burden among patients receiving palliative radiotherapy, with fatigue independently accounting for variation in quality-of-life scores. This indicates that patients with palliative care are particularly susceptible to symptom-related deterioration and may benefit from early incorporation of supportive and palliative care services [22, 23]. Given the resource constraints in this region, prioritizing symptom management for palliative patients could yield significant QoL improvements. Strengths of the study include the use of internationally recognized patient-reported outcome measures, including the EORTC QLQ-C30, relevant site-specific and PRO-CTCAE, allowing for comprehensive assessment of symptom burden. Exclusion of patients receiving concurrent chemotherapy enabled clearer evaluation of radiotherapy-related effects, while mid-treatment, real-time data collection reduced recall bias. Several limitations should be considered. The cross-sectional design does not permit causal relationships. Although the sample size was sufficient to detect moderate correlations, it constrained more detailed subgroup analyses. In addition, a single institution setting may limit external validity. Based on these findings, recommendations are: incorporation of patient-reported outcome screening, particularly for fatigue and pain, into routine radiotherapy practice; and longitudinal studies to assess the effect of PRO-driven care on quality of life and treatment adherence among radiotherapy patients.

CONCLUSIONS

Adult patients undergoing active radiotherapy experience a substantial severity of patient-reported symptoms, particularly fatigue and pain, resulting in compromised health-related quality of life. Significant associations were

identified between specific symptom burdens and key HRQoL domains, with fatigue, pain, and palliative treatment intent confirmed as independent predictors of reduced global health status. Routine integration of patient-reported outcome measures and supportive care interventions is essential to address these impairments and improve patient well-being during radiotherapy.

Authors' Contribution

Conceptualization: AL, MH

Methodology: AL, MH

Formal analysis: AL, MH, WH

Writing and Drafting: AL, MH, WH

Review and Editing: AL, MH, WH

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

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Original Article



Comparative Analysis of Outcomes: Intra-Oral and Transbuccal Approach Using Trocar for Fixation of Mandibular Fractures

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ABSTRACT

Mandibular fractures are frequent maxillofacial injuries. Open reduction and internal fixation may be intraoral or transbuccal, with each having varying access, visualization, and aesthetic effects. **Objectives:** To compare intraoral and transbuccal methods of fixation of mandibular fractures. **Methods:** It was a prospective interventional study among 70 patients with unilateral displaced fracture of the mandible, who were divided into intraoral (n=35) and transbuccal (n=35) groups. All cases were subjected to standard intraoral access. The fixation was done intraorally & using a transbuccal trocar. They were assessed in relation to surgical time, ease of accessibility (VAS 13), post-operative occlusion, and radiographic fracture reduction (adequate 3 mm gap or below). The continuous variables were evaluated using the Mann-Whitney U test, and the chi-square test was applied to the categorical variables with a level of significance at $p < 0.050$. **Results:** Fracture reduction (82.9 vs. 80.0; $p = 0.759$) and post-operative occlusion (both 88.6; $p < 0.001$) did not reveal any significant difference. The transbuccal group had better access to surgery. The intraoral method was shorter in terms of the time of operations (median 45 vs. 70 minutes; $p < 0.001$). **Conclusions:** The transbuccal method enhances the accessibility of the surgery, and the intraoral method is faster. The choice of approach must take into account the position of fractures and the experience of the surgeon.

INTRODUCTION

The mandible is positioned prominently among the face bones and is, hence, a common target for both intended and inadvertent injuries. Almost two-thirds of all facial traumas are mandible fractures, accounting for nearly 70% for almost, with angle fractures contributing 26-35% for of all mandibular fractures [1]. Various strategies have been put forth depending on the type of fracture and financial circumstances. The best course of action for angle fractures remains up for debate. The decision on which strategy to use is typically based on variables like

accessibility, fracture parts displacement, and visualization. The operators' decision regarding the best course of action is based on several factors, including the patient's preferences, the simplicity of the treatment, the surgeon's skills, the instruments, and the accessibility to the area of the fracture. Two of the most popular methods for managing fractures are intraoral and transbuccal. The transbuccal trocar approach combines the biomechanical benefits of lateral fixation of plates with minimum visible scars by allowing percutaneous lateral accessibility for



screw installation while maintaining an intra-oral approach. Transbuccal approach frequently enhances plate/screw placement and aesthetic results, according to clinical trials and literature reviews; however, reports of variations in infection, malunion, as well as cumulative rate of complications as compared to purely intra-oral management vary. Every technique has its pros and cons of its own [2]. Management of angle fractures is difficult and uncertain due to their substantial complication incidence and biomechanical complexity [3]. The mandibular angle fractures are often treated with open reduction and internal fixation [4]. According to Champy et al., putting simply one plate to the optimal line for osteosynthesis is sufficient to endure the stresses that are commonly applied to the lower jaw bone [5]. To compensate for displacement pressures from the musculatures, particularly in unfavorable fracture patterns, some people prefer to utilize thicker plates along the lower end of the jaw [6]. The mandibular angle fractures could be surgically accessed using intraoral or transbuccal approaches [7]. In numerous situations, an intraoral technique including fixation with plates at the inferior borders necessitates the use of a transbuccal trocar via a tiny puncture on the skin for introduction of the cannula [8]. Infection, misalignment, or nonunion, which may vary from 0 to 32%, result from improper anatomical correction of the angle fracture in appropriate conditions [9]. Researchers discovered the transbuccal route as a substitute for the transoral technique due to its drawbacks. With this method, a transbuccal trocar is used to allow tools like the drill and screw driver to navigate via an incision that is made on the skin on the face, in addition to an intraoral puncture. Benefits include avoiding external wounds, fixing the plates against the mandible's thicker lateral cortex in the sagittal view increasing the amount of tissue protection, reducing the risk of plate damage because over bending weakens the plates, lowering the rate of infection because fewer bacteria from the third molar region move around, and directly visualizing and confirming the intended occlusion while fixation [10].

Although several studies have been conducted on the comparison of intraoral and transbuccal techniques, the available evidence is still incongruent as to their comparative efficacy concerning their relative accessibility to surgery, their operative duration, their ability to reduce fractures, and their ability to achieve post-operative occlusion. The majority of the studies available have small sample sizes, are not standardized in assessment criteria, or are not compared directly between the two techniques in a similar clinical setting. This brings a literature gap in the form of which is the best approach when offering clinical results, especially when dealing with mandibular angle fractures. Thus, this study had an

objective of comparing intraoral and transbuccal techniques of open reduction and internal fixation of fractures of the mandible angle. This study aimed to assess and compare surgical time, fracture reduction quality, post-operative occlusion, and accessibility of surgery in fixation. The current research offers recent comparative statistics to justify evidence-based choices of surgical methods to use in mandibular angle fractures.

METHODS

This prospective interventional study comparing two techniques was conducted at the Department of Oral and Maxillofacial Surgery, The University of Lahore, from January 2025 to June 2025. Ethical approval was obtained from the Institutional Review Board of The University of Lahore (Ref. number UCD/ERCA/24/1566; dated 10th December 2024). The primary outcome variable used to estimate the sample size was the operative time since it is an objective, continuous, and clinically significant variable of the two surgical methods. The sample size was estimated by the use of the already published comparative data, which showed that the mean difference in the operative time between intraoral and transbuccal methods is about 20 minutes with a pooled standard deviation of 25 minutes [11]. Based on the two-sided test to compare the means, with a significance level of 0.05 and a power of 80%, the sample size of 35 patients per group was obtained. A non-probability convenience sampling technique was used to recruit participants who met the inclusion criteria. The patients who met the eligibility criteria were recruited sequentially and placed into two groups (intraoral or transbuccal) until 35 patients per group were recruited according to the clinical judgment and discretion of the operating surgeon, because there were no preset criteria that allowed patients to be assigned a particular group. Inclusion criteria were patients with displaced unilateral mandibular angle fractures. Patients with bone disorders affecting healing, contraindications for general anesthesia, active infection at the fracture site, or other facial fractures were excluded. Written informed consent was obtained from all participants after explaining the procedure, risks, benefits, and alternatives. Participants were allocated into two equal groups (n = 35 each) based on the surgical approach planned by the attending surgeon: Group 1 (intraoral approach) and Group 2 (transbuccal approach). All patients underwent preoperative evaluation, including routine blood tests and anesthesia assessment. All surgeries were performed under general anesthesia with nasotracheal intubation, supplemented with 2% lignocaine with 1:100,000 adrenaline at the surgical site for hemostasis for both groups. After general anesthesia and sterile draping, a conventional intraoral vestibular incision was made to expose the fracture. In Group 1, fracture

reduction was performed intraorally and fixed with a 5-hole miniplate and screws. In Group 2, a transbuccal cannula with a trocar was used in addition to the intraoral incision to insert screws through a small skin stab incision while protecting facial nerve branches. Surgical accessibility was evaluated using a visual analogue scale (1 = good, 2 = fair, 3 = poor) [12], and the duration of surgery was recorded. All patients had panoramic radiographs on the first postoperative day. A senior registrar, who was blinded by the surgical approach, measured fracture reduction. The interval between the fractures at the angle point was measured digitally on the X-ray. A fracture gap of ≤ 3 mm was considered adequate, while >3 mm was inadequate [13]. The reduction of fractures in representative postoperative panoramic radiographs in both groups is illustrated. There was adequate fracture reduction (≤ 3 mm gap) in transbuccal group. Panoramic radiographs were obtained using a Sirona Orthophos® orthopantomograph machine (Sirona Dental Systems, Bensheim, Germany). The fracture gap was measured on the Sirona software digitally. Postoperative occlusion was evaluated on the first postoperative day and categorized as satisfactory (minimal/no deviation from pre-trauma occlusion, normal intercuspation, comfortable mastication) or non-satisfactory (malocclusion, open bite, premature contacts, or functional difficulty). Postoperative panoramic radiograph (orthopantomogram) that shows the patient who was treated with a transbuccal approach has an adequate reduction of the fracture (less than 3 mm gap) (Figure 1).

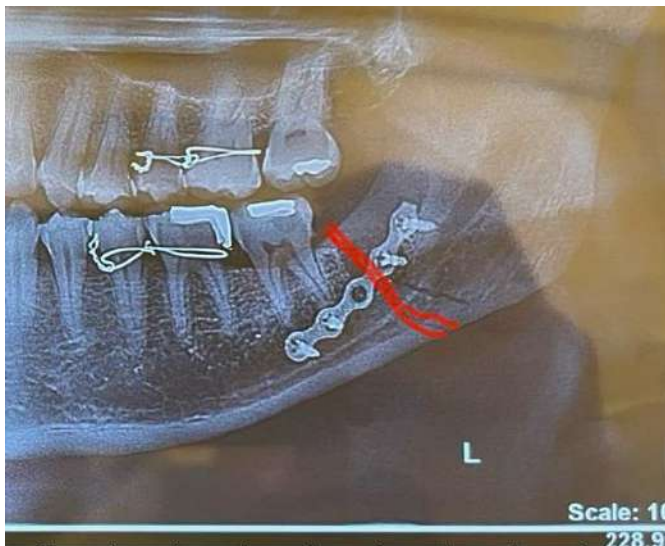


Figure 1: Postoperative Panoramic Radiograph (Orthopantomogram)

The study shows inadequate reduction (>3 mm gap) in the intraoral group. All the measurements were taken, and data were utilized to work out percentages of satisfactory reductions in each group (Figure 2).

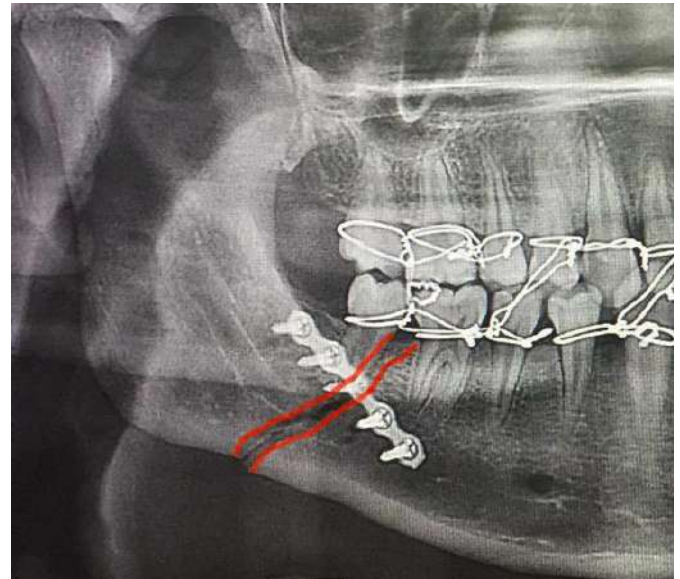


Figure 2: Panoramic Radiograph (Orthopantomogram) Showing Inadequate Fracture Reduction (>3 mm) Used in the Intraoral Technique

Continuous variables (age, surgical time) were assessed for normality using the Shapiro-Wilk test. As they were not normally distributed, the Mann-Whitney U test was used for group comparisons. Categorical variables (postoperative occlusion, fracture reduction, and surgical accessibility) were compared using the Chi-square test. All analyses were performed using SPSS version 24.0, with $p < 0.050$ considered statistically significant.

RESULTS

A total of 70 patients were included, with 35 in the intraoral group and 35 in the transbuccal group. The study evaluated surgical time, fracture reduction, post-operative occlusion, and surgical accessibility, corresponding to the stated objectives. The fracture reduction was measured on the digital software of the radiograph. Adequate fracture reduction was observed in 82.9% of the intraoral group and 80.0% of the transbuccal group. There was no statistically significant difference between the two groups ($\chi^2 = 0.094$, $p = 0.759$), indicating that both approaches are equally effective in achieving anatomical alignment of the mandible. Satisfactory occlusion was achieved in 88.6% of patients in both groups, with no statistically significant difference ($\chi^2 = 0.000$, $p < 0.001$). This demonstrates that both techniques reliably restore pre-trauma occlusion. The transbuccal approach provided significantly better surgical accessibility compared to the intraoral approach, with 77.1% rated as "good" versus 17.1% in the intraoral group ($\chi^2 = 25.675$, $p < 0.001$). The intraoral approach was predominantly rated as "fair" (71.4%), highlighting the advantage of transbuccal access for plate placement, especially in posterior fractures (Table 1).

Table 1: Comparison of Categorical Variables between Intraoral and Transbuccal Approaches

Variables		Intraoral, n (%)	Transbuccal, n (%)	χ^2 (df)	p-value
Post-Operative Occlusion	Satisfactory	31 (88.6%)	31 (88.6%)	0.000 (1)	<0.001
	Unsatisfactory	4 (11.4%)	4 (11.4%)		
Fracture Reduction on Radiograph	Adequate	29 (82.9%)	28 (80.0%)	0.094 (1)	0.759
	Inadequate	6 (17.1%)	7 (20.0%)		
Ease of Accessibility	Good	6 (17.1%)	27 (77.1%)	25.675 (2)	<0.001
	Fair	25 (71.4%)	6 (17.1%)		
	Poor	4 (11.4%)	2 (5.7%)		

χ^2 = Pearson Chi-square statistics

The median surgical time was significantly shorter for the intraoral group (45 minutes [IQR 42–48]) compared to the transbuccal group (70 minutes [IQR 65–75], $p < 0.001$), reflecting the additional steps required for transbuccal instrumentation. Age distribution did not differ significantly between groups ($p = 0.090$), ensuring comparability (Table 2).

Table 2: Comparison of Continuous Variables (Age and Surgical Time) Between Intraoral and Transbuccal Groups

Variables	Intraoral (n = 35) Median [IQR]	Transbuccal (n = 35) Median [IQR]	p-value
Age (Years)	28.0 [24.0–33.0]	27.0 [23.0–32.0]	0.090
Surgical Time (Minutes)	45.0 [42.0–48.0]	70.0 [65.0–75.0]	<0.001**

IQR: Interquartile range; the Mann-Whitney U test was used for all comparisons. **Statistically significant at $p < 0.050$

DISCUSSION

Open reduction and internal fixation of mandibular fractures can be achieved using various techniques, including intraoral, extraoral (submandibular/retromandibular), or transbuccal approaches. These techniques are often compared based on accessibility, operative duration, ease of use, and the skill required by the surgeon [14]. This study specifically evaluated the clinical outcomes of intraoral versus transbuccal approaches for mandibular angle fractures. In terms of fracture reduction, 82.9% of patients in the intraoral group and 80.0% in the transbuccal group achieved adequate reduction ($\chi^2 = 0.094$, $p = 0.759$). Similarly, post-operative occlusion was satisfactory in 88.6% of patients in both groups ($\chi^2 = 0.000$, $p < 0.001$). These findings indicate that both approaches are equally effective in achieving anatomical alignment and functional rehabilitation of the mandible. These results are consistent with previous studies by Said and Lee et al. which reported similar outcomes in occlusion and fracture reduction between intraoral and transbuccal techniques [15, 16]. However, a significant difference was observed in surgical accessibility, with 77.1% of patients in the transbuccal group rated as having “good” accessibility compared to 17.1% in the intraoral group ($\chi^2 = 25.675$,

$p < 0.001$). The improved exposure and mobility provided by the transbuccal approach facilitated accurate plate placement, particularly in posterior mandibular regions. Similar findings have been reported by Wusiman et al. and Kumar et al. highlighting the advantage of the transbuccal technique in reducing technical challenges during fixation [17, 18]. Regarding operative duration, the transbuccal approach required longer surgical time due to additional instrumentation. This balance between improved accessibility and procedural complexity aligns with previous studies [11]. Chari also reported longer operating times for transbuccal procedures [19], although recent evidence suggests that surgical time decreases as surgeons gain experience with this technique [20].

There are a few limitations associated with this study. First, it was performed in one center, and the sample size is quite small, which can restrict the extrapolation of the results. Even though surgical accessibility was chosen as the main outcome in the estimation of the sample size since only limited access to similar data used as categories of outcomes existed in the literature, this might have decreased the statistical power to observe the difference in the secondary outcomes, which included postoperative occlusion, adequacy of fracture reduction, and the operative time. Second, the allocation of patients was not randomized and was done linearly depending on the clinical judgment and preference of the operating surgeon, and the patient selection method presents a possible risk of selection bias. Third, assessment of radiographic outcomes, surgical accessibility, and postoperative occlusion was done by one evaluator, and this could have been used to influence observer bias despite the use of standard assessment criteria. Lastly, the limited time of postoperative follow-up did not allow for the prolonged analysis of the functional stability, occlusal, and aesthetic outcomes. To enhance the evidence base and add to the validity of comparative outcomes, future studies need to involve multicenter designs, larger sample sizes, randomized allocation, multiple blinded assessors, and longer follow-up.

CONCLUSIONS

Intraoral and transbuccal techniques are equally effective in the fixation of mandibular angle fractures with similar results in fracture correction and subsequent occlusion. The transbuccal technique is more surgically available, especially in posterior fractures, yet it has a high operative time. The choice of the operational methodology is to be determined by the fracture site, level of experience, and patient-related aspects such as anatomy and cosmetic interests. Irrespective of these results, the single-center design, non-randomized assignment, and short-term follow-up of the study restrict the extrapolation of findings,

and bigger, multicenter studies with extended post-treatment follow-up should support these findings.

Authors' Contribution

Conceptualization: MR

Methodology: MR, AUR, AKN, AM, ARN

Formal analysis: AUR

Writing and Drafting: MR, MAB, AUR, AKN, IT, AM

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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



Role of Vitamin D in Prevention of Preeclampsia Recurrence in Pregnant Women with Previous History of Preeclampsia: A Randomized Controlled Trial

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ABSTRACT

Vitamin D deficiency may contribute to abnormal placentation and endothelial dysfunction leading to preeclampsia (PE). **Objectives:** To compare the recurrence of preeclampsia in pregnant females having a previous history of PE receiving vitamin D supplementation versus placebo. **Methods:** This double-blind randomized controlled trial was done at the Department of Obstetrics and Gynecology, Nishtar Hospital, Multan, over six months from August 2025 to February 2026. A total of 146 pregnant ladies, 20-45 years old, with singleton pregnancy, gestational age ≥ 20 weeks, and previous preeclampsia were enrolled. Women with chronic hypertension, cardiac diseases, renal disease, and thyrotoxicosis were excluded. Participants were randomized to receive either oral vitamin D 4000 IU daily or a placebo. Follow-up continued until 36 weeks. Preeclampsia recurrence was defined as hypertension $\geq 140/90$ mmHg with proteinuria $\geq +1$ on spot urine test. Data were analyzed through SPSS version 27.0, descriptive statistics were run, group comparisons were done through chi-square and independent sample t-test as required, and a p-value < 0.050 was considered significant. **Results:** Mean age was 27.9 ± 4.6 years, and mean gestational age was 30.5 ± 2.8 weeks. Age and gestational age differed between the groups. Overall recurrence of preeclampsia was 21.9%. Recurrence was markedly less in the vitamin D compared to placebo (13.7% vs. 30.1%, relative risks 0.46, $p=0.016$) groups. Significant reductions were observed among women aged < 30 years, gestational age 24-30 weeks, and non-obese participants. **Conclusions:** Vitamin D therapy decreased recurrence of preeclampsia in high-risk pregnant females, supporting its potential role as an effective preventive strategy in antenatal care.

INTRODUCTION

Preeclampsia (PE) is characterized by raised blood pressure (BP) and proteins excreted in urine after the 20th week of gestation [1]. It is responsible for one-fourth of all maternal deaths and neonatal morbidity and mortality, and it complicates 2-8% of pregnancies [2]. Excreting > 300 mg of protein in a 24-hour collection of urine sample, or a protein-creatinine ratio of minimum 0.3 in a random urine specimen, or consistently having proteinuria of 30 mg/dl in random urine samples (i.e., +1 finding on dipstick) are all indicators of proteinuria [3]. Conditions of calcium homeostasis, e.g., hypocalciuria and decreased vitamin D levels, have been commonly documented in pregnant women who subsequently experienced preeclampsia [4]. The presence of PE in one pregnancy does not guarantee

that it will again develop in subsequent pregnancies. However, a larger likelihood of it occurring in later pregnancies is linked to its initial development [5]. Because low maternal vitamin D stores may raise the risk of maternal comorbidities and difficulties, e.g., small for gestational age infants and low birth weight, vitamin D is especially important during pregnancy [6]. According to past observations, preeclampsia patients are more likely to have increased Th1 expression in the presence of vitamin D deficiency [7]. Behjat Sasan et al. conducted a randomized controlled trial. While 70 pregnant patients were randomly assigned to the intervention group (vitamin D3), 72 pregnant women were placed in the control group (placebo). Preeclampsia was much less common in the



intervention group's patients (15.7% vs. 30.6%, p -value=0.036) than in the control group [8]. Dahma et al. Enrolled 139 pregnant females in the cases group, who had a history of PE and who confirmed daily supplementation of vitamin D in 2000 IU or 4000 IU up to the 36th week of gestation, while 59 individuals were enrolled in the control group with no vitamin D addition during pregnancy. Preeclampsia was more prevalent in the control group at 36 weeks of pregnancy (18.6% vs. 9.5% (low dosage) vs. 5.3% (high dose), $p=0.041$) [9]. Given that the increased need for vitamin D during pregnancy is one of the potential causes of preeclampsia, vitamin supplements are prescribed to meet this increased need. In Pakistan and other South Asian populations, vitamin D deficiency is highly prevalent among pregnant women, with several regional studies reporting deficiency rates exceeding 60–80% [10]. The study's findings will emphasize the necessity of taking vitamin D supplements throughout pregnancy, particularly for women who have previously experienced preeclampsia. By reducing the chances of PE, the associated maternal and neonatal complications and death rate may be reduced.

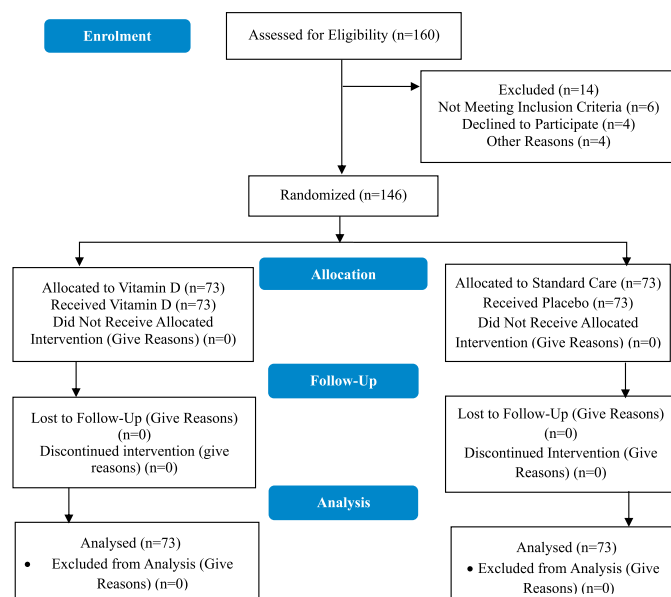
Pakistan does not have strong data from randomized controlled trials on vitamin D supplementation to prevent recurrence of preeclampsia in women at high risk; most of the evidence in the country is based on observational studies or small, insensitive trials. Although randomized, there were large baseline differences between groups in terms of age (27.2 vs 28.7 years, $p=0.038$) and gestational age (31.2 vs 29.8 weeks, $p=0.002$), which might confound even adjusted analysis. This study aims to evaluate how vitamin D may help prevent preeclampsia recurrence in our community.

METHODS

This double blind, parallel-group, randomized controlled trial (Trial Registry No. NCT07288801) was conducted at the Department of Obstetrics and Gynaecology, Nishtar Hospital, Multan, after taking approval from the institutional ethical review committee (No. 14538/NMU; dated 8th August 2025). The study lasted a period of six months from 9th August 2025 to 8th February 2026. A total of 146 pregnant females, gestational age ≥ 20 -weeks, singleton pregnancy, 20–45 years of age, and history of preeclampsia were recruited through non-probability consecutive sampling after taking written informed consent. A minimum sample size of 146 participants was calculated using Open Epi online software through the formula for a randomized controlled trial (https://www.openepi.com/PDFDocs/SS_CohortDoc.pdf). $n = (Z_{\alpha/2} + Z_{1-\beta})^2 pq(r+1) / r(p_1 - p_2)^2$. Preeclampsia recurrence of 18.6% in the placebo group, 5.3% in the vitamin D supplementation group [9], with a power of 80% and a significance level of

5%. Women with chronic hypertension, cardiac diseases, renal disease, thyrotoxicosis, and intrauterine fetal demise were excluded. Through simple random sampling using the lottery method, the participants were assigned to the vitamin D supplementation (intervention group) and placebo group in a 1:1 ratio. The group assignment was concealed in sequentially placed numbered and sealed opaque envelopes. The enrolling gynecologist opened the envelopes to assign the participants to allocated groups. Patients' characteristics like age (years), gestational age (weeks), BMI, obesity (yes/no), parity (primiparous/multiparous), and gestational diabetes were recorded. The women in the intervention group were given 4000 IU of vitamin D orally, while women in the placebo group were given the same amount of oil emulsion provided by the hospital pharmacy department. The participants were not aware of the assigned drug. The study medicine was prescribed till 36-weeks of gestation. Patients were followed fortnightly in the outpatient department, and blood pressure was measured according to standard procedure. The researcher measuring blood pressure was not aware of the treatment assigned to participants. If blood pressure was $\geq 140/90$ mmHg in sitting posture, a spot urine test to look for proteinuria was advised. Presence of proteinuria (+1 or higher) in the presence of hypertension was used to label preeclampsia. All women with recurrent preeclampsia were managed according to hospital protocol.

Normally distributed numerical data were presented as mean $\pm$ SD, and categorical data as frequency and percentages. Preeclampsia recurrence between the groups is compared through a chi-square test, and a p -value < 0.050 is taken as significant. The study followed Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting of randomized controlled trials [11] (Figure 1).

**Figure 1:** CONSORT 2010 Flow Diagram

RESULTS

The mean age of patients was 27.9 ± 4.6 years, and 91 (62.3%) were below 30-years of age. The mean body mass index (BMI) was 24.6 ± 3.2 , and 24 (16.4%) were obese. The mean gestational age was 30.5 ± 2.8 weeks, and 80 (54.8%) were between 31 and 36 weeks of gestation. In 110 (75.3%) of the cases, women were multiparous. In 27 (18.5%) of the cases, women had gestational diabetes. Women were significantly younger in the vitamin D supplementation group in contrast to the placebo group (27.2 ± 4.3 vs. 28.7 ± 4.8 years, p -value=0.038). The mean gestational age was remarkably high in the vitamin D group in comparison to the

placebo (31.2 ± 2.5 vs. 29.8 ± 3.1 weeks, p -value=0.002) (Table 1).

Table 1: Characteristics of Pregnant Women with Previous Preeclampsia History (n=146)

Characteristics	All, (n=146)	Vitamin D Group, (n=73)	Placebo Group, (n=73)	p-value*
Age (Years)	27.9 ± 4.6	27.2 ± 4.3	28.7 ± 4.8	0.038
< 30-Years	91 (62.3%)	51 (56%)	40 (44%)	0.060
> 30-Years	55 (37.7%)	22 (40%)	33 (60%)	
BMI (kg/m ²)	24.6 ± 3.2	24.2 ± 3.1	24.9 ± 3.3	0.164
Obese – Yes	24 (16.4%)	10 (41.7%)	14 (58.3%)	0.372
Gestational Age (Weeks)	30.5 ± 2.8	31.2 ± 2.5	29.8 ± 3.1	0.002
Parity – Primiparous	36 (24.7%)	21 (58.3%)	15 (41.7%)	0.249
Multiparous	110 (75.3%)	52 (47.3%)	58 (52.7%)	
Gestational Diabetes –Yes	27 (18.5%)	11 (40.7%)	16 (59.3%)	0.286

*Independent sample t-test for numeric and chi-square test for categorical comparisons

The incidence of preeclampsia recurrence was 32 (21.9%) in the study participants. Incidence of preeclampsia was remarkably less in patients receiving vitamin D compared to those taking a placebo (13.7% vs. 30.1%, relative risk 0.46 (0.23–0.89), p -value=0.016) (Table 2).

Table 2: Pre-Eclampsia Recurrence in Women with Previous Preeclampsia History (n=146)

Treatment Group	Preeclampsia Recurrence, n (%)		Relative Risk (95% CI)	p-value*
	Yes	No		
All (n=146)	32 (21.9%)	114 (78.1%)	—	—
Vitamin D Group (n=73)	10 (13.7%)	63 (86.3%)	0.46 (0.23 – 0.89)	0.016
Placebo Group (n=73)	22 (30.1%)	51 (69.9%)		

*chi-square test

In women < 30-years of age, the incidence of pre-eclampsia was remarkably less in the vitamin D group in contrast to the placebo (9.8% vs. 27.5%, relative risk 0.36 (0.14–0.94), p -value=0.028). In women 24–30 weeks of gestational age, the incidence of pre-eclampsia was significantly lower in the vitamin D supplementation group compared to the placebo group (11.1% vs. 38.5%, relative risk 0.29 (0.09–0.90), p -value=0.023). Incidence of pre-eclampsia was significantly lower in the vitamin D supplementation group compared to the placebo group (3.2% vs. 15.3%, relative risk 0.21 (0.05–0.92), p -value=0.026) only in the non-obese group (Table 3).

Table 3: Effect of Patient Characteristics on Distribution of Preeclampsia Recurrence Between Vitamin D and Placebo Groups (n=146)

Characteristics	Treatment Group	Preeclampsia Recurrence, n (%)		Relative Risk (95% CI)	p-value*
		Yes	No		
Age					
<30 Years	Vitamin D Group	5 (9.8)	46 (90.2)	0.36 (0.14 – 0.94)	0.028
	Placebo Group	11 (27.5)	29 (72.5)		
≥30 Years	Vitamin D Group	5 (22.7)	17 (77.3)	0.68 (0.28 – 1.70)	0.396
	Placebo Group	11 (33.3)	22 (66.7)		
Gestational Age					
24–30	Vitamin D Group	3 (11.1)	24 (88.9)	0.29 (0.09 – 0.90)	0.023
	Placebo Group	15 (38.5)	24 (61.5)		
31–36	Vitamin D Group	7 (15.2)	39 (84.8)	0.74 (0.28 – 1.91)	0.564
	Placebo Group	7 (20.6)	27 (79.4)		

Obesity					
Yes	Vitamin D Group	8 (80)	2 (20)	0.86 (0.61 – 1.21)	0.550
	Placebo Group	13 (92.9)	1 (7.1)		
No	Vitamin D Group	2 (3.2)	61 (96.8)	0.21 (0.05 – 0.92)	0.026
	Placebo Group	9 (15.3)	50 (84.7)		
Parity					
Primiparous	Vitamin D Group	0 (0.0)	21 (100)	—	0.008
	Placebo Group	5 (33.3)	10 (66.7)		
Multiparous	Vitamin D Group	10 (19.2)	42 (80.8)	0.66 (0.33 – 1.30)	0.220
	Placebo Group	17 (29.3)	41 (70.7)		

*chi-square test (Fisher's exact test where cell count <5).

DISCUSSION

The results of our research suggest that the overall incidence of preeclampsia recurrence was 21.9%. Incidence of preeclampsia was less in the vitamin D group in comparison to the placebo group (13.7% vs. 30.1%, p -value=0.016). A meta-analysis of RCTs on vitamin D and preeclampsia was carried out in 2024 by Kokkinari *et al.* They found that taking vitamin D supplements significantly decreased the risk of preeclampsia (pooled RR = 0.61) [12]. This is in line with our findings and demonstrates that vitamin D protects against preeclampsia, especially in areas where baseline deficiency is prevalent. Patients in the intervention group had a considerably decreased (p -value=0.036) likelihood of PE compared to women in the control group, according to a randomized trial by Behjat Sasan *et al.* which administered 50,000 IU of vitamin D every two weeks. Preeclampsia was 1.94 times more likely to occur in the control group than in the vitamin D group [8]. This closely resembles the decrease in recurrence risk that this study has observed. According to reports, vitamin D lowers endothelial dysfunction and systemic inflammation linked to the pathophysiology of preeclampsia [13]. Some factors, like dose regimens, timing of supplementation, and study populations, also make a difference. Some trials administered high-dose intermittent vitamin D (e.g., 50,000 IU every two weeks until late pregnancy), while others used lower daily doses (400–600 IU), which may lead to different biological effects on placental function and endothelial regulation. In 2023, Dahma carried out a systematic review on vitamin D supplementation before 20 weeks. In several trials, early pregnancy vitamin D supplementation was linked to a lower incidence of preeclampsia (ORs=0.26–0.31) [14]. This further validates the use of early supplementation as a preventative measure, as demonstrated in our RCT. Early in pregnancy, enough vitamin D may have a positive impact on placental vascular remodeling and trophoblast invasion [15]. In a Moghib *et al.* 4956 people were examined in a meta-analysis. Vitamin D supplementation dramatically decreased the risk of preeclampsia by 45% (RR=0.55) in 33 RCTs. This greater synthesis confirmed that maternal

vascular and inflammatory pathways were impacted by vitamin D in a quantifiable way [16]. A systematic review was carried out by AlSubai *et al.* The supplementation of vitamin D reduced the chance of preeclampsia by half (OR ~0.50), while deficiency was linked to an increased risk, according to pooled data from randomized and observational trials [17]. Their conclusion that supplementing vitamin D reduces recurrence is consistent with our findings. Increased levels of 25-hydroxyvitamin D decrease the anti-angiogenic imbalance linked to preeclampsia and raise angiogenic factors. The authors of a smaller RCT from Faisalabad, Pakistan, demonstrated that the vitamin D versus placebo difference in preeclampsia incidence (4% vs. 8%) did not reach statistical significance [18]. This is not consistent with what we found. A lower dosage and a different baseline vitamin D level could be the most likely cause. In the present study, it was seen that in women < 30-years of age, the incidence of pre-eclampsia was markedly less in vitamin D group in contrast to the group without vitamin D. Subgroup analysis in a study by Moghib *et al.* showed greater risk reductions in younger or earlier-treated women, indicating that early gestational intervention or age may increase the protective effect [16]. Younger women frequently have greater placental adaptability and fewer comorbidities; early or adequate vitamin D dose can enhance immune modulation and placental vascularization more successfully, resulting in higher preventative effects in these subgroups. This study also observed that in women at 24–30 weeks of gestational age, the incidence of preeclampsia was considerably less in women who received vitamin D in contrast to those who did not (11.1% vs. 38.5%). Vitamin D supplementation beginning early in pregnancy (median GA of 15 weeks) significantly decreased the incidence of preeclampsia (RR = 0.36; p =0.001) when compared to no supplementation, according to a randomized clinical trial from the Democratic Republic of Congo [19]. The substantial protective impact confirms our results that vitamin D supplementation started before or during mid-gestation reduces the incidence of

preeclampsia, even when the supplementation started earlier than 24–30 weeks. Adequate vitamin D may support healthy immunological and endothelial function during the crucial mid-gestational phase for placental remodeling and maternal vascular adaptation, hence reducing hypertensive problems [20]. In the present study, the incidence of pre-eclampsia was considerably less in the vitamin D group in contrast to placebo (3.2% vs. 15.3%) only in the non-obese group. While higher dosing improved serum 25OHD levels, there were no significant improvements in maternal or birth outcomes, according to a randomized trial comparing 800 IU vs. 400 IU vitamin D supplementation in pregnant women with overweight/obesity [21]. This suggests that standard supplementation may not adequately modify outcomes like hypertension or preeclampsia in obese pregnancies. This corroborates our findings that there is no discernible advantage of vitamin D in the obese group. Obesity may affect vitamin D metabolism and response; therefore, conventional pregnancy supplementation may be less successful in lowering the risk of preeclampsia in obese women unless significantly greater doses are employed. The strengths of our study include its experimental study design. By reducing observer bias and selection, double-blind randomized controlled trials improved causal inference. Clinical relevance and applicability to preventive obstetric care were improved by including women who had already experienced preeclampsia. Internal validity was guaranteed by using a fixed, evidence-based vitamin D dose (4000 IU/day) with a placebo control.

One of the study's limitations was a single-center study; its conclusions might not be as applicable to different populations or healthcare environments. Baseline imbalance was observed in maternal age and gestational age between the groups despite randomization. Since these variables are clinically relevant, an adjusted analysis was carried out to assess for potential confounding. Only outcomes up to 36 weeks were studied; perinatal outcomes and late-onset preeclampsia were not studied. Underpowered subgroup analyses raise the possibility of type II error. Baseline vitamin D levels in serum were not measured, and vitamin D toxicity monitoring during supplementation was not performed, limiting assessment of dose-response relationships and safety profiling. Larger sample sizes and multi-center trials should be carried out in the future to verify efficacy across a range of demographics. To establish a correlation between biochemical correction and clinical results, baseline and repeated vitamin D values should be included. Future research studies should be conducted on long-term maternal and neonatal outcomes, such as preterm birth, fetal growth, and newborn morbidity.

CONCLUSIONS

In conclusion, vitamin D supplementation at 4000 IU daily significantly reduces the recurrence of preeclampsia in females with a prior history of the disorder, with the greatest benefit observed among younger, non-obese women and those treated earlier in gestation. These results underscore the need for customized strategies in obese groups and additional large-scale validation.

Authors' Contribution

Conceptualization: TA, MK

Methodology: SAJ, FA, AR

Formal analysis: FA, AR

Writing and Drafting: TA, SAJ, MK

Review and Editing: TA, SAJ, MK, FA, AR

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Relationship of Serum Ferritin Levels with Haemoglobin Percentage and Its Impact on Fetomaternal Outcome of the Pregnancy

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ABSTRACT

Iron stores in the body exist primarily in the form of ferritin. Low serum ferritin levels, even in females with ideal haemoglobin levels, can lead to poor fetal-maternal outcome. **Objective:** To determine the frequency of low serum ferritin in non-anaemic pregnant females and its Fetomaternal outcomes. **Methods:** This Comparative analytical study was carried out in the Department of Gynaecology and Obstetrics, Fauji Foundation Hospital, Rawalpindi. Patients were enrolled from the Fauji Foundation Hospital, Rawalpindi. Detailed history was taken, and pregnant females with normal haemoglobin were selected; their serum ferritin was followed. Patients with low serum ferritin levels were observed for maternal and fetal outcomes. Data were entered and analysed by SPSS version 25.0. **Results:** The mean age of cases was 29.95 ± 3.57 years, with minimum and maximum ages of 25 and 35 years. Low serum ferritin levels were found in 248 (46.44%) cases, while in 286 (53.56%) cases serum ferritin levels were normal. 16 (21.72%) neonates were born preterm, 285 (53.37%) females had C-section, 41 (7.68%) had PPH, 96 (17.98%) neonates had low birth weight, and 94 (17.60%) neonates needed an ICU admission. Significant association of this outcome with low serum levels was found, p -value < 0.001. **Conclusions:** The females with Hb levels ≥ 11 g/dl should be screened for their serum ferritin levels, as females with low serum ferritin levels were associated with poor maternal outcome, like C-section, NICU admission, PPH, and poor fetal outcome, like preterm birth and low birth weight.

INTRODUCTION

During pregnancy, there is an increase in the requirement of some nutrients, like iron, to help in foetal growth and also in the physiological and metabolic changes. Iron is one of the trace metals that are important to numerous biological processes [1]. Since there is nearly a tenfold increment of iron needs during pregnancy to facilitate fetoplacental growth and the needs of the mother herself, iron deficiency anaemia (IDA) is common among pregnant women [2]. Important morbidity, including increased risks of

postpartum infection, blood transfusion, and postnatal depression, premature birth, and reduced low birth weights in both the parturient and her unborn baby, may serve as the consequences of IDA [3]. Anaemia of a severe form causes ineffective compensation by the mother's body, cardiac overload, high risk of bleeding, low tolerance to blood losses, and, possibly, cardiovascular shock and death [4]. Low levels of maternal ferritin may reflect an iron deficiency that can lead to anaemia and other problems



with pregnancy-related health [5]. Ferritin is considered a crucial biomarker and vital in supporting defence when there is bacterial invasion, since iron is one of the key elements in the growth of bacteria [6]. Whereas the levels of ferritin and haemoglobin are reflective of iron insufficiency, the levels of haemoglobin are late indicators that may not be a true reflection of tissue iron status. However, serum ferritin (SR) is, at most times, considered the most precise measure of iron deficit in pregnancy [7]. A prospective cohort study (n=412) assessed the prognosis of the connection between low birth weight (LBW) and maternal iron status in rural eastern Ethiopia. The LBW was 20.2 percent. The probability of a pregnancy delivering LBW infants was also higher by 5 times with women with IDA (serum ferritin <15 µg/L) [8]. On the same note, recent cohort evidence has shown that maternal serum ferritin levels during pregnancy are associated with adverse maternal and fetal outcomes, highlighting the importance of monitoring maternal iron status [9]. Nonetheless, another cohort study did not show any association at week 14; however, increased ferritin at week 30 was linked to 2-fold higher risks of low birth weight (OR = 2.27) and lower birth weight (-93g; p=0.021). [10] Moreover, another retrospective study identified that gestational diabetes and small for gestation age babies were associated with increased serum ferritin (SF) concentration. The levels of ferritin are to be observed and regulated, as hyper SF during pregnancy can increase the chance of having GDM and SGA [9]. These findings point out a contradiction in the literature concerning the level of serum ferritin and the Fetomaternal outcome.

Even though some studies have observed that low ferritin levels may cause such problems as preterm births, low birth weight, and the risk of caesarean delivery, other studies point out the dangers of high ferritin. This study aimed to clarify the relationship of serum ferritin levels with haemoglobin percentage and its impact on the Fetomaternal outcome of the pregnancy.

METHODS

The Comparative analytical study was carried out from June 11, 2025 to Dec 10, 2025, in the Department of Gynaecology and Obstetrics, Fauji Foundation Hospital, Rawalpindi. 534 cases of pregnant ladies. Sample size was calculated using the WHO sample size calculator, taking a confidence level 95%, an iron deficiency rate in pregnant women as 15% [11], by taking 4% margin of error, out rate after approval of the Ethical review committee (Ref No: 977/RC//FFH/RWP; dated 11th June 2025). Patients were enrolled by a non-probability consecutive technique. All pregnant women between the ages of 25-35 years with singleton pregnancy and gestational age between 27- 40 weeks admitted to the labour room for delivery with Hb

levels ≥ 11 g/dl. Women with comorbid conditions like pre-eclampsia/essential hypertension, diabetes/GDM, renal disease, cardiac disease, and febrile conditions. Patients with thalassemia, chronic anaemia, elderly primigravida, and those with two or more previous caesarean sections were also excluded. Patients were enrolled from the Department of Gynaecology and Obstetrics, Fauji Foundation Hospital, Rawalpindi. Detailed history was taken, and pregnant females with normal haemoglobin were selected; their serum ferritin was followed. Patients with low serum ferritin levels were observed for maternal and fetal outcome in terms of preterm birth, low birth weight, post-partum haemorrhage, caesarean section, and NICU admissions. The mode of delivery was also noted, and in the case of caesarean section, the indication was taken into account. The following definitions and clinical criteria were used in this study to assess maternal and fetal outcomes. Serum ferritin was considered low when levels were less than 15 µg/L. Haemoglobin was regarded as normal when equal to or greater than 11 g/dL. Iron deficiency was defined using a single serum ferritin cut-off value of < 15 µg/L, in accordance with World Health Organization recommendations for assessment of depleted iron stores in adult women [12]. Maternal outcomes included preterm delivery, defined as the birth of a baby before 37 completed weeks of gestation. Caesarean section was defined as the surgical delivery of the baby through an incision in the maternal abdomen and uterus, performed under spinal or general anaesthesia. Indications for caesarean section, such as fetal distress observed on cardiotocography (CTG) as a non-reactive trace, and obstructed labour, were also documented. Post-partum haemorrhage (PPH) was defined as blood loss exceeding 500 mL (for vaginal delivery) or 1000 mL (for caesarean section) within the first 24 hours following childbirth. Blood loss was clinically estimated using calibrated instruments such as a kidney tray, with one tray approximately equating to 500 mL. Fetal outcomes included low birth weight, defined as a birth weight less than 2.5 kg, and NICU admission, which referred to the admission of the newborn to the neonatal intensive care unit within the first 24 hours after birth. All the patients who met the inclusion criteria were included in the study. After preoperative assessment, informed consent was taken for inclusion in the study. Data were collected on a pre-formatted proforma, and the results were compiled.

Statistical analysis was performed using SPSS version 25.0. Quantitative variables, including age, gestational age, serum ferritin, and haemoglobin, were measured as mean $\pm$ S.D. Qualitative variables like preterm birth, caesarean section, post-partum haemorrhage, low birth weight, NICU admissions, and low serum ferritin were measured as frequency and percentage. Effect modifiers like age,

gravidity, parity, and gestational age were controlled by stratification. Post-stratification chi-square test was applied. The p -value ≤ 0.050 was significant.

RESULTS

The mean age of cases was 29.95 ± 3.57 years, with minimum and maximum ages of 25 and 35 years. There were 256 (47.94%) cases that were 25–29 years old, and 278 (52.06%) cases were 30–35 years of age. A total of 238 (44.57%) had < 3 Gravida, and 296 (55.43%) had Gravida ≥ 3 , while 385 (72.10%) cases had < 3 parity and 149 (27.90%) cases had parity ≥ 3 . The average gestational age was 37.12 ± 2.47 weeks with a range of 13 weeks (27 and 40 weeks). The mean Hb of all females was 11.54 ± 0.77 with a minimum and maximum Hb of 10.25 and 14.29 mg/dL. The mean serum ferritin was 21.80 ± 15.03 with minimum and maximum values of 2 and 62, respectively (Table 1).

Table 1: Descriptive Statistics of Maternal and Clinical Variables (n=534)

Variables	Mean $\pm$ SD	Range	Minimum	Maximum
Age (years)	29.95 ± 3.57	10.00	25.00	35.00
Gestational Age (weeks)	37.12 ± 2.47	13.00	27.00	40.00
Haemoglobin (g/dL)	11.54 ± 0.77	3.04	10.25	14.29
Serum Ferritin (μ g/L)	21.80 ± 15.03	60.00	2.00	62.00

According to the operational definition, low serum ferritin levels were found in 248 (46.44%) cases while in 286 (53.56%) cases serum ferritin levels were normal. According to the outcome, 116 (21.72%) neonates were born preterm, 285 (53.37%) females had C-section, 41 (7.68%) had PPH, 96 (17.98%) neonates had low birth weight, and 94 (17.60%) neonates needed an ICU admission (Figure 1).

section (54.0% vs. 46.0%, $p < 0.001$), and postpartum haemorrhage (90.2% vs. 9.8%, $p < 0.0001$) than those with normal levels of serum ferritin. Equally, low birth weight (88.5% vs. 11.5% $p < 0.001$) and NICU admission (71.3% vs. 28.7% $p < 0.001$) were also significantly higher among the neonates of mothers with low serum ferritin. All the observed relationships were very significant, suggesting a strong correlation between maternal iron deficiency and the risk of poor obstetric and neonatal outcomes. The findings indicate that low levels of maternal ferritin can be a significant predictor of complications in pregnancy (Table 3).

Table 3: Comparison of Low Serum Levels with Respect to Outcome

Low Serum Ferritin	Preterm Birth		C-section		PPH		Low Birth Weight		NICU Admission	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Yes	96 (75.0%)	152 (37.4%)	154 (54.0%)	94 (37.8%)	37 (90.2%)	211 (42.8%)	85 (88.5%)	163 (37.2%)	67 (71.3%)	181 (41.1%)
No	32 (25.0%)	254 (62.6%)	131 (46.0%)	155 (62.2%)	4 (9.8%)	282 (57.2%)	11 (11.5%)	275 (62.8%)	27 (28.7%)	259 (58.9%)
Chi-square (df) p-value	111.2 (1), 0.001		34.7 (1), 0.001		80.6 (1), 0.001		120.4 (1), 0.001		52.8 (1), 0.001	

Low serum ferritin was more frequent among women aged 25–29 years than among women aged 30–35 years (58.5% vs. 41.5%, $p < 0.001$) and was also significantly related to gestational age < 37 weeks (38.7% vs. 11.2%, $p < 0.001$). The preterm birth was not greatly correlated with maternal age ($p = 0.770$), but, predictively, preterm birth only happened in the pregnancies below 37 weeks ($p < 0.001$). There was no significant relationship between age and gestational age with caesarean section and postpartum haemorrhage ($p > 0.050$). Conversely, low birth weight and NICU admission were frequent with pregnancies that were below 37 weeks ($p < 0.001$ and $p = 0.001$, respectively), and there was no significant association with maternal age. On the whole, gestational age less than 37 weeks played a major factor in unfavourable types of neonatal outcome (Table 4).

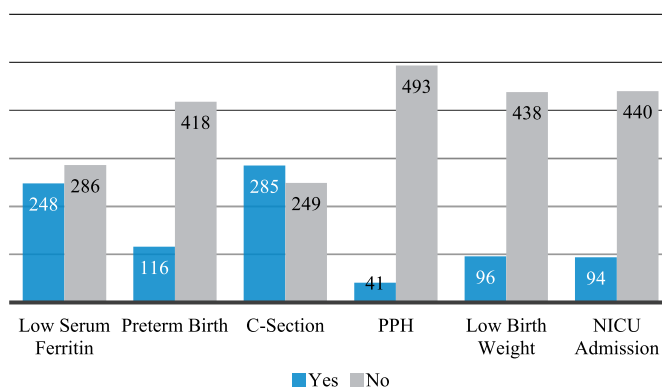


Figure 1: Distribution of Maternal and Fetal Outcomes

Women with low serum ferritin were much more likely to have anaemia (Hb < 11 g/dL) than those with normal ferritin (64.5% vs. 15.7%). In contrast, women with normal ferritin mostly had healthy haemoglobin levels (84.3%). This strong, statistically significant association ($p < 0.001$) highlights how closely a mother's iron stores are linked to her haemoglobin levels (Table 2).

Table 2: Cross-Tabulation Between Serum Ferritin Status and Haemoglobin Level

Serum Ferritin	Hb < 11 g/dL	Hb ≥ 11 g/dL	Total	Chi-square (df)	p-value
Low (n=248)	160 (64.5%)	88 (35.5%)	248	133.6 (1)	< 0.001
Normal (n=286)	45 (15.7%)	241 (84.3%)	286		
Total (n=534)	205	329	534		

The low serum ferritin was significantly associated with poor maternal and neonatal outcomes. The proportion of women with low serum ferritin had a significantly higher preterm birth (75.0% vs. 25.0%, $p < 0.001$), caesarean

Table 4: Comparison of Maternal and Fetal Outcomes by Different Strata

Outcomes	Sub-category	Yes, n (%)	No, n (%)	χ^2	df	P-value
Low Serum Ferritin	Age 25-29	145 (58.5%)	111 (38.8%)	38.2	1	<0.001
	Age 30-35	103 (41.5%)	175 (61.2%)			
	GA <37 Weeks	96 (38.7%)	32 (11.2%)	49.1	1	<0.001
	GA ≥37 Weeks	152 (61.3%)	254 (88.8%)			
Preterm Birth	Age 25-29	57 (49.1%)	199 (47.6%)	0.09	1	0.770
	Age 30-35	59 (50.9%)	219 (52.4%)			
	GA <37 Weeks	116 (100%)	0 (0%)	534	1	<0.001
	GA ≥37 Weeks	0 (0%)	406 (100%)			
C-Section	Age 25-29	139 (48.8%)	117 (47.0%)	0.16	1	0.681
	Age 30-35	146 (51.2%)	132 (53.0%)			
	GA <37 Weeks	63 (22.1%)	65 (26.1%)	1.16	1	0.280
	GA ≥37 Weeks	222 (77.9%)	184 (73.9%)			
Postpartum Hemorrhage (PPH)	Age 25-29	22 (53.7%)	234 (47.5%)	0.58	1	0.446
	Age 30-35	19 (46.3%)	259 (52.5%)			
	GA <37 Weeks	6 (14.6%)	122 (24.7%)	2.08	1	0.145
	GA ≥37 Weeks	35 (85.4%)	371 (75.3%)			
Low Birth Weight	Age 25-29	47 (49.0%)	209 (47.7%)	0.04	1	0.852
	Age 30-35	49 (51.0%)	229 (52.3%)			
	GA <37 Weeks	53 (55.2%)	75 (17.1%)	87.1	1	0.001
	GA ≥37 Weeks	43 (44.8%)	363 (82.9%)			
NICU Admission	Age 25-29	45 (47.9%)	211 (48.0%)	0.0001	1	0.998
	Age 30-35	49 (52.1%)	229 (52.0%)			
	GA <37 Weeks	48 (51.1%)	80 (18.2%)	45.2	1	0.001
	GA ≥37 Weeks	46 (48.9%)	360 (81.8%)			

DISCUSSION

Gestational anaemia may be typically due to depleted iron stores of depleted reserves or poor dietary intake. Pregnant women have a daily iron requirement of around 45mg of iron, relative to 12mg in non-pregnant women, and are therefore especially prone to iron deficiency. The main storage protein of iron is serum ferritin, and it is the most sensitive biomarker to identify iron deficiency during pregnancy and is increasingly used in preference to haemoglobin alone, which only indicates iron deficiency in later stages [13]. The median maternal age of our cohort was 29.95 with SD 3.57, with more than half (52) of the cohort aged between 30 and 35 years. This is in line with other researchers, including Thaichana *et al.* who have indicated that advanced maternal age can be a risk factor on its own, in increasing the chances of obstetric complications, including preterm birth and caesarean section [14]. The majority of the subjects were multiparous and multigravida (≥3), which is in agreement with the published literature that indicated an increasing parity to be the major cause of cumulative iron depletion leading to anaemia of iron deficiency [15]. The current study found the mean gestational age (37.12 ± 2.47 weeks), mean haemoglobin (12.43 ± 0.77 g/dl), and this lies in the lower normal range. The mean serum ferritin was, however, 21.80

15.03 ng/mL, and 46.44 percent of the respondents were found to possess low ferritin, meaning that most of the women were iron deficient despite not having anaemia. It has been found that local studies reported similar findings; e.g., a study by Khan *et al.* determined that maternal iron deficiency played a significant role in preterm birth [16], and a different study by local researchers indicated that 33 percent of women who had low ferritin levels delivered low-weight children [17]. These associations are also reinforced by regional studies conducted in Asia, which focus on the fact that maternal ferritin deficiency is a strong predictor of poor perinatal outcomes [18, 19]. These findings are supported by systematic reviews and meta-analyses conducted worldwide. The pooled analysis of 38 studies (that consist of more than 31 million pregnant women) found that anaemia was linked with increased incidence of intrauterine growth restriction by 30% (OR = 1.30, 95% CI 1.051.62) [20]. The future studies have also indicated trimester-specific relationships with high haemoglobin in early to mid-pregnancy related to gestational diabetes and PIH, and low haemoglobin and ferritin in late pregnancy to preterm birth and PROM [5]. These results highlight the significance of early diagnosis as well as trimester-specific observation. WHO recommends that serum ferritin levels less than 15ng/mL during the first trimester and less than 30ng/mL during the second and third trimesters present iron deficiency [21]. Even though our study used one cut-off of 15 µg/L across all gestational ages, current findings support the clinical significance of even moderately low levels of ferritin, which were also linked with severe maternal and child risks. The main intervention is the iron supplementation, although oral iron is recommended in mild cases and intravenous iron is used in the severe or unresponsive cases [22]. Concluding on this, it is possible to note that the current results underline the necessity to implement proactive ferritin-based screening and individual iron supplementation in pregnancy to minimize the premature burden of preventable adverse outcomes.

This research is characterized by some limitations. The study was a single centre, and it is possible that the results could not be applied to a general population. The sample size was somewhat small, and this might interfere with the degree of association between serum ferritin and Fetomaternal outcomes. Moreover, we used one time point of serum ferritin, and this may not completely show iron status during pregnancy. Also, the possible confounding factors were not controlled, including iron supplementation, inter-pregnancy intervals, maternal BMI, socioeconomic status, and overall nutritional status, which might have had an independent impact on ferritin levels as well as on maternal or neonatal outcomes. Conditions of inflammation, which may increase ferritin, were not always

excluded. Lastly, there is no possibility of a causal relationship since it is an observational study.

CONCLUSIONS

The females with Hb levels $\geq 11\text{g/dl}$ should be screened for their serum ferritin levels, as females with low serum ferritin levels have poor maternal outcomes, such as C-section, NICU admission, PPH, and poor fetal outcomes like preterm birth and low birth weight. Despite the strong association between low maternal serum ferritin and adverse maternal and neonatal outcomes, the descriptive case series design does not allow for establishing a causal relationship.

Authors' Contribution

Conceptualization: NS

Methodology: ASA, TF, UQ

Formal analysis: ASA, MA

Writing and Drafting: NS, TF, UQ, SK

Review and Editing: NS, ASA, TF, UQ, SK, MA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article

Etiology, Treatment, and Early Postoperative Outcomes of Neonatal Hydrocephalus

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ABSTRACT

Neonatal hydrocephalus is a neurological condition characterized by abnormal accumulation of cerebrospinal fluid (CSF) in the ventricular system of the brain, leading to increased intracranial pressure. **Objective:** To determine the etiology and early postoperative outcomes in neonatal hydrocephalus. **Methods:** This prospective observational study was conducted at the Pediatric Neurosurgery Department of the Children's Hospital and the Institute of Child Health, Multan, Pakistan, from September 2023 to March 2025. A total of 120 newborns aged 0-28 days, who were diagnosed with hydrocephalus on clinical and radiological grounds and subsequently underwent surgical intervention, were analyzed. Postoperative complications and their association with demographic and clinical characteristics were assessed up to 30 days. Data were analyzed using IBM-SPSS Statistics, version 26.0. $P < 0.05$ was taken as significant. **Results:** Among 120 neonates, the mean age at presentation was 14.28 ± 7.53 days, gestational age 36.61 ± 1.93 weeks, and birth weight 2508.89 ± 375.78 grams. Preterm birth and low birth weight were seen in 64.2% and 52.5% neonates, respectively. Common etiologies included congenital (30.0%) and intraventricular hemorrhage (28.3%). Early postoperative complications occurred in 15.8%, with significantly longer hospital stays (9.21 ± 3.44 vs. 6.54 ± 1.78 days, $p < 0.001$). Prematurity ($p = 0.022$), low birth weight ($p = 0.044$), maternal infection ($p = 0.009$), congenital anomalies ($p = 0.033$), intraventricular hemorrhage ($p = 0.045$), and post-infectious hydrocephalus ($p = 0.033$) were significantly associated with complications. **Conclusions:** In neonates with hydrocephalus undergoing surgical management, intraventricular hemorrhage, post-infectious etiologies, prematurity, low birth weight, and abnormal antenatal history were significantly associated with early postoperative complications.

INTRODUCTION

Neonatal hydrocephalus is a neurological condition characterized by abnormal accumulation of cerebrospinal fluid (CSF) in the ventricular system of the brain, leading to increased intracranial pressure [1]. It may be congenital or acquired and poses significant risks to neurodevelopmental outcomes in infants [2]. The incidence of congenital hydrocephalus ranges between 0.5 and 1 per 1,000 live births worldwide [3]. Neonatal hydrocephalus contributes significantly to neurodevelopmental impairment and mortality, particularly in settings with limited access to neurosurgical

services. In low- and middle-income countries, post-infectious hydrocephalus accounts for a substantial proportion of cases [4]. The causes are diverse, including intraventricular hemorrhage (particularly in preterm infants), congenital anomalies such as aqueductal stenosis, infections like meningitis, and neoplasms [5, 6]. Early diagnosis and an appropriate surgical intervention are crucial in neonatal hydrocephalus for optimizing outcomes and minimizing long-term disabilities. The standard treatment involves CSF diversion techniques, most commonly ventriculoperitoneal (VP) shunting [7].

While shunt placement can alleviate symptoms and prevent further damage, complications such as infection, obstruction, or the need for revision are not uncommon [8]. Early postoperative outcomes are variable and influenced by factors including etiology, timing of intervention, and perioperative care [9]. Shunt-related complications can occur in 30-50% of cases within the first year of surgery [10].

Despite advancements in neuroimaging and surgical techniques, neonatal hydrocephalus remains a challenging condition with variable outcomes. There is a pressing need to understand the local etiological profile better, preferred surgical interventions, and early postoperative results to improve clinical protocols. By analyzing the causes, treatment approaches, and short-term surgical outcomes in neonates diagnosed with hydrocephalus, the findings would not only fill the knowledge gap but also help clinicians develop early intervention strategies, anticipate complications, and tailor postoperative care plans to achieve better patient outcomes. Therefore, the study aimed to determine the etiology and early postoperative outcomes in neonates diagnosed with hydrocephalus at a tertiary care center.

METHODS

This prospective observational study was conducted at the Department of Pediatric Neurosurgery of the Children's Hospital and the Institute of Child Health, Multan, Pakistan, from September 2023 to March 2025, after obtaining prior approval from the institutional ethical committee (letter number: ERC/78/23; dated 16th August 2023). A sample size of 120 was calculated using the WHO online sample size calculator based on the post-procedure infection rate of 27.6%, with 95% confidence level and 8% margin of error [11]. The inclusion criteria were neonates of any gender, aged 0-28 days, who were diagnosed with hydrocephalus on clinical and radiological grounds and subsequently underwent surgical intervention. Exclusion criteria were neonates with gestational age below 32 weeks, birth weight below 1000 grams, multiple congenital anomalies incompatible with life, previously operated hydrocephalus, or those who expired before surgery. Hydrocephalus was labeled based on clinical assessment, which included an abnormally enlarging head circumference, bulging anterior fontanelle, irritability, vomiting, and downward gaze (sun setting sign), along with confirmatory findings on neuroimaging (cranial ultrasound, CT scan, or MRI) demonstrating dilatation of the cerebral ventricles [12]. A non-probability consecutive sampling technique was used to recruit eligible participants. Data were collected on a structured proforma after obtaining informed written consent from the parents or legal guardians. Detailed demographic data, including age at presentation, gender,

mode of delivery, birth weight, gestational age, and antenatal history, were recorded. Etiological classification was done based on clinical history and radiological findings. Congenital aqueductal stenosis, intraventricular hemorrhage (IVH), neural tube defects (e.g., myelomeningocele), and post-infectious causes (e.g., ventriculitis or meningitis) were the main categories, along with other structural anomalies. The treatment plan, type of surgical procedure performed (most commonly ventriculo-peritoneal shunting), duration of surgery, and any intraoperative complications were noted. Postoperative follow-up was done for up to 30 days to assess early outcomes. Early postoperative outcomes included shunt malfunction (defined as clinical or radiological evidence of persistent or recurrent hydrocephalus due to obstruction, or displacement of the shunt), shunt infection (defined as fever, signs of meningitis, positive CSF culture, or signs of wound infection), and mortality (death occurring within 30 days of surgery regardless of cause).

The statistical analysis was carried out using "IBM-SPSS Statistics" version 26.0. The normality of the data was checked by applying the Shapiro-Wilk test. The quantitative variables, which included age, gestational age, duration of surgery, and birth weight, were expressed as mean and standard deviation (SD) or median and inter-quartile range (IQR). The qualitative data, comprising gender, mode of delivery, etiological classification, type of surgical procedure performed, intra-operative complications, and early postoperative outcomes (shunt malfunction, shunt infection, and mortality), were presented as frequency and percentage. The chi-square test was applied, considering a p-value of 0.05 for significance.

RESULTS

In a total of 120 neonates with hydrocephalus undergoing surgical interventions, the mean $\pm$ SD age at presentation, gestational age, and birth weight were 14.28 ± 7.53 days, 36.61 ± 1.93 weeks, and 2508.89 ± 375.78 grams, respectively. There were 74 (61.7%) males, and 77 (64.2%) were born preterm. Low birth weight (<2500 g) was observed in 63 (52.5%) neonates. The most common presenting features were enlarged head in 19 neonates (15.8%), poor feeding in 18 (15.0%), lethargy in 18 (15.0%), seizures in 16 (13.3%), irritability in 15 (12.5%), sun setting eyes in 12 (10.0%), bulging fontanelle in 11 (9.2%), and vomiting in 11 (9.2%). Etiologically, congenital aqueductal stenosis accounted for 30.0% of cases, followed by intraventricular hemorrhage (28.3%), post-infectious causes (19.2%), Dandy-Walker malformation (10.0%), myelomeningocele (5.8%), and other structural anomalies (6.7%). Table-1 is showing demographical, clinical, and

diagnostic characteristics of neonates.

Table 1: Demographical, clinical, and diagnostic characteristics of neonates (n=120)

Characteristics		Frequency (%)
Gender	Male	74 (61.7%)
	Female	46 (38.3%)
Age at Presentation (Days)	≤7	25 (20.8%)
	8-28	95 (79.2%)
Gestational Age	Preterm	77 (64.2%)
	Term	43 (35.8%)
Low Birth Weight		62 (51.7%)
Maternal Age (Years)	<30	61 (50.8%)
	≥30	59 (49.2%)
Mode of Delivery	Assisted	15 (12.5%)
	Cesarean	48 (40.0%)
	Vaginal	57 (47.5%)
Place of Birth	Hospital	109 (90.8%)
	Home	11 (9.2%)
Antenatal History	Normal	50 (41.7%)
	Maternal Infection	28 (23.3%)
	Congenital Anomaly	23 (19.2%)
	Polyhydramnions	19 (15.8%)
Etiology	Congenital	36 (30.0%)
	Dandy-Walker	12 (10.0%)
	Intraventricular Hemorrhage	34 (28.3%)
	Myelomeningocele	7 (5.8%)
	Post-Infectious	23 (19.2%)
	Other	8 (6.7%)

The mean duration of hospitalization was 6.97 ± 2.33 days, ranging between 2-16 days. Early postoperative complications were observed in 19 neonates (15.8%) (Figure 1).

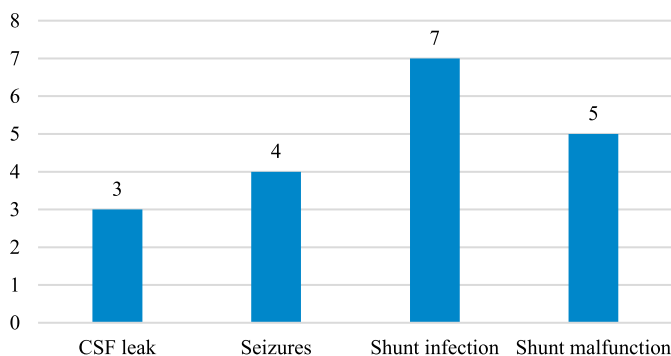


Figure 1: Post-operative complications (n=19)

The mean duration of postoperative hospitalization was significantly longer among neonates with complications than among those without complications (9.21 ± 3.44 vs. 6.54 ± 1.78 days, $p < 0.001$). Readmission due to complications was noted in 6 cases (5.0%). No mortality was reported during the study period (Figure 2).

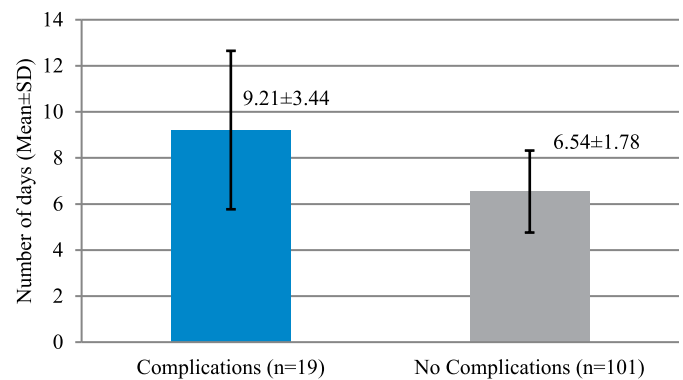


Figure 2: Duration of Hospitalization Among Neonates with and Without Post-Operative Complications (n=120)

Prematurity (78.9% vs. 50.5%; $p = 0.022$) and low birth weight (73.7% vs. 48.5%; $p = 0.044$) were significantly associated with postoperative complications. Abnormal antenatal history, including maternal infection ($p = 0.009$), and presence of congenital anomalies ($p = 0.033$) also showed significant associations. In terms of etiologies, intraventricular hemorrhage ($p = 0.045$) and post-infectious hydrocephalus ($p = 0.033$) were significantly more frequent in neonates with complications (Table 2).

Table 2: Association of Post-Operative Complications with Demographic and Clinical Characteristics of Neonates (n=120)

Characteristics		Post-Operative Complications		p-value
		Yes (n=19)	No (n=101)	
Gender	Male	9 (47.4%)	65 (64.4%)	0.162
	Female	10 (52.6%)	36 (35.6%)	
Age at Presentation (Days)	≤7	6 (31.6%)	19 (18.8%)	0.209
	8-28	13 (68.4%)	82 (81.2%)	
Gestational Age	Preterm	15 (78.9%)	51 (50.5%)	0.022
	Term	4 (21.1%)	50 (49.5%)	
Low Birth Weight		14 (73.7%)	49 (48.5%)	0.044
Maternal Age (Years)	<30	11 (57.9%)	50 (49.5%)	0.502
	≥30	8 (42.1%)	51 (50.5%)	
Mode of Delivery	Assisted	3 (15.8%)	12 (11.9%)	0.836
	Cesarean	8 (42.1%)	40 (39.6%)	
	Vaginal	8 (42.1%)	49 (48.5%)	
Place of Birth	Hospital	17 (89.5%)	92 (91.1%)	0.823
	Home	2 (10.5%)	9 (8.9%)	
Abnormal Antenatal History	Maternal Infection	8	16	0.009
	Congenital Anomaly	7	16	0.033
	Polyhydramnions	4	15	0.497
Etiology	Congenital	2	34	0.070
	Dandy-Walker	—	12	0.113
	Intraventricular Hemorrhage	9	25	0.045
	Myelomeningocele	1	6	0.908
	Post-Infectious	7	16	0.033
	Other	—	8	0.204

Surgical Procedure	Endoscopic Third Ventriculostomy	1(5.3%)	5(5.0%)	0.716
	External Ventricular Drain	4(21.1%)	14(13.9%)	
	Ventriculoperitoneal Shunt	14(73.7%)	82(81.2%)	

DISCUSSION

In the present neonatal hydrocephalus cohort, the predominance of preterm births (64.2%) and low birth weight (52.5%) corresponds closely with Mandzukovska et al. who found 60.8% of hydrocephalic neonates to be preterm, and a birth weight of 2120 grams [13]. The higher frequency of IVH underscores the pathophysiological vulnerability of preterm infants to germinal matrix hemorrhage, a known precursor of post-hemorrhagic hydrocephalus. In this study, IVH was significantly associated with postoperative complications ($p=0.045$), a finding echoed in the cost-analysis study by Mancha et al. where 40% of infants undergoing neurosurgical procedures had IVH, and infection rates reached 11% within 30 days of surgery [14]. Congenital aqueductal stenosis, representing 30.0% of cases in the current analysis, remains one of the most commonly encountered causes of obstructive hydrocephalus in neonates. This is consistent with the descriptive study conducted by Deshmukh and Yadav who identified aqueductal stenosis as the leading congenital cause [15]. Congenital hydrocephalus was not significantly associated with early postoperative complications ($p=0.070$), possibly due to the absence of inflammatory debris and better anatomical delineation, facilitating more effective shunt function. Post-infectious hydrocephalus was significantly associated with early complications ($p=0.033$), including shunt infection and malfunction. This aligns with findings from a local study by Bakhsh who documented a 14% shunt infection rate and a 10% failure rate in infants with post-meningitic hydrocephalus [16]. The higher risk in this subgroup is biologically plausible given the altered CSF characteristics, inflammation-mediated adhesions, and higher rates of colonization during shunt placement. Mottolese et al. observed a 90.9% complication rate in children with abnormal CSF findings at the time of shunt insertion, reinforcing the idea that infected or proteinaceous CSF predisposes to mechanical and infective shunt failure [17]. Early and appropriate preoperative management of infection may be pivotal in mitigating adverse outcomes in this high-risk population. The overall postoperative complication rate of 15.8% in this study is relatively lower than rates observed in several retrospective and prospective studies. Kumar et al. reported a 32.0% overall complication rate, with shunt malfunction (29.2%) and infection (4.4%) being the most common [18]. The comparatively lower complication rate in the current study

may be attributed to strict exclusion criteria, which omitted neonates with birth weight below 1000 g and those with multiple anomalies incompatible with life. Rigorous aseptic surgical protocols and specialized pediatric neurosurgical care may have contributed to improved short-term outcomes. No early mortality was recorded during the 30-day follow-up period in the present study. This contrasts with the findings of Lodha et al. who reported a 17.5% mortality rate, predominantly in infants younger than 3 months following endoscopic third ventriculostomy (ETV) [19]. The zero mortality in this study reflects both the inclusion of only hemodynamically stable neonates and the efficacy of perioperative management. The possibility of delayed complications beyond 30 days, such as shunt dependency or neurodevelopmental deficits, remains a concern and was not captured in the current follow-up window. In terms of procedure type, ventriculoperitoneal shunting was performed in 80.0% of cases, consistent with its continued designation as the standard of care for neonatal hydrocephalus. Although not significantly associated with early complications in this study ($p=0.716$), VP shunts inherently carry a long-term risk of mechanical failure and infection. Ji et al. have shown that both ETV and VPS can result in cognitive improvement, although VPS yielded more significant gains in infants [20]. Sharafat et al. found a 57.1% success rate of ETV in infants under one year, with low rates of complications [21]. The present study reaffirms that ETV remains underutilized in neonates, largely due to anatomical and physiological limitations, and its effectiveness remains lower in children under 3–6 months of age, as supported by Kim et al. and Lodha et al [19, 22]. This study also found that the mean duration of hospitalization was significantly prolonged among neonates with complications (9.21 ± 3.44 days vs. 6.54 ± 1.78 days, $p<0.001$). This observation corroborates the findings of Mancha et al. who reported that postoperative infections extended NICU stay by approximately 10.6%, thereby increasing overall healthcare costs [14]. This reinforces the clinical and economic imperative to prevent shunt-related complications in the neonatal population. The importance of antenatal history, particularly maternal infection and polyhydramnios, is underscored in the current data, where maternal infection demonstrated a statistically significant association with complications ($p=0.009$). This parallels findings from Abebe et al. who emphasized antenatal infections as a key risk factor for congenital hydrocephalus [2]. While polyhydramnios was not significantly associated with complications in this study ($p=0.497$), it remains an important antenatal marker and has been linked to neural tube defects such as myelomeningocele in previous literature, like Venkataramana and Mukundan who found that even children with spina bifida can achieve favorable

developmental outcomes post-shunting if managed early [23]. The presence of seizures (21.1%) and CSF leaks (15.8%) among those with postoperative complications corresponds to the complication spectrum reported in similar populations. The present study contributes valuable data from a low-to-middle-income country (LMIC) context, where resource limitations, late presentation, and inconsistent antenatal care frequently influence surgical outcomes. This setting makes the relatively low complication and mortality rates particularly noteworthy and offers a benchmark for similar tertiary centers in the region. The findings in this study carry important clinical implications. The identification of prematurity, low birth weight, and specific etiologies (post-infectious and IVH) as predictors of early complications underscores the need for risk-stratified perioperative planning. Antenatal screening for infections and structural anomalies should be reinforced, particularly in settings with limited resources. The study also reaffirms that while VP shunting remains the primary intervention, attention to patient selection, early diagnosis, and meticulous surgical technique can substantially reduce complication rates. Incorporating protocols for preoperative CSF drainage in high-risk neonates may further reduce morbidity [17, 24]. Several limitations of this study must also be acknowledged as well. The follow-up period was limited to 30 days, precluding assessment of long-term complications, such as shunt dependency, neurodevelopmental delay, or cognitive impairment. The exclusion of neonates with birth weight <1000 grams or gestational age <32 weeks may have introduced selection bias, limiting the generalizability of the findings to extremely low birth weight and extremely premature infants. While this study relied on structured clinical and radiologic criteria for hydrocephalus classification, volumetric imaging tools such as FOHR or Evan's Index were not routinely employed, which could enhance risk stratification and guide intervention decisions.

CONCLUSIONS

In neonates with hydrocephalus undergoing surgical management, intraventricular hemorrhage, post-infectious etiologies, prematurity, low birth weight, and abnormal antenatal history were significantly associated with early postoperative complications. The use of ventriculoperitoneal shunts remained the predominant surgical modality, with a relatively lower complication rate and no reported mortality within 30 days. These findings highlight the prognostic relevance of birth and etiological characteristics in predicting early outcomes and underscore the need for targeted perioperative strategies to improve the care and outcomes of neonates with hydrocephalus, particularly in resource-constrained settings.

Authors' Contribution

Conceptualization: SA, SZHS, ZK

Methodology: SA, SSK, MAW

Formal analysis: SA, SSK, SZHS, MAW, ZK

Writing and Drafting: SSK, UU

Review and Editing: SA, SSK, SZHS, MAW, UU, 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



Comparison of Induction of Labour with Sublingual Versus Vaginal Misoprostol 25 UG in a Primigravida with Post-Date Pregnancy

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ABSTRACT

In obstetrics, the induction of labour has been widely used in clinical practice for a decade. Misoprostol is effective for the induction of labour. It can be administered either sublingually or via the vaginal route. **Objective:** To compare the induction of labour with sublingual versus vaginal Misoprostol 25 ug in primigravida with postdate pregnancy. **Methods:** Our Study Prospective Comparative Study with consecutive sampling, conducted at the department of Gynecology, and Obstetrics at Saidu Group of Teaching Hospitals Swat, from March 2025 to September 2025 (6 months duration). **Results:** 160 participants were analyzed, with 80 in Group A (sublingual) and 80 in Group B per-vaginal route). Vaginal delivery within 24 hours occurred in 84.4% of the sublingual group and 80.8% of the vaginal group ($p=0.612$), while the mean induction-to-delivery time was significantly shorter in the sublingual group (9.1 ± 2.9 hrs vs. 10.4 ± 3.2 hrs; $p=0.04$). Maternal side effects and neonatal outcomes, including Apgar scores and birth weights, were comparable between the two groups. **Conclusions:** Both sublingual and vaginal misoprostol (25 μ g) were effective for labour induction in post-date primigravida. The sublingual route demonstrated a significantly shorter induction-to-delivery interval with comparable safety outcomes, offering a practical alternative for routine clinical use.

INTRODUCTION

Induction of labour was first described by Thomas Denman, who explained amniotomy in his textbook in the 1780s [1]. In obstetrics, induction of labour has been widely used in clinical practice for decades. This trend has significantly increased, especially in the last few years, during which around 9.6% of worldwide deliveries have been medically induced. These statistics are particularly high in the United States and Europe, where around 27% and 33% of overall deliveries are induced through medical therapy [2, 3]. There are several indications for the Induction of labour (IoL); the most common ones are when maternal or fetal life is at risk with an ongoing pregnancy and gestational age

above 41 weeks. According to the literature, in a high-risk pregnancy, one can induce labour preterm (<37 weeks), and, whenever possible, IoL should be delayed until 39 weeks of pregnancy. Most international guidelines recommend induction of labour at or after 41 weeks of gestation [4, 5]. In obstetrics, induction of labour is one of the most significant practices, and over the past decade, the number of women undergoing induction of labour has increased substantially [6]. The mechanical methods were previously used for labour induction, but these conventional methods have largely been replaced by medical therapy, including Prostaglandins and synthetic



oxytocin. Misoprostol is currently a topic of interest among scholars as it is a more convenient and much safer alternative for the induction of labour [7]. It promotes cervical ripening and enhances cervical dilatation, resulting in shorter duration of labour and facilitates vaginal delivery [8]. Misoprostol is effective for the induction of labour. It can be administered either sublingually or via the vaginal route. Current international guidelines support dose-adjusted misoprostol, which should not exceed 25mg to prevent maternal and neonatal adverse outcomes [9]. Women often prefer to take misoprostol orally due to various concerns, one of which is that oral administration is more convenient and provides privacy compared to the vaginal route. However, the literature does not provide strong evidence regarding the best route for misoprostol administration in induction of labour [10].

Although multiple studies in the literature described different administration routes, the existing literature lacks research studies evaluating how sublingual misoprostol compares to vaginal administration in terms of safety and efficacy. Therefore, our study aimed to address the literature gap by answering the question: Is sub-lingual misoprostol (25mg) as effective and safe as vaginal misoprostol (25mg) for the induction of labor in primigravida women with post-dated pregnancy in our set-up? our study aims to compare the induction of labour with sublingual versus vaginal Misoprostol 25 ug in primigravida with postdate pregnancy at the tertiary care hospital of the northern region of Pakistan. Finding the optimal route of misoprostol administration would help the clinician to improve maternal comfort, effective labor induction, and minimize adverse effects.

METHODS

This was a prospective comparative study employing consecutive sampling conducted at the Department of Gynecology and Obstetrics of Saidu Group of Teaching Hospitals, Swat from July 2025 to December 2025 (6 months duration). Ethical approval was obtained from the Institutional Review Board of Saidu Medical College (IRB-SMC number = 90-ERB/024; dated 3rd June 2024). The required sample size was calculated using a WHO sample size calculator based on the following specifications: level of significance = 5%, statistical power of 80%, an expected prevalence of 91.0% for population group A and 89.0% for population Group B [11]. For the given population, the optimal sample size for the study was 160 patients. Data were collected using a preformed questionnaire through the consecutive sampling technique. To control cofounders and minimize bias, patients were recruited after obtaining written informed consent using a predefine inclusion and exclusion criteria. Inclusion criteria include:

maternal age ranging from 15 to 45 years, Primigravida with singleton pregnancy, single gestation with viable fetus in cephalic position, live fetus with cephalic presentations, and gestational age exceeding ≥ 40 weeks. While exclusion criteria include those having history of uterine surgery, major fetal malformation, patients having premature rupture of membrane, antepartum hemorrhage, Patients with documented known medical comorbidities, or any other contraindication to vaginal delivery. For this study, labor induction was defined as the initiation of uterine contraction before the spontaneous onset of labor for vaginal delivery, using either pharmacological or mechanical methods [12]. Uterine tachysystole was defined as excessively frequent uterine contractions during pregnancy, typically more than 5 uterine contractions per 10 min in consecutive. Failed induction was defined as the necessity for cesarean delivery due to failure to establish active labor (cervical dilation ≥ 4 cm with adequate contractions) after completion of the maximum six doses of misoprostol (25 μ g every 4 hours for 24 hours). Intervals [13]. Fetal distress was defined as compromised fetal well-being indicated by pathological pattern of fetal heart rate including late decelerations, and persistent bradycardia (< 110 bpm), or loss of variability on continuous CTG interpreted by an obstetrician. [14]. Uterine hypertonus, as a single contraction lasting > 2 minutes or baseline intrauterine pressure > 25 mmHg, whereas hyperstimulation involves hypertonic activities associated with non-reassuring fetal heart rate patterns, both are well-recognized complications of labor induction with prostaglandins. After obtaining approval of Ethical Committee of Saidu Medical College, Swat, all 160 patients were stratified into two groups i.e. Group A, and Group B. The group-A received vaginal misoprostol (25 μ g) and Group B sublingual misoprostol (25 μ g), administered 4-hourly up to six doses. Continuous electronic fetal monitoring (cardiotocography) was performed for 20-30 minutes prior to administering each repeat dose to confirm fetal well-being and absence of uterine tachysystole. Detailed history, physical, and obstetric examinations, and Bishop scoring were performed at admission. Bishop scoring was performed by a single trained obstetrician at admission to ensure consistency. Labor progress and fetal heart rate were monitored; subsequent doses were administered until effective uterine contractions (3 contractions every 10 mins), cervical dilation > 3 cm, Bishop score > 8 , or complications (tachysystole, hypertonus, or hyperstimulation) occurred. In the event of such complications, patients were managed with left lateral positioning, oxygen (8 L/min) via face mask, and subcutaneous terbutaline (250 μ g). The principal outcome assessed was the frequency of vaginal birth. The study also identified total drug administration, duration from drug

administration to birth completion, failure of induction within 24 hours, pathological uterine contractions, undesired maternal response, fetal compromise, newborn Apgar scores, and requirement for NICU admissions.

For data analysis SPSS software version 22.0 was employed. For descriptive variables, mean $\pm$ standard deviation was computed for continuous variables (age, mean birth weight, and Apgar score), and frequencies and percentages for categorical variables (mode of delivery, uterine activity abnormalities, side effects, fetal distress, and NICU admissions). Comparative analysis between the two groups was performed for all key outcomes. Effect modifiers such as age, uterine tachysystole, hypertonus, hyperstimulation, side effects, and fetal outcomes were stratified, and post-stratification comparisons were made using the Chi-square test. The primary outcome (vaginal birth rate within 24 hours) was analyzed using the Chi-square test (or Fisher's exact test, as appropriate for cell counts) to compare proportions between Group A (sublingual) and Group B (vaginal). Independent t-test or Mann-Whitney U test were used for continuous variables. p -value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 160 primigravida with post-date pregnancy were recruited into two groups for the study over six months of duration. In Group A, three patients and 2 in group B underwent cesarean section and were excluded from final data analysis. 77 patients in group A received sublingual misoprostol 25 mg, and 78 patients in group B received vaginal misoprostol. Mean age of participants in group A was 25.9 ± 3.4 years and 26.3 ± 3.9 years in group B. In group A, the mean gestational age was 41.1 ± 0.6 weeks, while in group B it was 41.3 ± 0.8 weeks. The mean Bishop score at admission in group A was 3.1 ± 0.9 , while in group B it was 3.0 ± 1.1 . The comparison shows that there were no statistically significant differences between the two groups regarding mean age, gestational age, and Bishop score (Table 1).

Table 1: Baseline Characteristics among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Mean Age (Years)	25.9 ± 3.4	26.3 ± 3.9	0.61
Mean Gestational Age (Weeks)	41.1 ± 0.6	41.3 ± 0.8	0.46
Mean Bishop Score (at Admission)	3.1 ± 0.9	3.0 ± 1.1	0.71

Among group A, 65 out of 77 participants (84.41%) achieved vaginal delivery within 24 hours, while in group B, 63 participants achieved that ($p=0.612$). Moreover, the mean induction to delivery interval was calculated and compared between the two groups. This interval was significantly shorter in the sublingual group (9.1 ± 2.9 hours) compared to the vaginal misoprostol group (10.4 ± 3.2 hours) ($p=0.04$).

Additionally, the average misoprostol dose required in the sublingual group was relatively lower (i.e., 3.1 ± 0.7) compared to the vaginal misoprostol group (3.5 ± 1.1) ($p=0.735$). The labor and delivery outcomes in Group A (sublingual) and Group B (per-vaginal route). While the two cohorts showed similar success rates for vaginal delivery within a 24-hour window ($p>0.05$), Group A exhibited a statistically significant reduction in the mean induction-to-delivery time compared with Group B ($p<0.05$). Additionally, the mean dose requirement did not differ significantly between the groups (Table 2).

Table 2: Labor and Delivery Outcomes among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Vaginal Delivery within 24 hours	n=65 (84.41%)	n=63 (80.76%)	0.61
Mean induction delivery interval (Hours)	9.1 ± 2.9 hours	10.4 ± 3.2 hours	0.04
Mean number of doses required	3.1 ± 0.7	3.5 ± 1.1	0.73

Maternal side effects and uterine activity were assessed in both groups. In Group A (Sublingual), 10 participants developed tachysystole, 4 developed hypertonus, 3 developed hyperstimulation syndrome, 3 developed fever, and 08 patients experienced nausea and vomiting. In Group B (Vaginal misoprostol), 6 developed tachysystole, 3 developed hypertonus, 2 developed hyperstimulation syndrome, 5 developed fever, and 6 experienced nausea and vomiting. The incidence of tachysystole, hypertonus, hyperstimulation syndrome, fever, and nausea/vomiting was comparable between the sublingual and per-vaginal groups. There were no statistically significant differences between any parameter ($p>0.05$) (Table 3).

Table 3: Maternal Side Effects and Uterine Activity among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Tachysystole	n= 10	n= 06	0.30
Hypertonus	n= 04	n= 03	0.71
Hyperstimulation Syndrome	n= 03	n= 02	0.65
Fever ($>38^{\circ}\text{C}$)	n= 03	n= 05	0.54
Nausea and Vomiting	n= 08	n= 06	0.62

Neonatal outcomes were also assessed in both groups. In Group A, the mean birth weight was 3.31 ± 0.30 kg, while in Group B the mean birth weight was 3.28 ± 0.34 kg ($p=0.60$). The mean 5-minute Apgar score for neonates delivered in Group A was 8.8 ± 0.5 , while in Group B, the mean 5-min Apgar score was 8.6 ± 0.5 with no statistical significance ($p=0.43$). Five patients in Group A and four in Group B developed fetal distress ($p=0.73$). Mean birth weight and 5-minute Apgar scores were comparable between the

sublingual and per-vaginal groups, and the incidence of fetal distress was low in both. No statistically significant differences were observed ($p > 0.05$) (Table 4).

Table 4: Neonatal outcomes among study participants

Variables	Group A (Sublingual)	Group B (Per-Vaginal route)	Level of Significance (p)
Mean Birth weight (in Kg)	3.31 ± 0.30	3.28 ± 0.34	0.60
Mean 5-min Apgar score	8.8 ± 0.5	8.6 ± 0.5	0.43
Fetal Distress	n=5	n=4	0.73

DISCUSSION

Initiation of labour is one of the most common obstetrical interventions. A decade or more ago, mechanical techniques such as balloon catheter and amniotomy were used for cervical ripening. However, at present, pharmacological agents, including prostaglandins, are more commonly used in case of an unfavorable cervix, as they act on both the cervix and the uterus to increase contractions [15]. In our study, we compared induction of labour using sublingual versus per-vaginal misoprostol in primitive gravida. Our principal finding indicated that participants receiving sublingual misoprostol exhibited a shorter induction to delivery interval compared to those administered vaginal misoprostol ($p = 0.04$), our findings do support by multiple studies in literature including the study carried out by Shafqat et al. in Peshawar Pakistan (the population with same cultural and demographic profile like our study population) concluded that, the use of misoprostol could reduce mean induction to delivery time [16]. A meta-analysis conducted by Pergialiotis et al. [17] concluded that the sublingual misoprostol administration could lead to a decrease in induction to delivery time compared to the per-vaginal route without any accompanying side effects. Although both of them are equally safe in terms of induction of labour. Moreover, aside from comparison with per-vaginal administration, sublingual administration also had reduced induction to delivery time when compared with per-oral administration of misoprostol [18]. All these studies support our study findings. Additionally, in contrast to our study findings, some studies in the literature have found no difference between the two groups. A study conducted by Galidevara et al. [19], comparing oral, vaginal, and sublingual routes of misoprostol administration, concluded that all three routes of misoprostol administration are equally effective for labor induction. However, there was no statistical significance difference ($p = 0.88$). Moreover, the maternal and neonatal side effects in both groups were also compared in our study. Maternal side effects included Tachysystole, Hypertension, and Hyperstimulation syndrome. Several studies in the literature have also reported the maternal side effects associated with

sublingual and vaginal misoprostol use [20].

Overall, the incidence of side effects varies and depends upon the route, dose, and population. The prospective comparative design represents a notable strength of this study, which helps in minimizing bias. The use of consecutive sampling and adherence to standard protocols ensures consistency in data collection and analysis between groups. However, our study has certain limitations: because the data were collected from only one, the findings may not be readily generalizable to wider populations. Future research should consider multicenter studies with larger cohorts to validate these findings. Despite these limitations, our study can assist the clinician in identifying the more effective and safer route of misoprostol administration for the induction of labour, improving overall maternal and neonatal outcomes. Implementation of the results could enhance safe, cost-effective, and standardized labour induction practice.

CONCLUSIONS

In this study, both the sublingual, and vaginal misoprostol (25 µg) were equally effective for labour induction in post-date primigravida women with comparable vaginal delivery rates and safety outcomes. However, the sublingual route shows a significantly shorter induction-to-delivery interval and offers the practical advantage of non-invasive administration. Overall, sublingual misoprostol can be considered an effective and practical alternative to the vaginal route for routine clinical use.

Authors' Contribution

Conceptualization: HG, STK

Methodology: HG, SK, S

Formal analysis: STK, KJ, N

Writing and Drafting: KJ, SK, ZI

Review and Editing: HG, STK, KJ, SK, ZI, S, N

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



Patient Preferences and Concerns Regarding Stoma Formation Versus Sphincter-Sparing Surgery in Rectal Cancer

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ABSTRACT

The outcome of the decision between stoma construction and sphincter-sparing procedures is critical to the quality of life of the patients after a rectal cancer operation. In a socio-culturally diverse society like Pakistan, clinical outcomes are significant to the surgeon to reach a decision, but the views of the patients are significant as well. **Objectives:** To assess the preferences and concerns of rectal cancer patients regarding permanent stoma formation versus sphincter-preserving surgery in Khyber Pakhtunkhwa (KPK), Pakistan. **Methods:** This analytical cross-sectional study was carried out in the Department of General Surgery, Hayatabad Medical Complex, Peshawar, between January 2022 and December 2024. A total of 250 patients with rectal cancer were enrolled. The final analysis included 220 patients after excluding those who had undergone previous surgery (n=12), cognitive impairment (n=8), recurrent rectal cancer (n=6), and those who refused participation (n=4). **Results:** Among 220 respondents, 63.6% preferred sphincter-sparing surgery and 36.4% preferred abdominoperineal resection (APR). Female gender (p<0.069), rural residence (p=0.024), and a high concern level (p<0.001) were significant predictors of preference for APR, while knowledge of stoma was associated with lower odds of APR preference (p<0.012). Higher education (p=0.165) and age (p=0.271) were not statistically significant. **Conclusions:** Psychosocial, informational, and demographic factors all affect patient preferences for rectal cancer surgery. Patients with greater preoperative concerns, female gender, and those who lived in rural areas were all linked to a stoma favor. However, prior experience with stoma care was protective of this choice.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common causes of cancer morbidity and mortality globally, and noticeably, rectal cancer represents a considerable proportion of cases [1]. Rectal cancer surgery requires decision-making between sphincter-sparing procedures (SSP) and abdominoperineal resection (APR), with a permanent stoma. Although oncological outcomes are still the main issue, patient-related endpoints, such as QoL, body image, and psychosocial adjustment, have attracted more attention in the decision-making process of surgical treatment [2, 3]. The principles of sphincter-saving operation are to enhance sphincter function while

achieving tumor clearance [4]. But such interventions may not always be practical because of tumor placement, size, or anatomic limitations of the patient. When this is not possible, APR, colorectal resection with permanent stoma (APR) is mandatory [5, 6]. Despite improvements in stoma care and education, a lot of patients maintain a great deal of anxiety about having to live with a stoma, including fears about social stigma, intimacy, alteration of lifestyle, and long-term psychological burden [7]. On the other hand, SSPs retaining the anal sphincter interim a low anterior resection syndrome (LARS) with urgency, incontinence, and frequent bowel motion may affect QoL aspects [8].



Therefore, the balances of each of these options are intricate and frequently tied to a patient's desire, cultural influences, and socioeconomic considerations [9]. The results of this survey should guide shared decision-making, enhance preoperative counselling, and shape culturally sensitive strategies for care.

In low- and middle-income countries (LMICs) such as Pakistan, where health literacy is variable, and stoma care facilities are not universal, it is important to understand patient experiences of undergoing rectal cancer surgery. There is no local literature available about patients' perception and preferences regarding these surgical options, more so in the local population of Khyber Pakhtunkhwa with its own cultural and health care trends. This study aimed to evaluate patients' preferences and concerns for stoma creation and sphincter-saving surgery in rectal cancer patients of Khyber Pakhtunkhwa.

METHODS

This analytical cross-sectional study was conducted in the Department of General Surgery, Hayatabad Medical Complex, Peshawar, Khyber Pakhtunkhwa (KPK), Pakistan, from January 2022 to December 2024. Approval was taken from the Institutional Review Board (IRB) of Hayatabad Medical Complex, Peshawar, before the start of the study under reference no: 1110 on 19th December 2021. A total of 250 rectal cancer patients were assessed for eligibility during the study period. After excluding patients who had undergone prior surgery ($n=12$), had cognitive impairment ($n=8$), recurrent rectal cancer ($n=6$), or declined participation ($n=4$), 220 patients were included in the final analysis (88%). The sample size was calculated using the formula $n = Z^2 p (1-p) / d^2$ for cross-sectional prevalence studies [10]. Taking the anticipated prevalence of preference for APR as 38% from Lee *et al.* [11], with 95% confidence level and 6.5% absolute precision, the minimum required sample size was 214; hence, the final sample of 220 patients was adequate. Inclusion criteria were: age > 18 years, having histological evidence of rectal adenocarcinoma, and being a known case for radical surgical therapy (i.e., undergoing either abdominoperineal resection or sphincter-preserving surgery). Patients with recurrent disease, cognitive impairment, or previous surgery were excluded in order to prevent bias in preference reporting. The standardized interviewer-administered questionnaire was designed to collect the data after the written and informed consent was received. The English-language questionnaire was translated into Urdu and Pashto so that it would be easy to understand. It contained demographic data, clinical history, the knowledge of surgical choices, and perception and particular concerns on stoma or sphincter-sparing surgery. The relevance of the questions and their clarity

were identified after the pre-test on a sample of 20 patients, and the required changes were made. A surgical resident used standardized materials to teach patients about the two main surgical options: abdominal perineal resections (APR) and sphincter-preserving procedures. Following that, they were asked if they had a preference, if they thought either operation had benefits or drawbacks, and whether they were afraid of or unwilling to do any of the suggested procedures.

IBM SPSS 25.0 was used to process and input all of the data. Descriptive statistics were used to summarize clinical and demographic features. Numbers and percentages were used to represent categorical variables. The relationships between patient preferences and clinical and demographic factors were assessed using the chi-square test, or Fisher's exact test if necessary. A statistically significant difference was defined as $P \leq 0.05$.

RESULTS

Among the 220 respondents, most patients preferred sphincter-sparing surgery, with approximately two-thirds selecting SSP compared with about one-third preferring APR. Nevertheless, the proportion of patients who expressed major concerns in the case of the sphincter group was 75 (53.6%), with most of the concerns being related to bowel control, urgency, and disruption in lifestyle. Conversely, 65 (81.3%) patients in the stoma group raised serious concerns, which included the fear of social stigmatization, body image, and practical difficulties of dealing with the stoma. Regional distribution showed a total of 120 (54.5%) belong to urban areas of the KPK, and the remaining 100 (45.5%) belong to rural areas (Table 1).

Table 1: Summary of Patient Enrolment and Preferences

Variables	n (%)
Preferred Sphincter-Sparing Surgery	140 (63.6%)
Preferred Stoma (APR)	80 (36.4%)
Major Concerns - Sphincter Group	75 (53.6%)
Major Concerns - Stoma Group	65 (81.3%)
Urban	120 (54.5%)
Rural	100 (45.5%)

Gender distribution differed between surgical preference groups. Among patients preferring sphincter-sparing surgery, 85 (60.7%) were male, and 55 (39.3%) were female. In contrast, among patients preferring APR, 35 (43.7%) were male and 45 (56.3%) were female, indicating a relatively higher proportion of females opting for permanent stoma formation (Figure 1).

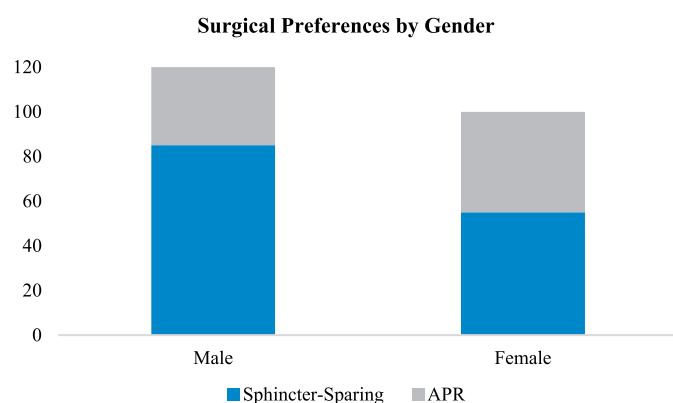


Figure 1: Surgical Preference by Gender

Similarly, residence was associated with surgical preference. Among urban residents, 90 patients (40.9%) preferred sphincter-sparing surgery, while 30 (13.6%) opted for APR. Among rural residents, 50 patients (22.7%) preferred sphincter-sparing surgery and 50 (22.7%) preferred APR, suggesting a comparatively higher inclination toward permanent stoma formation among rural patients (Figure 2).

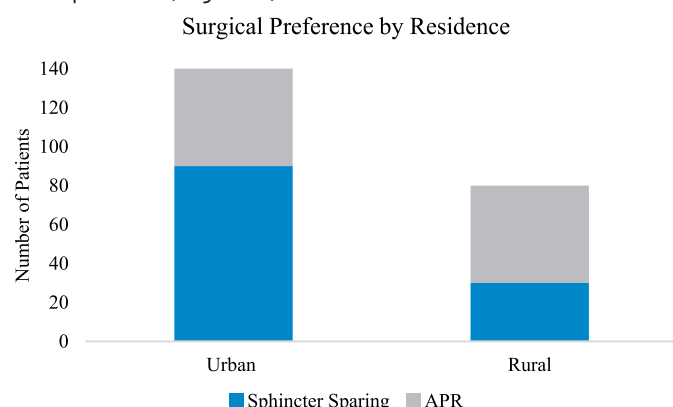


Figure 2: Surgical Preference by Residence

Univariate analysis was conducted to analyse the relationship between patient attributes and preference for permanent stoma formation (APR). There was a strong correlation between female gender and preference for APR with rural residence. On the same note, patients who were more concerned were also much more likely to choose APR, and good knowledge of stoma care also correlated with low chances of opting to permanently form the stoma. The higher education exhibited the trend of sphincter-preserving surgery; however, not statistically significant. The variables that might have a connection in the univariate analysis were later incorporated in the multivariate logistic regression model to come up with independent predictors of surgical preference (Table 2).

Table 2: Univariate Analysis of Factors Associated with Preference for Permanent Stoma (APR)

Variables	SSP, n (%)	APR, n (%)	COR	95% CI	p-value
Gender					
Male	85 (60.7%)	35 (43.7%)	1.00	Reference	—
Female	55 (39.3%)	45 (56.3%)	1.98	1.13–3.46	0.017*
Residence					
Urban	90 (64.3%)	30 (37.5%)	1.00	Reference	—
Rural	50 (35.7%)	50 (62.5%)	3.00	1.67–5.37	<0.001*
Education Level					
Lower education	70 (50.0%)	50 (62.5%)	1.00	Reference	—
Higher education	70 (50.0%)	30 (37.5%)	0.60	0.34–1.06	0.079
Knowledge of Stoma Care					
Poor Knowledge	60 (42.9%)	55 (68.8%)	1.00	Reference	—
Good Knowledge	80 (57.1%)	25 (31.2%)	0.34	0.18–0.64	0.001*
Concern level					
Low Concern	95 (67.9%)	15 (18.8%)	1.00	Reference	—
High Concern	45 (32.1%)	65 (81.2%)	9.13	4.73–17.6	<0.001*

COR = Crude Odds Ratio, CI = Confidence Interval, APR = Abdominoperineal Resection, SSP = Sphincter-Sparing Procedure, *Statistically significant at $p \leq 0.050$

To identify independent predictors of surgical preference, binary logistic regression analysis was performed with preference for APR as the dependent variable. The analysis demonstrated that female gender (OR = 2.31, 95% CI: 1.26–4.24; $p < 0.069$) and rural residence (OR = 2.67, 95% CI: 1.42–5.03; $p < 0.024$) were significant predictors of preference for APR. Additionally, higher levels of concern were strongly associated with choosing APR (OR = 3.86, 95% CI: 2.10–7.11; $p < 0.001$). Conversely, knowledge of stoma care was associated with lower odds of preferring APR (OR = 0.36, 95% CI: 0.19–0.67; $p < 0.012$). In contrast, higher education (OR = 1.52; $p = 0.165$) and age (OR = 1.01; $p = 0.271$) were not statistically significant predictors of surgical preference (Table 3).

Table 3: Results of Multivariable Binary Logistic Regression for Preference for APR

Variables	AOR	95% CI (Lower–Upper)	p-value
Female Gender	2.31	1.26–4.24	<0.069*
Rural Residence	2.67	1.42–5.03	<0.024*
Higher Education	1.52	0.84–2.76	0.165
Knowledge of Stoma	0.36	0.19–0.67	<0.012*
High Concern Level	3.86	2.10–7.11	<0.001*
Age (Years)	1.01	0.99–1.04	0.271

AOR = Adjusted Odds Ratio; CI = Confidence Interval. * Statistically significant at $p \leq 0.050$

DISCUSSION

In this study, women were much more likely than men to choose permanent stoma formation (OR = 2.31; $p < 0.069$). Mak *et al.* stated that male patients were not as willing to accept APR due to uremic concerns like sexual function

and appearance after the creation of a stoma [12]. On the other hand, our results are in line with Eid *et al.* who showed that female patients showed much more anxiety about the postoperative bowel dysfunction and fecal incontinence, which resulted in a greater acceptance of a permanent stoma as a more reliable functional outcome [13]. Other gender-based variations have been found in South Asian colorectal cancer decision-making studies, where the considerations related to hygiene, control of continence, and sustaining daily social functions appear more often among the female patients [14]. The cultural concept of bowel control may also become an issue that affects the preference of surgery, where the fear of bowel control being unpredictable is a factor in more conservative communities like Pakistan, and a permanent stoma is assumed to be a better option than the risk of postoperative incontinence in sphincter-preserving surgery. Research carried out in similar cultural contexts has indicated that patients tend to value functional predictability over anatomical preservation in cases where the results of continence are questionable [15]. This study indicated that rural residence was among the important independent predictors of preference to stoma formation (OR 2.67; $p < 0.024$). Nevertheless, other variables such as female gender, familiarity with stoma care, and increased level of concern were also found to be independent variables with surgical preference during the multivariate analysis. This finding is in line with Jung [16], who similarly found that patients from nonrecourse-limited or rural locations were more likely to favor a definitive treatment, hence avoiding the need for additional postoperative care. Similarly, Abelson *et al.* found that rural communities lacked access to specialized continence treatment, which led to surgeons and patients being persuaded to use APR [17]. On the other hand, if oncological safety is not compromised, the urban patient should have better access to rehabilitative services and be better informed about and able to get radical sphincter preservation. In current study, those with greater levels of education were more likely to favor sphincter preservation (OR 1.52), but this difference was not statistically significant ($p = 0.165$). Prior research, such as that conducted by Gadan *et al.* revealed that patients with higher levels of education were more likely to participate in shared decision-making, prioritized better quality of life outcomes, and preferred sphincter-sparing treatments [18]. The lack of public health education in the local context that is not connected to formal education or variations in educational quality could be the reason we were unable to find a meaningful effect. In this analysis, choosing APR seems to be significantly protected by having a good understanding of stoma care (OR = 0.36; $p < 0.012$). This is in accordance with Nassar *et al.* findings,

which showed that prior planning considerably reduces anxiety and boosts acceptance of temporary or permanent stomas [19]. Given that not all temporary stomas become permanent and can be adequately managed, patients in our cohort who had prior experience with stoma care—whether from personal experience or exposure in the community were more likely to consent to sphincter preservation. The strongest independent predictor of choosing a stoma in this research was perceived high distress (OR 3.86; $p < 0.001$). This pattern was also discovered by Abdalla, who reported that a significant factor of patient preference was the degree of post-sphincter saving surgery quality of life and fear of postoperative incontinence [20]. In general, patients' fears of "not reaching the toilet in time" or social embarrassment exceeded their worries about stoma stigma, according to Crippa *et al.* [21]. Our findings support the notion that addressing psychosocial concerns is a key objective of preoperative counseling. In our investigation, age did not significantly predict outcomes ($p = 0.271$), some trends suggest that older patients might be more likely to undergo decisive operations. This partially contradicts the findings of Denost *et al.* who discovered that older patients were more inclined to accept a permanent stoma [22]. This finding seems to be related to rehabilitation and functional level after major procedures. Concern level and expertise appear to predict preferences more accurately in our sample than age alone.

There are certain limitations of the study that must be recognized. These findings might not be generalizable to other regions, or even to other private healthcare providers in Pakistan, since it was performed at a public tertiary care hospital in Khyber Pakhtunkhwa. The cross-sectional design also complicates the anticipation of how the preferences of the patients might change over time or over the process of counseling. Moreover, the multivariate analysis lacked the pertinent confounding factors such as socioeconomic status, mental health, and the influence of the surgeon in the selection of the patient. Despite these shortcomings, we do recommend that future research should utilize multi-center and longitudinal studies in terms of tracking the alterations in patient preferences and perceptions over time. Extra insights into patient motivations and psychological impacts can be achieved with the help of the qualitative research methods, when some focus groups or interviews are conducted. Interventional studies of the effect of structured counseling, decision aids, and stoma education programs are also proposed to improve patient-centered surgical planning of rectal cancer.

CONCLUSIONS

This research shows that most rectal cancer patients had been choosing sphincter-sparing surgery instead of permanent stoma formation. Nevertheless, both groups showed significant concerns, with bowel functionalities and lifestyle disruption being the most common in those who preferred sphincter-sparing surgeries, and social stigma, body image, and realistic stoma-related challenges being the most important in patients undergoing abdominoperineal resection (APR). Rural residency and female gender were found to be independently related to increased chances of preferring permanent stoma formation, and enhanced knowledge of stoma care was correlated with less preference for a stoma. These results show that patient-centered counseling, specific patient education, and context-dependent communication are necessary to make informed decisions during surgery in patients with rectal cancer.

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Authors' Contribution

Conceptualization: FOS, TAR

Methodology: FOS, HJA, TAR, HI

Formal analysis: HJA, TAR, HI

Writing and Drafting: HJA, HI

Review and Editing: FOS, HJA, TAR, HI

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



Effect of Hemodialysis on Serum Phosphate Levels in Patients with End-Stage Renal Disease: A Quasi-Experimental Study at Sir Ganga Ram Hospital, Lahore

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ABSTRACT

Hyperphosphatemia is a common complication in patients with end-stage renal disease (ESRD). Hemodialysis remains the primary mode of phosphate elimination; however, the impact of demographic and clinical factors on individual patients' clearance is still being studied.

Objective: To determine the mean change in serum phosphate levels before and after a single session of hemodialysis in patients with ESRD. **Methods:** This quasi-experimental study included 115 adult patients undergoing maintenance hemodialysis three times a week at the Department of Nephrology, Sir Ganga Ram Hospital, Lahore, between February and July 2025, and were recruited. Serum phosphate concentration was measured at the beginning and end of the dialysis session. The statistical analysis was performed using SPSS version 26.0, with significance set at $p < 0.050$. **Results:** Among the 115 patients (mean age, 46.5 years), a statistically significant decrease in mean serum phosphate levels from 5.44 ± 1.71 mmol/L to 2.53 ± 0.98 mmol/L was observed as a result of hemodialysis. Multivariate regression supported the view that the model explained 77.3% of the variance in phosphate reduction ($R^2 = 0.773$, $p < 0.001$), with pre-dialysis levels being the only significant independent predictor ($\beta = -0.892$, $p < 0.001$). There was no statistically significant influence of age, gender, or BMI on the magnitude of reduction ($p > 0.050$). **Conclusions:** A single maintenance hemodialysis session significantly reduced serum phosphate levels in patients with ESRD. Although reductions were observed across all demographic variables, the magnitude of reduction did not differ significantly between these groups.

INTRODUCTION

End-stage renal disease (ESRD) is a rising but underreported national health problem in Pakistan, which has a significant impact on the global burden of chronic kidney disease (CKD) [1, 2]. In the absence of a national nephrology registry, the incidence of new ESRD cases is estimated at 150 per million population per year, which provides about 16,000 new cases per year [3]. Hyperphosphatemia is a frequent biochemical imbalance in patients with ESRD and is linked to increased mortality and morbidity [4, 5]. Continuous high levels of serum phosphate can trigger cardiovascular calcification, secondary hyperparathyroidism, and renal osteodystrophy [6, 7]. Although hemodialysis helps remove phosphates to some degree, it is often insufficient to reach target levels.

Treatment of phosphate is generally achieved through a combination of dietary phosphorus restriction and oral phosphate binders; however, adherence to phosphate binder regimens is challenging for many patients because binders often contribute a high daily pill burden and require multiple tablets with meals, which can negatively impact compliance [8-10]. Past studies have shown that hemodialysis can significantly reduce circulating phosphate levels. In one study, patients had elevated phosphate levels before dialysis, which decreased significantly after dialysis. Over the next 10 years, the time series of blood phosphate levels in dialysis patients is expected to vary across regions. Between 2002 and 2012, the average phosphate levels decreased in Japan, Europe,



and the United States. These levels have, however, changed in recent years, with the United States showing an increase, Europe a slight decrease, and Japan showing stable values [11, 12]. The current study results can guide the optimization of dialysis procedures and improve phosphate management among ESRD patients in Pakistan, where adherence to treatment and resource shortages remain a persistent issue.

No study has compared phosphate rebound in Pakistani ESRD patients following dialysis or the effect of dietary phosphate intake, binder use, and dialysis efficiency on phosphate control. The quasi-experimental design has no control group to make cause-and-effect conclusions, and the single-center setting of the Sir Ganga Ram Hospital has limits to cause and effect and generalization to other dialysis centers with different protocols and resources. This study aims to establish the average intradialytic variation in serum phosphate levels among hemodialysis patients, particularly in a local setting using modern high-flux dialyzers.

METHODS

This quasi-experimental study was conducted at the Department of Nephrology, Sir Ganga Ram Hospital, Lahore, from February 2025 to July 2025. A sample size of 115 patients was calculated using an expected mean difference in serum phosphate levels before and after hemodialysis of -2.57 ± 1.64 [11], with a 3% absolute precision and a 95% confidence level. Non-probability consecutive sampling was used to select participants. Patients aged 18-70, of either gender, receiving regular hemodialysis (at least three sessions weekly) for chronic kidney disease were enrolled. CKD was defined by an eGFR below $15 \text{ ml/min/1.73m}^2$ or current dialysis treatment, regardless of eGFR. Those with active viral infections such as HIV, CMV, or HBV, and patients who had undergone parathyroidectomy, were excluded. Approval for the study was obtained from the hospital ethics committee (vide letter 168-FCPS-Nephro/IRB-ERC; dated 12th July 2024), and informed consent was taken from all participants. Basic demographic and clinical data, including name, age, gender, and body mass index, were recorded. Hemodialysis was performed through an arteriovenous fistula, with each session lasting four hours. The average ultrafiltration volume per session ranged between 2 and 2.5 liters. Biomocompatible capillary filters (polysulfone F60 or F70, surface area $1.2\text{--}1.4 \text{ m}^2$) of high flux and high efficiency were used, along with the 4008S dialysis machine (Fresenius Medical Care, Germany). To determine serum phosphate levels, venous blood samples were collected at the start and end of each session via the venous line connected to the dialysis set. The difference in phosphate levels before and after dialysis was recorded on a predesigned pro forma.

All data were analyzed using SPSS version 26.0. Normality was assessed using the Shapiro-Wilk test, and parametric tests were applied accordingly. Differences in serum phosphate levels before and after dialysis were evaluated using the paired-samples t-test. The magnitude of phosphate reduction between gender groups was compared using an independent-samples t-test. In contrast, comparisons across age groups and BMI categories were performed using a one-way analysis of variance (ANOVA). Multiple linear regression analysis was conducted to determine whether age, gender, body mass index (BMI), and pre-dialysis phosphate levels were significant independent predictors of phosphate reduction. A $p\text{-value} < 0.050$ was considered statistically significant.

RESULTS

A total of 115 patients were included in the study. The mean age of participants was 46.5 ± 15.47 years. The mean body mass index was $21.51 \pm 2.20 \text{ kg/m}^2$. Among the study population, 57 patients (49.6%) were female, and 58 patients (50.4%) were male. The mean pre-dialysis serum phosphate level was $5.44 \pm 1.71 \text{ mg/dL}$, and the post-dialysis level was $2.53 \pm 0.98 \text{ mg/dL}$. A paired samples t-test revealed a statistically significant reduction, with an average decrease of $-2.91 \pm 2.04 \text{ mg/dL}$ ($t(114) = 15.298$, $p < 0.001$). The findings present a comparison of pre-dialysis and post-dialysis serum phosphate levels across age groups, gender, and BMI categories using a paired-samples t-test. A statistically significant reduction in serum phosphate levels was observed in all age groups following hemodialysis, as determined by paired-sample analysis. Among patients aged 18-30 years, the mean phosphate level decreased from $5.92 \pm 1.60 \text{ mg/dL}$ to $2.59 \pm 0.88 \text{ mg/dL}$ ($p < 0.001$). In those aged 31-40 years, levels declined from $5.83 \pm 1.51 \text{ mg/dL}$ to $2.46 \pm 0.89 \text{ mg/dL}$ ($p < 0.001$). Patients aged 41-50 years showed a decrease from $5.03 \pm 1.78 \text{ mg/dL}$ to $2.55 \pm 0.99 \text{ mg/dL}$ ($p < 0.001$). In the 51-60 years group, phosphate levels reduced from $5.20 \pm 2.13 \text{ mg/dL}$ to $2.49 \pm 1.14 \text{ mg/dL}$ ($p < 0.001$). Similarly, patients aged 61-70 years demonstrated a decline from $5.34 \pm 1.38 \text{ mg/dL}$ to $2.54 \pm 1.02 \text{ mg/dL}$ ($p < 0.001$). When stratified by gender, both female and male patients demonstrated significant reductions in serum phosphate levels after dialysis. In female patients, the mean level decreased from $5.57 \pm 1.88 \text{ mg/dL}$ to $2.48 \pm 1.06 \text{ mg/dL}$ ($p < 0.001$). In male patients, levels declined from $5.32 \pm 1.53 \text{ mg/dL}$ to $2.58 \pm 0.90 \text{ mg/dL}$ ($p < 0.001$). Across BMI categories, a significant reduction was also observed. Underweight patients showed a decrease from $4.16 \pm 0.32 \text{ mg/dL}$ to $2.27 \pm 1.31 \text{ mg/dL}$ ($p = 0.010$). Patients with normal BMI demonstrated a reduction from $5.41 \pm 1.68 \text{ mg/dL}$ to $2.54 \pm 0.97 \text{ mg/dL}$ ($p < 0.001$). In overweight patients, phosphate levels

declined from 6.64 ± 2.33 mg/dL to 2.11 ± 0.66 mg/dL; however, this change was not statistically significant ($p=0.162$). Obese patients showed a decrease from 8.09 ± 1.30 mg/dL to 2.93 ± 1.15 mg/dL ($p<0.001$) (Table 1).

Table 1: Comparison of Pre- and Post-Dialysis Serum Phosphate Levels Across Demographic and BMI Categories

Groups	n	Pre-Dialysis (mg/dL)	Post-Dialysis (mg/dL)	Paired Sample t-test
Age Groups				
18–30 Years	25 (21.74%)	5.92 ± 1.60	2.59 ± 0.88	$t(24) = 9.04, p<0.001$
31–40 Years	15 (13.04%)	5.83 ± 1.51	2.46 ± 0.89	$t(14) = 8.14, p<0.001$
41–50 Years	22 (19.13%)	5.03 ± 1.78	2.55 ± 0.99	$t(21) = 4.89, p<0.001$
51–60 Years	25 (21.74%)	5.20 ± 2.13	2.49 ± 1.14	$t(24) = 5.41, p<0.001$
61–70 Years	28 (24.35%)	5.34 ± 1.38	2.54 ± 1.02	$t(27) = 8.92, p<0.001$
Gender				
Female	57 (49.57%)	5.57 ± 1.88	2.48 ± 1.06	$t(56) = 10.73, p<0.001$
Male	58 (50.43%)	5.32 ± 1.53	2.58 ± 0.90	$t(57) = 10.95, p<0.001$
Body Mass Index				
Underweight	104 (90.43%)	4.16 ± 0.32	2.27 ± 1.31	$t(5) = 4.03, p=0.010$
Normal	6 (5.22%)	5.41 ± 1.68	2.54 ± 0.97	$t(103) = 14.20, p<0.001$
Overweight	2 (1.74%)	6.64 ± 2.33	2.11 ± 0.66	$t(1) = 3.85, p=0.162$
Obese	3 (2.61%)	8.09 ± 1.30	2.93 ± 1.15	$t(2) = 61.01, p<0.001$

The results present the comparison of mean phosphate reduction (pre-post dialysis difference) across gender, age groups, and BMI categories. Independent samples t-test showed no statistically significant difference in phosphate reduction between female (-3.09 ± 2.17 mg/dL) and male patients (-2.74 ± 1.90 mg/dL) ($t(113) = -0.917, p=0.361$), indicating that gender did not influence the magnitude of reduction. One-way ANOVA showed no significant difference in mean phosphate reduction among age groups ($F(4,110) = 0.775, p=0.544$), with comparable reductions across all age groups. When analyzed by BMI category, one-way ANOVA revealed a trend toward variation; however, the difference did not reach statistical significance ($F(3,111) = 2.204, p=0.092$). Although obese and overweight patients showed numerically greater reductions, these differences were not statistically significant (Table 2).

Table 2: Comparison of Magnitude of Phosphate Reduction Across Gender, Age Groups, and BMI Categories

Variables	Groups	Difference (Pre-post Dialysis), Mean $\pm$ SD (mg/dL)	Test Statistic	p-value
Age Group	18–30 Years	-3.34 ± 2.23	$F(4,110) = 0.775$	0.544
	31–40 Years	-3.37 ± 2.36		
	41–50 Years	-2.48 ± 1.85		
	51–60 Years	-2.71 ± 1.88		
	61–70 Years	-2.80 ± 2.05		
Gender	Female	-3.09 ± 2.17	$T(113) = -0.917$	0.361
	Male	-2.74 ± 1.90		
BMI Category	Normal	-2.87 ± 2.03	$F(3,111) = 2.204$	0.092
	Underweight	-1.89 ± 1.58		
	Overweight	-4.53 ± 1.62		
	Obese	-5.16 ± 1.94		

The linear regression model produced a significant prediction of change in phosphate, $F(4,110) = 93.68$,

$p<0.001$, with a substantial proportion of variance explained ($R^2 = 0.773$). The pre-dialysis phosphate level was the only significant independent predictor of reduction ($\beta = -0.892, p=0.001$). The age, BMI, and gender did not have a significant impact on the level of phosphate reduction ($p>0.050$) (Table 3).

Table 3: Multiple Linear Regression Analysis for Predictors of Serum Phosphate Reduction

Predictor Variables	Unstandardized B	SD Error	Standardised Beta (β)	t-value	p-value
(Constant)	2.135	0.958	—	2.228	0.028
Pre-Dialysis Phosphate	-1.064	0.058	-0.892	-18.476	<0.001
Age	-0.003	0.006	-0.024	-0.515	0.608
Body Mass Index	0.041	0.048	0.044	0.844	0.401
Gender	0.008	0.205	0.002	0.041	0.968

DISCUSSION

In the current study, a single maintenance hemodialysis session resulted in a statistically significant reduction in serum phosphate levels among patients with end-stage renal disease. The decline was consistently observed across all age groups, in both genders, and in most BMI categories. However, when the magnitude of phosphate reduction was compared across demographic and anthropometric groups, no statistically significant differences were identified. Multivariable analysis further demonstrated that the extent of phosphate reduction was independently predicted only by the pre-dialysis serum phosphate level, while age, gender, and body mass index were not significant independent predictors. These findings indicate that although hemodialysis effectively lowers serum phosphate levels, the degree of reduction is primarily determined by baseline phosphate levels rather

than patient demographic characteristics. The regulation of phosphates is significantly impaired in CKD patients, especially in ESRD, due to grossly impaired renal excretion [13, 14]. Hyperphosphatemia is common in this population and is associated with an increased risk of vascular calcification, secondary hyperparathyroidism, and left ventricular hypertrophy, which together increase cardiovascular morbidity and mortality. Accurate phosphate management is one of the pillars of CKD-related mineral and bone disorder management, as outlined in existing clinical guidelines. Current clinical practice guidelines recommend that in patients with CKD stages G3a to G5D, elevated serum phosphate levels should be reduced toward the normal range through a combination of dietary phosphate restriction, use of phosphate-lowering therapies, and optimization of dialysis regimens, with regular monitoring of phosphate as part of CKD-MBD management. Recent guideline updates emphasize individualized phosphate targets and reinforce the role of multidisciplinary management in achieving these goals. Although dialysis can aid in the elimination of phosphates, this mode is often insufficient to achieve and maintain target serum concentrations [15-17]. As a result, most patients require additional measures, such as dietary restriction of phosphorus and the use of phosphate-binding agents. Maintaining adequate phosphate control is also a clinical concern, particularly given non-adherence to complex binder regimens that require multiple daily doses with meals. The management of phosphate balance in dialysis patients involves optimizing dialysis performance and regularly monitoring nutrition and medication compliance [18, 19]. Current study observed a statistically significant decrease in serum phosphate in the current study, with 115 patients on routine high-flux hemodialysis, from a pre-dialysis mean of 5.44 ± 1.71 to a post-dialysis mean of 2.53 ± 0.98 mg/dL ($p < 0.001$), and an average intradialytic change of 2.91 ± 2.04 mg/dL. These results support the use of modern high-efficiency dialysis filters in significantly reducing serum phosphate in a single session. The extent of decrease was uniform across sex, age groups, and body mass index groups. However, underweight patients showed a slightly smaller mean decrease, possibly due to a lower total body phosphate burden or changes in distribution kinetics. The current study findings are consistent with previous studies evaluating phosphate kinetics during hemodialysis. A similar reduction was reported by Ardalan *et al.* from 5.24 ± 1.83 /dl to 2.72 ± 1.00 /dl, with a mean difference of -2.52 ± 1.64 /dl, which is quite similar to the 2.91/dl change in our cohort [11]. Al-Khafaji *et al.* also found that phosphate levels decreased from 5.68 ± 1.64 to 4.17 ± 1.43 mg/dL after dialysis, whereas the remaining levels were higher than

those reported in the current study [20]. This difference could be attributed to variations in dialyzer efficiency, session duration, dietary phosphorus intake, or compliance with phosphate binders. Hamid *et al.* studied the long-term dialysis vintage and phosphate levels and found that they fluctuated over time: 4.7 ± 1.56 mg/dL in those with 10-15 years on dialysis, 5.1 ± 0.85 mg/dL in those with 15-20 years, and 4.4 ± 1.3 mg/dL in those over 20 years. Such trends can be indicative of adaptive changes in bone buffering capacity, nutrition, or remaining renal function with age [3]. The geographic and time-mediated changes in serum phosphate, as shown by the DOPPS study, include regional differences that have decreased gradually in Japan, Europe, and the United States between 2002 and 2012, but have increased or levelled off in 2021. The present results (mean pre-dialysis level = 5.44 mg/dL) align with this international scenario and underscore the ongoing challenges in controlling phosphate levels, despite advancements in dialysis technology [12]. Elias *et al.* examined the kinetics of phosphate removal and found a sharp decline in the initial hour of dialysis; however, only 25% of the total phosphate was removed during this period. Even though serum phosphate can be normalized early in the course of dialysis, a significant proportion is retained, underscoring the importance of completing each session and the potential role of adjunctive phosphate management [21]. Their finding that patients with pre-dialysis phosphate levels ≥ 5.5 mg/dL had higher overall phosphate removal is consistent with our results, which show larger decreases in younger and obese subgroups who might have higher initial phosphate levels. In a mathematically modelled analysis, Yu *et al.* reported a statistically significant decrease from 2.00 ± 0.53 to 0.84 ± 0.21 mmol/L, consistent with our findings and supporting the effectiveness of hemodialysis in reducing phosphate. The study also noted post-dialysis rebound, which was not considered in our present study [22]. Stremke *et al.* employed a novel methodology to evaluate phosphate rebound after dialysis in phosphate binder-free, controlled-diet patients. They found that in most participants, phosphate levels returned to more than 90 per cent of pre-dialysis levels within 24 hours, indicating that although hemodialysis temporarily reduces serum phosphate, post-treatment phosphate is released into tissue compartments, thereby initiating a rebound effect [23]. This has clinical implications, suggesting that measurement of serum phosphates immediately after dialysis can underestimate the total body phosphate burden, which is not considered in this study but is critical in future studies. This can be used clinically, implying that serum phosphate levels following dialysis may not reflect the total body phosphate burden, which was not

considered in this research but is essential in future studies. These findings are relevant to the Pakistani setting, particularly the need for systematized monitoring of pre-dialysis phosphate levels, optimization of dialysis adequacy, dietary counselling, and prudent use of phosphate binders to improve control of mineral metabolism in the resource-limited clinical environment. Enhancing guideline-driven phosphate management may be one possible measure to reduce cardiovascular complications among patients with end-stage renal disease in local practice [2,3].

The research was limited in several ways. Post-dialysis phosphate rebound was not assessed, which can occur due to the slow mobilization of phosphate from intracellular stores and bone to the extracellular space; thus, the sustainability of phosphate reduction after the dialysis session is unclear. Phosphorus intake in the diet and phosphate binder use were not documented or controlled, which may have influenced the pre-dialysis phosphate levels and changes. Also, parathyroid hormone and vitamin D measurements were not done, which limits the overall evaluation of mineral metabolism. In Pakistan, the management of ESRD and phosphate control is often challenged by limited access to phosphate binders, financial constraints, inconsistent dietary counselling, and variability in dialysis resources, which may affect the generalizability of findings to routine clinical practice. The factorial designs used should measure the relative effect of dietary phosphate restriction, binder adherence, and dialysis parameters in total phosphate management.

CONCLUSIONS

A single maintenance hemodialysis session significantly reduced serum phosphate levels in patients with end-stage renal disease. This reduction was consistently observed across all age groups, both genders, and most BMI categories in the pre-post comparison. However, the magnitude of phosphate reduction did not differ significantly between age groups, genders, or BMI categories. Multivariable analysis further confirmed that only the pre-dialysis serum phosphate level independently predicted the extent of reduction, whereas age, gender, and body mass index were not significant independent determinants.

Authors' Contribution

Conceptualization: IF, SA

Methodology: IF, SA

Formal analysis: IF, SA

Writing and Drafting: IF, SA

Review and Editing: IF, SA

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



Impact of Surgical Duration on Morbidity after Monopolar Transurethral Resection of the Prostate: A Prospective Analysis

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ABSTRACT

Benign prostatic hyperplasia (BPH) is associated with high morbidity and poses serious health problems in elderly males. The most effective surgical treatment for BPH that effectively relieves lower urinary tract symptoms is transurethral resection of the prostate (TURP). Still, TURP is not without complications, which can impact patient issues. **Objective:** To contribute to the existing knowledge on TURP complications with respect to resection time duration. **Methods:** From January 2021 to June 2022, this prospective cross-sectional study included 639 individuals with benign prostatic hyperplasia (BPH) and a prostate volume of 30 – 80 milliliters who underwent monopolar transurethral resection of the prostate (M-TURP) at Sindh Institute of Urology and Transplantation between the periods of 50 and 80. Complications were noted throughout a one-month follow-up period, and cases were grouped according to the length of surgery. The purpose of the study was to assess the results and benefits of M-TURP in BPH cases. **Results:** In 639 cases undergoing monopolar TURP, postoperative complications were observed in 11.6 % of cases, with a significant association between complications and surgical duration ($p=0.006$). Sepsis was more common in longer procedures ($p=0.025$), followed by Incontinence (6%), hematuria (4.6%), and urinary tract infections (1.5%). **Conclusions:** M-TURP is a dependable and effective treatment for enlarged prostate, with careful case selection and optimized surgical duration being pivotal to minimizing complications.

INTRODUCTION

In urology, prostate pathologies are common, with benign prostatic hyperplasia (BPH) being the most common [1]. Age-related differences in glandular tissue composition and cell proliferation exertion are the cause of BPH, which generally starts in the fourth decade of life [1]. Lower urinary tract symptoms (LUTS) are common in BPH cases and can have a substantial negative influence on their quality of life. An estimated 1.2 million surgical treatments are carried out encyclopedically each time to reduce symptoms and enhance patient issues due to the significant burden of BPH [2]. Medical remedy is generally the first line of treatment for benign prostatic hyperplasia

(BPH) [3]. Still, surgery is constantly the best course of action for cases with severe symptoms or those who don't respond to conventional remedies [4]. Although transurethral resection of the prostate (TURP) has long been honored as the main surgical fashion for treating BPH, surgeons must be conscious of its possible side effects. Both mono-polar and bipolar TURP methods are effective in managing benign prostatic hyperplasia, offering feasible options for cases requiring surgical intervention [5, 6]. Several studies and meta-analyses have estimated the morbidity and mortality of transurethral resection of prostate (TURP) [7]. Recent substantiation suggests that



while the operative duration of TURP is similar to other surgical technologies for benign prostatic enlargement, bipolar TURP appears to have advantages in terms of reduced transfusion rates, clot retention, and early reoperation rates [8]. Nonetheless, postoperative complications remain a significant concern, occurring in roughly 36% of cases. Specifically, Clot retention and gross hematuria are among the most common complications. [9] Urethral stricture is also commonly seen in patient have a prolonged operative time and a large prostate volume. [10-12] Similarly, urologists need to be apprehensive of these implicit complications and take measures to alleviate them, eventually improving patient outcomes. Recent substantiation highlights the significance of surgical duration in determining the threat of complications following TURP. Studies have shown that procedures lasting longer than 120 minutes are associated with a significant increase in major complications, including sepsis, deep vein thrombosis, transfusion, pulmonary embolism, and reoperation. Again, TURP procedures completed within 90 minutes are considered safest, emphasizing the need for effective and timely surgical ways to minimize morbidity and optimize case outcomes [4,5].

Whereas the existing studies point out the relationship between the duration of surgery and postoperative complications in TURP, there are no multicenter, long-term studies or comparative studies that assess the various surgical methods and patient outcomes. The primary research question is to establish the joint effects of the duration of operation and the patient-related factors on morbidity and maximize surgical safety. This study aimed to contribute to the existing knowledge on TURP complications with respect to resection time duration.

METHODS

This prospective cross-sectional study was conducted in the Sindh Institute of Urology and Transplantation, Karachi, over 18 months (January 2021 to June 2022) following synopsis approval from the institutional ERC with ref no: 157 approved on 28th February 2020. A non-probability consecutive sampling technique was used. Using the Open Epi sample size calculator, the total population of TURP patients in 18 months is 750. Considering the proportion of any complication was observed in 8.2% in 0-30 minutes with a margin of error 1% and 95% confidence level, and accounting for accounting 7% attribution rate. A total of 639 patients, between the ages of 50 and 80 years and with BPH (Volume 30-80ml) were recruited for the study. Patients with active urinary tract infections (UTI) or coagulation disorders were excluded. After written informed consent, demographic and clinical data (age, gender, comorbidities, TRUS volume, PSA, Coagulation

profile, Urine culture, hemoglobin and renal functions, Uroflow-metry, Ultrasound PVR) were abstracted onto a standardized proforma. Prophylactic antibiotics were administered according to institutional protocol. All procedure done under spinal anesthesia/ General anesthesia (in case of failed Spinal Anesthesia). The position of the patient was modified to the lithotomy position after providing anesthesia. Cystourethroscopy was done with a 22 FR cystoscopy, and then, urethral calibration was done up to 26 FR with Urethral sound dilators. 26 FR Continuous irrigations, a ceramic beak sheath is used for monopolar TURP with 1.5% Glycine as an irrigation fluid. Resection and fulguration of the adenoma were done, and the patient was discharged on the 1st post-operative day. Patients were categorized based on surgical duration. The catheter was removed according to the departmental protocol (3-5 days). Follow-up assessments were conducted at one week and one-month post-surgery to observe complications.

Data entry and analysis were performed in SPSS version 20.0. Continuous variables (age, duration of procedure) were summarized as mean $\pm$ SD or median $\pm$ IQR based on Shapiro-Wilk normality testing. Categorical variables (gender, comorbidities, indications, prostate volume, urine sterility) were expressed as n (%). Analyses employed chi-square or Fisher's exact tests as applicable. The $p \leq 0.050$ was considered statistically significant.

RESULTS

This study investigated the outcomes and complications of monopolar transurethral resection of the prostate (TURP) in 639 patients with benign prostatic enlargement. The mean age was 64.10 ± 8.36 years, with a median of 65 years (IQR: 11 years). Transrectal ultrasound (TRUS) revealed a mean prostate volume of 59.70 ± 16.55 grams, with a median of 61 grams (IQR: 30 grams). Uroflowmetry showed a mean maximum flow rate (Qmax) of 4.74 ± 6.96 mL/s, with a median of 2.25 mL/s (IQR: 8 mL/s), and the mean post-void residual volume was 94.37 ± 171.20 mL, with a median of 15 mL (IQR: 120 mL) (Table 1).

Table 1: Descriptive Statistics of Characteristics of Patients

Variables	Mean $\pm$ SD
Age (Years)	64.10 $\pm$ 8.36
PSA	4.74 $\pm$ 7.07
TRUS Volume (gm)	59.70 $\pm$ 16.55
Qmax	4.74 $\pm$ 6.96
Post Void	94.37 $\pm$ 171.20

Preoperatively, lower urinary tract symptoms (LUTS), including renal failure (n=121, 18.9%), hematuria (n=31, 4.9%), recurrent urinary tract infections (n=103, 16.1%), and bladder stones (n=34, 5.3%), were observed (Table 2).

Table 2: Presentation of the Patients(n=639)

Indication	n (%)
With Renal Failure	121 (18.9%)
Without Renal Failure	518 (81.1%)
Recurrent Hematuria	31 (4.9%)
Recurrent UTI	103 (16.1%)
Bladder Stone	34 (5.3%)

The average surgical duration was 20.19 ± 10.95 minutes, with an average fluid usage of 11.37 ± 5.92 liters (Table 3).

Table 3: Statistics of Mean Operative Time, the Amount of Fluid (n=639)

Variables	Point Estimate
Operative time (min)	20.19 ± 10.95
Amount of Fluid (liter)	11.37 ± 5.92

Results are presented as mean with Standard Deviation

Postoperative complications occurred in 11.6% of patients. Those were significantly associated with surgical duration (18.5% Vs 9.8%, $p=0.006$). Specifically, sepsis (8.5% vs 4.1%) was more common in the longer procedures group ($p=0.025$). While other complications, such as acute urinary retention ($n=16$, 2.5%) hematuria ($n=25$, 4.7%), incontinence ($n=30$, 4.7%), and urinary tract infections (UTIs) ($n=13$, 2%), were observed, their relationship with surgical duration did not reach statistical significance except for Blood transfusion (1.5% vs 0.2%, $p=0.048$) which were more in patients having longer operative time. The findings suggest that longer surgical durations are associated with increased morbidity, emphasizing the importance of efficient surgical techniques in minimizing complications (Table 4).

Table 4: Relationship of Surgical Duration with Complications After Monopolar Transurethral Resection of Prostate(n=639)

Complications	Surgical Duration		
	≤ 30 min, n=509	≥ 31 min, n=130	p-value
Acute Urinary Retention	14 (2.8%)	2 (1.5%)	0.381
Hematuria	19 (3.7%)	6 (4.6%)	0.642
Incontinence	21 (4.1%)	9 (6.9%)	0.181
Uti	11 (2.2%)	2 (1.5%)	0.621
Sepsis	21 (4.1%)	11 (8.5%)	0.025*
Tur Syndrome	2 (0.4%)	0 (0%)	0.458
Blood Transfusion	1 (0.2%)	2 (1.5%)	0.048*
Overall	50 (9.8%)	24 (18.5%)	0.006*

DISCUSSION

Due to acute urine retention, numerous cases in underdeveloped nations have surgery for benign prostatic hyperplasia (BPH), constantly following an unprofitable catheter-free trial. In discrepancy, the main reason for surgery in Western nations is irritable lower urinary tract symptoms (LUTS) [11]. Due to fiscal enterprises, monopolar transurethral resection of the prostate (M- TURP)

continues to be the most commonly performed treatment despite the inadequacy of newer modalities [12]. For BPH that's resistant to drugs, M- TURP is a tried- and-true standard surgical procedure, especially for prostate volumes between 30 and 80 cc. In our study, a significant proportion of cases presented with preoperative complications of BPH, including renal failure (18.9%), hematuria (4.9%), repeated urinary tract infections (16.1%), and bladder calculi (5.3%). These findings are harmonious with former studies, similar to those conducted in Nigeria, and maybe it's among the top list of suggestions according to the current EAU guidelines [13]. The prevalence of postoperative complications following TURP varies across studies. In this series, complications were observed in 11.6% of cases (74/639), with sepsis being the most common at 5% (32/639), followed by incontinence and hematuria, each at 4.7% (30/639 and 25/639, independently). Other complications included acute urinary retention (2.5%), urinary tract infections (2%), and blood transfusions (0.5%). A meta-analysis across 103 RCTs found TUR syndrome (2%), hematuria (8%), urinary incontinence (8%), and stricture of the urethra (3%) [12]. Specifically, our complication rates were lower compared to some studies, which have reported advanced rates of complications, particularly infections in cases with urinary retention [4]. A study by Khan et al. reported a 2.3% prevalence of sepsis after transurethral resection of the prostate (TURP), with 19 out of 837 cases developing sepsis [14]. Specifically, these cases had either an indwelling catheter or pre-existing bacteriuria and were receiving perioperative antibiotics. Another study reported UTI in 7.8% and 11.1% of the patients, respectively. In discrepancy, our study set up an advanced prevalence of sepsis at 5%, which increased with the duration of surgery. Specifically, the threat of sepsis was smallest in procedures lasting ≤ 30 minutes and highest in those exceeding 30 minutes. These findings punctuate the significance of surgical duration and patient factors in determining the threat of sepsis after TURP [15]. The reported frequency of postoperative urinary incontinence after transurethral resection of the prostate (TURP) varies across studies. Estimates range from 0.3% to 4%, with some studies suggesting that patient incontinence can trouble cases for several months postoperatively [16, 17]. The current study reported the prevalence of incontinence $n=30/639$ (4.7%), pressing the need for farther disquisition into the factors contributing to this complication. The reported prevalence of urinary tract infections (UTIs) after transurethral resection of the prostate (TURP) varies extensively, from 2.3% to 19% [18]. The current study set up a 2% prevalence, potentially due to shorter resection in a large proportion of cases. Urinary retention following TURP has been proven to occur in 3% to

9% of cases, and it's constantly linked to primary detrusor failure rather than partial resection [19]. The prevalence of urine retention in the current study was 16/639 (2.5%), emphasizing the significance of scrupulous case selection and postoperative care. A potentially dangerous consequence of dilutional hyponatremia, the TUR pattern is marked by symptoms including bradycardia, internal disorientation, hypertension, visual abnormalities, nausea, and vomiting. Over the past many decades, the prevalence of the TUR pattern has dropped dramatically, from roughly 3% to less than 1%. Another meta-analysis across 103 RCTs found TUR syndrome (2%) [5, 20]. The prevalence of TUR pattern in our study was 2/639 (0.3%), which is in line with the downward trend noted in recent exploration. In this study, the volume of irrigation fluid status and duration of the procedure were also studied. Our study employed 1.5 glycine irrigation fluid, with an average operation of 11.37 liters and a surgical duration of 20.19 minutes. Specifically, gill dragged TURP procedures (>120 minutes) are associated with increased pitfalls of major complications. Completing TURP within 90 minutes is recommended for optimal issues [5]. In line with the current study ($p=0.034$), the total complication rate was 9.0% and increased vastly with lesser surgical length ($p<0.001$). An increased threat of deep vein thrombosis or pulmonary embolism, transfusion, reoperation, and postoperative sepsis or shock was linked to longer operating times.

Nevertheless, the study has weaknesses of a single-center design, a limited follow-up duration, and non-probability sampling, which limit the generalization. Research in the future ought to concentrate on larger, multicenter longitudinal research, the incorporation of various populations, and the comparison of monopolar and bipolar methods to enhance clinical outcomes and evidence-based practice.

CONCLUSIONS

Monopolar transurethral resection of the prostate (M-TURP) remains a dependable and effective surgical option for managing an enlarged prostate. The current study underscores the significance of careful case selection and optimizing surgical duration to minimize complications, thereby ensuring the uninterrupted safety and efficacy of M-TURP in urological practice.

Authors' Contribution

Conceptualization: BZ

Methodology: FH

Formal analysis: AS, AUHR

Writing and Drafting: BZ, FH, SU, AS, AUHR

Review and Editing: BZ, FH, SU, AS, AUHR

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



Pattern and Distribution of Symphysis and Parasymphysis Fracture among Patients of Road Traffic Accident at Tertiary Care Hospital Karachi

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ABSTRACT

Maxillofacial trauma resulting from road traffic accidents (RTAs) constitutes a significant public health burden, particularly in developing countries. **Objectives:** To establish the trend and location of symphysis and parasymphysis mandibular injuries and their relationship with the road traffic accident mechanism. **Methods:** This cross-sectional research was done at the Department of Oral and Maxillofacial Surgery, Jinnah Postgraduate Medical Centre (JPMC), Karachi, during a period of six months after receiving ethical approval. Non-probability consecutive sampling was used to include 122 patients aged 18-60 years who sustained a mandibular fracture as a result of RTA either at the symphysis or parasymphysis. The structured Performa was utilized in data collection, and SPSS version 23.0 in data analysis. Descriptive statistics were used, and a chi-square test was used to identify the association, and a p-value less than 0.05 was taken to be significant. **Results:** The average age of patients was 34.6 ± 9.8 years with the male preponderance (79.5%). The majority were related to motorcycles (69.7% and 78.7% of the cases, respectively), and most of the victims did not take any preventive measures (69.7%). The most commonly associated was the parasymphysis region (53.3%), which was then followed by symphysis (32.0%), and most fractures were unilateral (68.0%) and displaced (55.7%). A statistically significant relationship between mechanism of injury and fracture site ($p=0.032$) and fracture pattern ($p=0.041$) existed. **Conclusion:** Symphysis and parasymphysis mandibular fractures are mostly caused by motorcycle road traffic accidents, especially in young males.

INTRODUCTION

Mandibular fractures lie in the category of the most common maxillofacial injuries, and the symphysis and parasymphysis areas are most susceptible to these fractures because they are the most exposed and anatomically prominent areas, and because road traffic accidents (RTAs) continue to be the leading cause of trauma [1]. Preservation of occlusion and mandibular continuity is the main objective of the treatment in parasymphysis and symphysis fractures, which necessitates proper and timely surgical intervention [2]. In most developing countries, such as Pakistan, the mandibular fracture is caused most often by a road traffic accident, which is caused by a combination of poor

enforcement of road traffic regulations, absence of wearing seat belts and helmets, and poor road facilities [3]. Wang et al. examined national trends, and they reported that mandibular fractures come at a high cost to the face, with mandibular fractures being the most frequent sustained injuries. In the South Asian context, road traffic accidents are the major cause of mandibular fracture, due to the impact forces generated during crashes, which may produce direct trauma to the mandible, leading to displacement, comminution, or multiple fracture sites depending on the direction and magnitude of the impact. There is considerable biomechanical work that indicates that stress-bearing areas of the mandible include the



symphyseal and parasymphyseal areas, which are more likely to fracture during anterior-posterior forces like those resulting from a car collision or a fall forward in an accident [4]. These patterns can be used to choose the proper fixation system and forecast potential complications. Investigations in other areas have also continued to highlight the presence of RTAs as a significant causal agent of mandibular fractures, including parasymphysis fractures, and this phenomenon necessitates region-specific prevention tactics. [5,]. Asya et al. in their extensive retrospective study, found that RTAs were one of the most frequent etiological factors in anterior mandibular fractures, especially in men aged 20-40 years [6]. In addition, the fracture location and severity are directly influenced by the mechanism of injury; Hesham et al. described high-velocity fractures caused by vehicular trauma as usually complex or multifocal fractures of the anterior mandible, and low-velocity injuries as localized ones involving only one part of the body [7]. Nogami et al. also reported that dental injuries often go along with mandibular fractures of road traffic origin, especially in the symphysis region, which makes recovery of dental functions difficult and thus makes treatment more challenging [8]. The Middle East and South Asian research also resulted in recent reports on increased incidences of maxillofacial trauma in terms of increased urbanization and car density, which are the same and must be taken into consideration as the source of prevention initiatives, including helmet use and road safety education [9, 10].

Symphysis and parasymphysis fractures are common consequences of road traffic accidents (RTAs), particularly in rapidly urbanizing settings of developing countries like Pakistan, where trauma incidence is on the rise. Despite this, there is limited local data from tertiary care centers in Karachi regarding the specific patterns, distribution, and associated risk factors of these fractures, highlighting a significant gap in the existing literature. Understanding these epidemiological trends is crucial for improving clinical outcomes and guiding preventive strategies. Therefore, this study aimed to identify the pattern and distribution of symphysis and parasymphysis fractures among patients involved in RTAs presenting to a tertiary care hospital in Karachi. Given that the mandible plays a vital role in mastication, speech, and facial aesthetics, and is highly susceptible to trauma due to its prominent position, such insights may contribute to better management protocols and a reduction in the burden of mandibular injuries.

METHODS

The cross-sectional research was carried out during the period between 3rd June 2025 and 30th November 2025 at the Department of Oral and Maxillofacial Surgery, Jinnah

Postgraduate Medical Centre (JPMC), Karachi, over a period of six months. The Institutional Review Board and Ethics Review Committee of JPMC (ERC No. F-2-81/2025-GENL/331-H/JPMC; dated 2nd June 2025) provided the ethical approval of the study on 2nd June 2025 and ensured that it was conducted in accordance with the Declaration of Helsinki and institutional guidelines on research ethics. All participants were enrolled using informed consent, which was signed. The outpatient department and inpatient units of the hospital were used to screen patients presented with fractures of the symphysis or parasymphysis of the mandible due to road traffic accidents (RTAs) until the required number of patients was obtained. The aged patients were included between 18 and 60 years of both genders who suffered fractures as a result of RTAs and were willing to take part after grasping the purpose and process of the study. Fracture patients, fracture of other parts of the maxillofacial, prior mandible fractures or surgeries, mentally unstable patients, pregnant or lactating women, and immunocompromised patients were excluded. Such exclusion criteria were used to limit confounding by non-RTA trauma, systemic conditions, or previous interventions that could influence fracture patterns, healing, or outcomes. The WHO Sample Size Calculator (version 2.0) was used to calculate the sample size. This was calculated using the prevalence of parasymphysis fractures of the mandibular fractures, as expected, which has been reported to be 28.33% in a study conducted by Pendyala KS et al. The choice of this outcome variable was due to the fact that the main goal of the study was to identify the distribution and the trend of symphysis and parasymphysis fractures in mandibular injury by RTAs. The minimum sample size calculated based on a 95% confidence level and an 8% margin of error was 122 patients. It was found that this sample size was adequate to be able to estimate the prevalence of these fracture patterns in the study population with reasonable accuracy. A non-probability consecutive sampling technique was used in this study. The data was gathered through a structured proforma based on earlier published research on the epidemiology of mandibular fracture and a few adjustments in relation to the goals of the current research. The proforma contained data on demographic factors (age, gender, occupation, residence), injury factors (mechanism of RTA, type of the vehicle involved, and use of protective factors, helmets or seatbelts), clinical findings, radiographic findings, fracture site (symphysis, parasymphysis, combined), laterality (unilateral or bilateral), and fracture pattern. Direct patient interview and examination of clinical and radiographic records were used as data collection methods. Clinical examination was carried out in the normal aseptic conditions, and radiographic confirmation was done by the use of

orthopantomogram (OPG) and/or computed tomography (CT) scan in cases where necessary. Fracture patterns were operationally defined in terms of the radiographic criteria that had been previously described in the maxillofacial trauma literature. The fracture that was referred to as a displaced fracture was a fracture that had lost its normal position in the anatomy. Fractures in which the anatomically set bone fragments were not moved far apart were termed a non-displaced fracture. A fracture that had three or more bone pieces was considered to be comminuted as exhibited through a radiograph. They were based on the standard radiographic classification criteria that are outlined in the former studies of mandibular trauma.

The statistical analysis and data input were done using SPSS version 23.0. The continuous variables, like age, were summarized as the mean and standard deviation, and the categorical variables, like gender, fracture site, and laterality, as well as fracture pattern, were summarized into frequencies and percentages. Besides the descriptive statistics, inferential analysis was also done to test the relationship among categorical variables, like the relationship between fracture site and mechanism of injury or use of protective equipment. The comparisons were done using the Chi-square test. A statistically significant p-value was considered to be 0.050 or less.

RESULTS

A total of 122 patients meeting the inclusion criteria were enrolled in the study. The mean age of participants was 34.6 ± 9.8 years (range: 18–58 years). Males predominated the study population ($n=97$; 79.5%), while females accounted for 25 (20.5%) participants. Most patients resided in urban areas of Karachi ($n=84$; 68.9%) and were primarily employed in manual or field-based occupations ($n=72$; 59.0%)(Table 1).

Table 1: Baseline Demographic Characteristics of the Study Population($n=122$)

Variables	Frequency (%)
Age (Years)	
18 – 30	48 (39.3%)
31 – 40	36 (29.5%)
41 – 50	27 (22.1%)
51 – 60	11 (9.0%)
Gender	
Male	97 (79.5%)
Female	25 (20.5%)
Occupation	
Field / labor-based	72 (59.0%)
Office/business	33 (27.0%)
Student	10 (8.2%)
Unemployed	7 (5.8%)

Residential Area	
Urban	84 (68.9%)
Rural	38 (31.1%)

Motorcycle-related accidents were the most common cause of mandibular fractures ($n=85$; 69.7%), followed by car accidents ($n=21$; 17.2%), bus/truck-related trauma ($n=10$; 8.2%), and pedestrian injuries ($n=6$; 4.9%). The majority of victims ($n=96$; 78.7%) were not using protective measures (helmets or seatbelts) at the time of the accident. Fractures predominantly involved the parasymphysis region (53.3%) followed by symphysis (32.0%), with most fractures being unilateral (68%) and displaced (55.7%). Motorcycle accidents were particularly associated with displaced parasymphysis fractures (Table 2).

Table 2: Mechanism of Injury and Fracture Characteristics($n=122$)

Variables	Frequency (%)
Type of Vehicle Involved in RTA	
Motorcycle	85 (69.7%)
Car	21 (17.2%)
Bus / Truck	10 (8.2%)
Pedestrian	6 (4.9%)
Use of Protective Measures	
Yes	26 (21.3%)
No	96 (78.7%)
Fracture Location	
Symphysis	39 (32.0%)
Parasymphysis	65 (53.3%)
Both	18 (14.7%)
Type of Fracture	
Unilateral	83 (68.0%)
Bilateral	39 (32.0%)
Fracture Pattern (on Imaging)	
Displaced	68 (55.7%)
Non-displaced	34 (27.9%)
Comminuted	20 (16.4%)
Site of Impact on Face	
Frontal	29 (23.8%)
Lateral	41 (33.6%)
Chin	39 (32.0%)
Other	13 (10.6%)

The association between the mechanism of injury and fracture characteristics was further analyzed. A statistically significant association was observed between mechanism of injury and both fracture location ($p=0.032$) and fracture pattern($p=0.041$), indicating that high-velocity motorcycle trauma was more likely to produce displaced parasymphysis fractures. No significant association was found between the mechanism of injury and use of protective measures ($p=0.058$). These findings are summarized in table 3.

Table 3: Association of Mechanism of Injury with Fracture Variables(n=122)

Characteristics	Motorcycle (n= 85)	Car (n=21)	Bus/Truck (n=10)	Pedestrian (n=6)	p-value
Fracture Location					
Symphysis	21(24.7%)	9(42.9%)	6(60.0%)	3(50.0%)	0.032*
Parasymphysis	56(65.9%)	10(47.6%)	3(30.0%)	2(33.3%)	
Both	8(9.4%)	2(9.5%)	1(10.0%)	1(16.7%)	
Fracture Pattern					
Displaced	54(63.5%)	7(33.3%)	5(50.0%)	2(33.3%)	0.041*
Non-displaced	22(25.9%)	9(42.9%)	3(30.0%)	2(33.3%)	
Comminuted	9(10.6%)	5(23.8%)	2(20.0%)	2(33.3%)	
Use of Protective Measures					
Yes	14(16.5%)	7(33.3%)	3(30.0%)	2(33.3%)	0.058
No	71(83.5%)	14(66.7%)	7(70.0%)	4(66.7%)	

*P<0.050 statistically significant(Chi-square test)

DISCUSSION

The current research evaluated the trend and the distribution of symphysis and parasymphysis fractures in patients who had road traffic accidents (RTA) in one of the tertiary care hospitals within Karachi. The results indicate that mandibular fractures continue to be among the most common consequences of facial trauma, especially after accidents on motorbikes, which contributed to almost 70% of all cases in this research. The mean age of the study sample was 34.6 ± 9.8 years, and the majority of them were young adult males working in the field. These results can be compared to Muralidhar *et al.* who also demonstrated the same demographic situation since males between their third and fourth decades were the majority of maxillofacial trauma victims [11]. A similar result was reported by Roccia *et al.* in the WORMAT project, where the same global predominance of young male patients with road-traffic-related facial injuries was observed, which is dependent on exposure and occupational mobility [12]. The most common mechanism of injury in the study (69.7%) was motorcycle collisions, and the next ones were car and bus/truck accidents. Similar findings were also reported in the works by Chuang *et al.* and Maharjan *et al.* which expressed a similar opinion by stating that motorcycles are the most common cause of facial fractures in the developing lands where helmet non-adherence is widespread [13, 14]. In the given study, it was also found that 78.7 % of patients were not wearing helmets or seatbelts during an injury, which supports the results reported by Wusiman *et al.* and Kanala *et al.* who state that the lack of compliance with the safety measures is one of the primary causes of mandibular injuries [15, 16]. Concerning the location of fracture, parasymphysis fractures were the most common (53.3%), symphysis (32.0%), and combined fracture(14.7%). These findings are consistent with the research of Hashmi *et al.* who

underlined the anatomical susceptibility of the parasymphysis area because it is thinner in the cortex and has an approach to the canine fossa [17]. Equally, Jamal *et al.* (2023) and Khan *et al.* (2025) emphasized that high-velocity trauma normally causes anterior mandibular fractures, which need to be fixed with surgery to achieve the best alignment and functionality [18, 19]. There was also a strong correlation between the mechanism of injury and the fracture site ($p=0.032$) and the fracture pattern ($p=0.041$), the motorcycle accidents were more likely to result in displaced parasymphysis fractures. These results are consistent with the literature of Kanala *et al.* (2021) and Roccia *et al.* (2022) that revealed that intense, high-velocity impacts of motorcycle collisions tend to produce intricate fracture patterns [16,12]. This observation was also reinforced by Gercek and Bayrakci (2025) who found that the degree and orientation of the parasymphysis and angle fractures after open reduction and internal fixation were of significant consideration in the remodeling of the mandibular condyles and alteration of the joint space. [20]. All these results together are used to underscore the fact that RTA, especially motorcycle accidents that do not involve protective gears, continue to be the number one cause of anterior mandibular fractures in Pakistan. Education on helmet use and enforcement of traffic laws and early surgical intervention on facial trauma would play a critical role in the reduction of the burden of facial trauma. This project was done in one tertiary care facility and might not represent the trend of the fractures in the general population. The number of the samples was small, and only the cases connected to RTA were considered, without falling or assault cases being considered as other etiologies. Radiological evaluation was mainly admired on the basis of two-dimensional assessment instead of CT-based reconstruction that could have limited accurate assessment of the anatomy. It is suggested that future multicenter research using bigger cohorts and more sophisticated imaging be used to confirm these results. Strict prevention measures by encouraging helmet wearing, good driving skills.

CONCLUSIONS

This study concludes that road traffic accidents, particularly motorcycle collisions, are the predominant cause of symphysis and parasymphysis mandibular fractures in young adult males. The parasymphysis region was most frequently involved, with displaced unilateral fractures being the most common pattern. A statistically significant relationship was found between mechanism of injury and both fracture location and pattern, indicating that high-velocity motorcycle trauma is more likely to produce displaced anterior mandibular fractures. These findings highlight the urgent need for public health

interventions focusing on road safety education, mandatory helmet use, and stricter traffic law enforcement to reduce the incidence and severity of mandibular fractures resulting from preventable road accidents.

Authors' Contribution

Conceptualization: HR

Methodology: HR, SG, AM, WB

Formal analysis: JA, HR, SG

Writing and Drafting: HR, AM, MM, WB

Review and Editing: HR, JA, SG, AM, MM, WB

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

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Original Article



Impact of Speech Sound Disorders on the Academic Performance of Children

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ABSTRACT

Speech sound disorders (SSD) have a high prevalence and impact an individual's capability to make and produce speech sounds, essential for humans to communicate. Children's participation in the educational environment may be restricted in children with SSD.

Objectives: To determine the impact of Speech Sound Disorders on the Academic Performance of children. **Methods:** This Cross-Sectional study was conducted at Riphah International University, Islamabad, from 1st June 2024 to 30th November 2024. The study recruited a sample of n=67 children of both genders, aged 5 to 11 years, diagnosed with SSD by qualified Speech-Language pathologists (SLPs), who used standardized and clinical evaluation processes to make the diagnosis. Children of The Spirit School, The Thinking School, and ASAS International School were recruited. Their academic performance was assessed utilizing the APRS, and previous academic grades of students were also noted. The Academic Performance Rating Scale was used for data collection. SPSS version 23.0 was used for data collection. **Results:** Students with mild SSD demonstrated performance in higher grade ranges (51-70%), indicating negligible academic influence. Conversely, individuals with moderate SSD predominantly scored in the mid-range (41-50%), but students with severe SSD were primarily situated in the lowest grade range (30-40%). **Conclusions:** The conclusion shows a direct and significant correlation between children's academic achievement and the severity of speech sound disorder. Academic achievement tends to decrease with increasing SSD severity, as seen by instructors' observations in the classroom and lower annual grades.

INTRODUCTION

Spoken communication facilitates humans to communicate and exchange ideas; however, the correct production of speech sounds needs both motor control and knowledge of the language system. The correct speech sound production is assumed if sounds are generated correctly by 75 to 90% by the children [1]. The development of plosives, approximants, fricatives, and nasals occurs before affricates and pre-nasalized consonants. Similarly, short syllable strings develop before the longer ones. Also, phonetically more complex sounds and syllables are more commonly produced by older children, indicating developmental progress [2]. A speech sound disorder (SSD) is a disorder of communication that impacts an individual's capability to make and produce speech sounds, and SSD includes issues in articulation, i.e., to make

sounds, and phonological process ie, sound patterns [3]. SSD is highly prevalent, with 2.1 to 23 percent of 4-6-year-old kids and 3.6 percent of 8-year-old children suffering from SSD, with higher prevalence in boys compared to girls 2:1 [4]. The prevalence of Speech Sound Disorders in primary school children of Pakistan is low at 1.3%, with a slightly greater incidence in males aged 5-6 years [5]. Both organic etiologies, like neurological or anatomical issues, and functional issues can result in SSD. It can also result from motor disorders; structural anomalies like clefts; sensory issues like reduced hearing, and may also be idiopathic [4]. In children with SSD, there may be additions, omissions, or substitutions of sounds in word strings [6]. Phonological issues of moderate to severe level may result in incomprehensible speech, thus affecting social



interactions as well as communication [7]. Impairment of motor skills can result in phonetic problems characterized by incorrect motor production of speech sounds, which may include airflow release laterally on /s/. Less developed cognitive-linguistic skills can also result in phonological problems, which may include a lack of meaningful contrasts in words, resulting in a consistent pattern of errors like velar fronting, causing the substitution of [t] for /k/, [d] for /g/, and [n] for /ŋ/ [8]. Phonological impairments refer to a reduction of the ability to acquire the speech-sound distinctions to differentiate between words and the rules dictating the permissible combinations of those sounds [6]. Lower literacy has also been reported in kindergarten kids who suffer speech sound disorders [4]. Teachers are crucial in helping kids grow academically, socially, and emotionally, but they might not be equipped to help kids with speech sound abnormalities [9]. Even while having an SSD is crippling in itself, the disorder is linked to poor literacy acquisition and reading mastery, which has serious consequences for academic performance and preparedness for school [10]. The child's views, emotions, and attitudes regarding how other people perceive their communication, as well as the opinions, feelings, and attitudes of those who engage with the child, are all part of the social impact of an SSD. Children's participation in the educational environment may be restricted as a result of these views, which may also restrict their access to normal social relationships in the school environment [11]. The study may be beneficial for academia and professional domains, advocating for evidence-based strategies that can improve the overall quality of care for children with speech sound problems and phonological difficulties. Hence, keeping in view the high prevalence of SSD and the fact that it may affect schooling, the current study aimed to determine the impact of speech sound disorders on the academic performance of children.

METHODS

This Cross-Sectional study was conducted at Riphah International University, Islamabad, from 1st June 2024 to 30th November 2024, using a purposive sampling. This study was initiated following ethical approval of the research proposal from the Research Ethical Committee, Riphah International University vide Reference # Riphah/RCRAHS-ISB/REC/MS-SLP/01974 approved on 6th May 2024, permission from the relevant school/ clinic, and informed consent of the participants/ parents of children. A sample size of n=67 was determined by the Open Epi tool with a confidence interval of 95% with 5% of margin of error. Children of both genders, aged 5 to 11 years, diagnosed with speech Sound Disorders (SSD) by qualified Speech-Language pathologists (SLPs). Children with language difficulties, who are not diagnosed with SSD and

who are not going to school, were excluded. The sample was obtained from inclusive schools in Islamabad, including The Spirit School, The Thinking School, and ASAS International School Pakistan. These children had reduced intelligibility and frequent speech sound problems, which hindered their ability to participate in class and communicate effectively. In order to accurately identify SSD for study inclusion, qualified speech-language pathologists used standardized and clinical evaluation processes to make the diagnosis. Teachers who had been teaching the participating children for a minimum duration of one academic year were utilized, since they were better aware of the children with learning difficulties, the effect of bullying, if any, the child's personal interests, etc., making it easier to exclude the effect of such conditions. Tools utilized for the study included basic demographic information and the Academic Performance Rating Scale (APRS). APRS is a 19-item scale, and every item has a 5-point Likert scale rating on a 1-5 scale, and the score ranges from a minimum of 19 to a maximum of 95. While lower scores show greater academic challenges, higher scores indicate better classroom functioning and academic accomplishment. The rating form assesses several aspects of classroom performance, such as accuracy, attention, task completion, and neatness. The raw score is averaged across items, and it tends to range from 1-5 or 1-6 for a good global estimation of student performance. The APRS is developed to be used with children between 6 and 12 years old, to assess teachers' perceptions of students' academic progress, to identify academic skills weaknesses, and to monitor progress after intervention. These children were recruited from The Spirit School, The Thinking School, and ASAS. Their academic performance was assessed utilizing the APRS, and previous academic grades of students were noted.

Following data collection, it was analyzed utilizing SPSS version 23.0. Descriptive statistics were utilized for demographic data and responses, while the chi-square test was used to determine the association between academic performance and SSD.

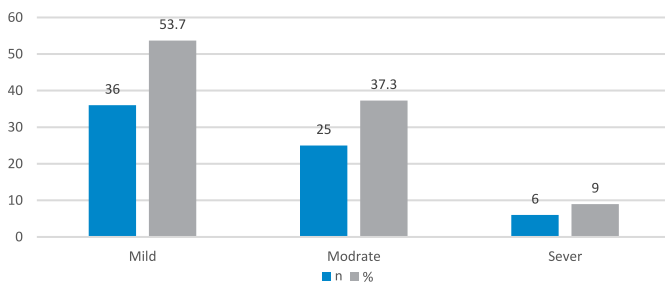
RESULTS

The current study sample (N=67) revealed that the largest age group, 30(44.8%), was 5 to 6.11 years of age with nearly equal gender distribution. Most children, 37(55.2%), were studying in KG, Adv, or Prep class. The annual grades obtained by students in the previous year were somewhat similar, 18(26.9%) each achieved grades 41-50%, 51-60%, and 61-70%, and only 13(19.4%) obtained grades 30-40% (Table 1).

Table 1: Demographic Characteristics of Sample (n=67)

Variables	Group	n (%)
Age Group (Years)	5 -6.11	30 (44.8%)
	7 -8.11	22 (32.8%)
	9 to 11	15 (22.4%)
Gender	Male	34 (50.7%)
	Female	33 (49.3%)
Grades	KG, Adv and Prep	37 (55.2%)
	Class 1	9 (13.4%)
	Class 2	7 (10.4%)
	Class 3	6 (9%)
	Class 4	7 (10.4%)
Previous Grades	Class 5	1 (1.5%)
	30-40	13 (19.3%)
	41-50	18 (26.9%)
	51-60	18 (26.9%)
	61-70	18 (26.9%)

Study revealed that mild 36(53.7%) SSD was predominant and severe was least 6(9%)(Figure 1).

**Figure 1:** Severity of Symptoms (Errors and Intelligibility) of the Sample (n=67)

The cross-tabulation and chi-square association revealed a significant difference in annual grades ($p < 0.001$) with majority i.e., 36 participants with mild SSD received grades 51-60 and 61-70% grades, while of the moderate SSD cases most i.e., 18 received grades 41-50% and 6 cases with severe SSD received low grades of 30-40% revealed a significant association ($p < 0.001$) between APRS based on observation of teachers and SSD with 13 students of SSD with performance score range of 41-60 and 23 in 61-80, while the 6 students achieved low APRS score of 20-40 only indicating worsening performance with increasing severity of SSD (Table 2).

Table 2: Cross Tabulation b/w severity of Speech Sound Disorder and Annual Grades: Chi-Square Association

Diagnosis, n (%)	Annual Grades			
	30-40%	41-50%	51-60%	61-70%
Mild, 36 (54%)	0	0	18	18
Moderate, 25 (37%)	7	18	0	0
Severe, 6 (9%)	6	0	0	0
Chi-Square Test	Value	df	p-value	
Pearson Chi-Square	89.266	6	<0.001	
Likelihood Ratio	105.026	6		

Linear By Linear Association	51.421	1	
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Results revealed a significant association ($p < 0.001$) between APRS based on observation of teachers and SSD, with 13 students of SSD with a performance score range of 41-60 and 23 in 61-80, while the 6 students achieved a low APRS score of 20-40, only indicating worsening performance with increasing severity of SSD (Table 3).

Table 3: Cross Tabulation b/w APRS Scoring and SSD: Chi-Square Association

Diagnosis	APRS Scoring		
	20-40	41-60	61-80
Mild (n=36)	0	13	23
Moderate (n=25)	3	18	4
Severe (n=6)	6	0	0
Chi-Square Test	Value	Df	p-value
Pearson Chi-Square	56.555	4	<0.001
Likelihood Ratio	46.696	4	
Linear-by-	32.508	1	

DISCUSSION

This study looked at how children's academic performance was affected by Speech Sound Disorder (SSD) and discovered a significant inverse link ($p < 0.001$) between academic accomplishment and SSD severity. Academic performance decreased as SSD severity grew, suggesting that speech issues affect overall academic results and go beyond communication deficiencies. An obvious inverse association was found when academic performance was examined in relation to annual grades. The majority of children with mild SSD scored between 51 and 70%, indicating minimal academic impairment. On the other hand, those with mild SSD were mostly found in the 41-50% range, indicating a discernible compromise in academic performance. Significant academic underachievement was indicated by the fact that children with severe SSD were mostly found in the 30-40% grade range. These results imply that classroom participation, oral replies, reading development, and general academic engagement are adversely impacted as speech intelligibility declines and phonological errors rise. The findings are in line with those of Gonzales, who found that children with moderate to severe SSD outperformed their peers without speech issues on standardized academic tests [12]. The link between SSD severity and academic performance did not significantly differ by gender, suggesting that severity rather than gender is the main factor influencing academic impact. Research by Hitchcock ER et al. who surveyed the residual speech errors, found that while children may experience social and emotional challenges, the extent of academic impact varies widely, and not all children with severe speech difficulties necessarily struggle academically [13]. In contrast, the current study found that children with severe SSD encountered more academic

difficulties at higher class levels, according to a class-wise comparison. Students with more severe speech impairments had trouble keeping up with classroom expectations as curriculum demands got more linguistically and intellectually rigorous. These results are consistent with those of Foster *et al.* and Wren *et al.* [14, 15]. The children with persistent speech impairments at age 8 had significantly worse scores in math and English at later academic stages (10-14 years) [15]. This suggests that if early speech issues are not adequately handled, they may persist throughout later schooling. Hitchcock *et al.* who noted that children with SSD have social, emotional, and academic difficulties even in milder cases with just one or two sound abnormalities, support the current findings [13]. Even though the current study's moderate SSD participants had comparatively higher academic results, research suggests that even minor speech errors might have an impact on more general developmental areas. Additionally, children with SSD are more likely to experience ongoing reading difficulties, which could further contribute to academic underachievement [16-18]. This validates the current study's conclusion that poorer academic grades are closely linked to severe SSD [19, 20]. The relatively small sample size and purposive sampling of the selected schools are also limitations of this study, as they can reduce the extrapolation of the results to the wider population. Also, there is the risk of subjective bias due to the use of teacher-reported measures (APRS). The cross-sectional study design also limits the causal inferences between academic performance and the severity of SSD. Future studies should involve larger, multi-centered samples, a longitudinal design, inclusion of objective academic measures, and standardized diagnostic measures to gain more insight into long-term effects and results of intervention.

CONCLUSIONS

This study's findings indicate a substantial correlation between the severity of Speech Sound Disorder (SSD) and children's academic achievement, as assessed by their annual grades and observation of their class teachers. The results underscore the significance of early diagnosis and intervention for children with SSD, especially those with moderate to severe symptoms, to alleviate academic difficulties and enhance educational outcomes.

Authors' Contribution

Conceptualization: HM

Methodology: HM

Formal analysis: MH

Writing and Drafting: TY, MF, GS

Review and Editing: HM, TY, MF, GS

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article


Comparison of the Effect of Insulin with Metformin on Neonatal Outcome in Booked Patients with Gestational Diabetes Mellitus

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ABSTRACT

Insulin has long been used as a treatment for gestational diabetes that is not well managed with diet. Metformin has been shown in several trials conducted in recent years to produce perinatal and obstetric results that are comparable to those of insulin. Studies have reported conflicting results regarding both modalities, and not all clinical recommendations support its usage.

Objective: To compare neonatal outcomes in patients with metformin-treated gestational diabetes mellitus versus those with insulin-treated gestational diabetes mellitus. **Methods:** An observational study took place at the Obstetrics and Gynaecology Unit-III of Lady Willingdon Hospital, Lahore, during the time period starting from January 1, 2023, until December 1, 2023. One hundred and eighty-eight patients (94 in each group) were included in the study. In Group A, metformin tablets were given, and patients in Group B were given insulin. Outcome variables were measured as per the operational definition, respectively. **Results:** Patients receiving insulin therapy developed macrosomia more frequently (10.6% in the Metformin group vs. 23.4% in the Insulin group, $p=0.029$), along with hypoglycaemia (19.2% for Metformin vs. 33% for Insulin, $p=0.031$) and respiratory distress (9.6% Metformin vs. 20.2% Insulin, $p=0.041$) statistically often. Research showed no meaningful differences in findings between study groups regarding jaundice occurrence, together with intrauterine growth restriction (IUGR) and amniotic fluid measurements. **Conclusions:** In comparison to insulin, metformin is equally effective in preventing neonatal complications such as macrosomia, hypoglycaemia, and respiratory distress in women with gestational diabetes.

INTRODUCTION

Insulin resistance is a characteristic of pregnancy, and insufficient insulin production to offset insulin resistance leads to gestational diabetes mellitus (GDM) [1]. Because of glucose intolerance, GDM is frequently discovered in the second trimester of pregnancy. Pregnancy-related obesity, autoimmune beta-cell dysfunction, modification of metabolism of carbohydrates, fats, proteins, decreased insulin production, and insulin resistance are important variables [2, 3]. When hyperglycemia is initially noticed with one or more abnormal readings on 75 g OGTT-fasting

plasma glucose 5.1-6.9 mmol/l, 1-hour plasma glucose 10.0 mmol/l, or 2-hour plasma glucose 8.5-11.0 mmol/l, the World Health Organization advises labeling it as GDM [4]. In many parts of the world, GDM is a growing health issue [5]. Global occurrence of diabetes is 16.9 percent, with 80 percent residing in low- and middle-income countries. About 16.2% of live births are exposed in utero to hyperglycemia, 85.1% of which is due to gestational diabetes mellitus. In Southeast Asia, the prevalence of GDM is highest, estimated at approximately 24.2 percent, mainly



in low or middle-income groups [6]. The survey within Pakistani healthcare facilities revealed that 11.8% of pregnant mothers received GDM diagnoses. The identification of gestational diabetes mellitus (GDM) occurred among 6.2% of women in their first trimester, and 51.1% during the third trimester, and 39.9% in the second trimester [7]. The goal of regulating high blood glucose levels in gestational diabetes mellitus patients makes insulin an established treatment option because of its proven effectiveness [8]. Research teams originally developed insulin as a life-saving medication for Type 1 diabetic patients before using it as the primary treatment for GDM because most oral hypoglycemic agents proved teratogenic [9]. The medical community considers insulin to be a dependable and secure treatment for diabetic pregnant women with diabetes. The use of insulin for managing gestational diabetes mellitus presents two main disadvantages due to its requirement for injections and potential risks for maternal hypoglycemia and excessive fetal growth, as well as increased costs [10]. The diabetes drug metformin, which entered clinical use in 1960 for type 2 diabetes patients, now serves as an acceptable option for the management of GDM. Medical professionals classify metformin as Category B because it does not cause congenital fetal malformations, maternal weight increases, or neonatal hypoglycemia during pregnancy [11]. The effect of metformin on insulin sensitivity, along with its ability to decrease gluconeogenesis, supports β -cell function according to studies [12, 13]. Medical science first employed metformin as an insulin resistance treatment for women, according to research available [14].

Although there is an increasing prevalence of gestational diabetes mellitus (GDM) and both insulin and metformin are available as treatment options, comparative evidence regarding their effect on neonatal outcomes, especially in low and middle-income countries such as Pakistan, is still scarce. This poses a clinical dilemma on the best treatment that leads to optimal efficacy, safety, and cost. Thus, the study aims to compare neonatal outcomes between patients who have undergone GDM treatment with metformin and those treated with insulin.

METHODS

It was a prospective comparative study was conducted at the Department of Obstetrics and Gynaecology Unit-I, Lady Willingdon Hospital, Lahore, from 1st January 2023 to 1st December 2023. The ethical approval for this study was obtained from King Edward Medical University, Lahore (Ref No. 493/RC/KEMU; dated 23rd May 2022). Patients were randomized using a computer-generated simple randomization sequence. Group assignment was done using sealed, opaque envelopes to ensure allocation concealment. The outcome assessors were blinded to the

treatment groups during data collection and outcome evaluation to reduce bias. A total sample size of 188 patients (94 in each group) is estimated by using 95% confidence interval level, 10% absolute precision, with expected percentage of neonatal hypoglycaemia associated with insulin as 28.2% and metformin as 4.4% [15]. All patients aged 18-36 years, having singleton pregnancies, who at 24-28 weeks of gestation, confirmed to have GDM (on the basis of oral glucose challenge test and oral glucose tolerance test) were included. The pre-gestational diabetes mellitus and multiple pregnancies were excluded. Patients were thoroughly assessed for study criteria and investigated during an outdoor appointment. Patients were assessed every 1-2 weeks throughout pregnancy for glycaemic control with HbA1C. Tests are advised at 24 and 32 weeks of gestation, and fetal outcome was monitored by ultrasound. at these visits. Advise women with gestational diabetes mellitus to maintain their plasma glucose below the target levels: Fasting 5.3 mg/dl, 1 hour after meal 7.8 mg/dl, and 2 hours after meal 6.4 mg/dl. Informed consent was obtained, patients were randomly assigned by parallel assignment with 94 in each group (in the second trimester, after confirmation of gestational diabetes mellitus with an oral glucose challenge test Metformin tablets with a 500 mg strength three times daily were provided to Group A patients (a total of 94 patients). The dosage increased from a single morning dose to three times daily based on blood sugar management. The patients whose numbers ended in even received subcutaneous insulin (Group B=94). Each insulin type was prescribed separately: short-acting insulin before meals (4-6 units), and intermediate or long-acting insulin (10-12 units) once daily, with doses adjusted based on glucose levels. The calculation of insulin dosage for the second trimester used 0.8 units per kilogram of body weight, and the amount was increased to 0.9 units per kilogram for the third trimester. Insulin was prescribed twice daily: short-acting insulin before meals and intermediate-acting insulin at bedtime, with doses adjusted according to blood glucose levels. Patients were advised through diet charts to strict diet control (1800-2000kcal/day. and were also prescribed at least thrice weekly for 30 minutes' walk. If a patient on metformin was not controlled during treatment, they were excluded from the study. Fetal outcome was monitored by using ultrasound scans at these visits in terms of macrosomia and polyhydramnios. Outcomes were measured with reference to the neonate regarding preterm, birth weight, Respiratory Distress Syndrome RDS, Jaundice, and polyhydramnios. It was a convenient sampling, including neonatal heart rate, neonatal blood sugar levels were assessed, and values below 2.6 mmol/l were labelled as hypoglycaemia. The sample size of 188 patients (94 in each

group) was calculated using a 95% confidence level, 10% absolute precision, and the expected percentage of neonatal hypoglycaemia of 28.2% in the insulin group and 4.4% in the metformin group, based on the findings reported by Akinyemi *et al.* [16].

Data was entered and analysed with SPSS-26. Quantitative variable outcome was compared between groups with the help of an independent sample t-test, and qualitative outcome variables were compared between groups with the help of the chi-square test. Data were entered and analysed using SPSS version 26. The quantitative variables included maternal age, amniotic fluid index (AFI), neonatal birth weight, and neonatal heart rate. These were compared between the metformin and insulin groups using the Independent Sample t-test. The qualitative variables included the presence or absence of jaundice, macrosomia, neonatal hypoglycaemia, respiratory distress syndrome (RDS), and intrauterine growth restriction (IUGR). These categorical outcomes were compared between the two groups using the Chi-square test. A p-value of less than 0.05 was considered statistically significant. The p-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of women in Group A was 27.47 ± 4.77 and 27.90 ± 4.92 years in Group B. There was statistically significant difference was noted between groups. The mean amniotic fluid was 16.16 ± 5.86 in group A, and 16.04 ± 5.88 in group B. No significant difference was seen for amniotic fluid between groups. The mean heart rate of neonates in Groups A and B was 142 ± 8.56 and 142.41 ± 8.45 , and the mean weight of neonates in Groups A and B was 3.37 ± 0.30 and 3.39 ± 0.28 kg, respectively. There was a statistically significant difference between heart rate and weight between the groups (Table 1).

Table 1: Comparison of Age and Amniotic Fluid of Patients in Both Groups

Variables	Group A	Group B	p-value ⁽¹⁾
Age (Years)	27.47 ± 4.77	27.90 ± 4.92	0.528
Amniotic fluid	16.16 ± 5.86	16.04 ± 5.88	0.911
Heart rate (bpm)	142.00 ± 8.56	142.41 ± 8.45	0.662
Weight (kg)	3.37 ± 0.30	3.39 ± 0.28	0.708

⁽¹⁾ Independent sample t-test

The frequency of jaundice showed no significant difference between groups, Group A 7.4% vs Group B 13.8%, with p-value=0.156. Macrosomia was significantly higher in group B as compared to group A, 10.6% vs. 23.4%, with a p-value of 0.020. Hypoglycaemia was significantly higher in group B as compared to group A, 19.2% vs. 33%, with a p-value of 0.031. Respiratory distress was significantly higher in group B as compared to group B 9.6% vs 20.2%, with a p-

value of 0.041. IUGR was seen in 3 (3.2%) neonates in Group A and 3 (3.2%) neonates in Group B, respectively (Table 2).

Table 2: Comparison of Jaundice, Macrosomia, Hypoglycaemia, and Respiratory Distress in Both Groups

Variables	Group A	Group B	X ² value	p-value
Jaundice				
Yes	7 (7.4%)	13 (13.8%)	2.01	0.156
No	87 (92.6%)	81 (86.2%)		
Macrosomia				
Yes	10 (10.6%)	22 (23.4%)	5.423	0.020*
No	84 (89.4%)	72 (76.6%)		
Hypoglycaemia				
Yes	18 (19.2%)	31 (33%)	4.66	0031*
No	76 (80.9%)	63 (67%)		
Respiratory distress				
Yes	9 (9.6%)	19 (20.2%)	4.196	0.041*
No	85 (90.4%)	75 (79.8%)		
IUGR				
Yes	3 (3.2%)	3 (3.2%)	0.000	-p < 0.001
No	91 (96.8%)	91 (96.8%)		

Chi-Square test, (*) p-value < 0.05

DISCUSSION

It is essential to control diabetes throughout pregnancy to reduce negative consequences on the mother and fetus. Two frequently used treatment options for managing GDM are metformin and insulin. Although the goal of both drugs is to manage blood sugar levels, their modes of action and possible effects on the health of newborns are different. In this trial, we have examined the comparison of newborn outcomes linked to metformin vs insulin usage for the treatment of GDM. The mean age of women in Groups A and B was calculated to be 27.47 years and 27.90 years, respectively, and the age range in both groups was 20-36 years. Comparison of neonatal outcomes was done among the study groups. Some outcomes have not shown any difference among comparison drugs, i.e., neonatal HR, amniotic fluid mean, and IUGR development. In both groups, the mean of neonatal HR calculated was similar, showing no significant difference, i.e., 142.00 (group A) and 142.41 (group B) bpm, respectively, p=0.662. Both study groups also have similar mean neonatal weights calculated, 3.37 kg in group A and 3.39 kg in group B, p=0.708. In both groups, 3.2% newborns developed intrauterine growth restriction. The mean of amniotic fluid calculated in both groups was also nearly equal, metformin group mean calculated was 16.16, and in the insulin group, 16.04, p=0.91. Fetal development may also be linked to diabetes during pregnancy. Type 1 diabetes that has been uncontrolled encompasses a variety of clinical problems, like diabetic vasculopathy leading to placental malfunction and consequent fetal growth limitation since the placenta

is an organ made almost entirely of vessels [17]. It was observed previously that there was no change in newborn length or IUGR, but metformin usage was linked to lower birth weights and decreased likelihood of macrosomia (OR 0.59) [2]. Jaundice was detected in 7.4% neonates in the metformin group and 13.8% in the insulin group. The total number of cases with jaundice was 20, accounting for 10.6% of the total sample size of 188 neonates. However, the difference between groups was not statistically significant ($p=0.156$). In women with GDM, metformin along with insulin has been demonstrated to reduce newborn jaundice. 10.71% neonates developed jaundice on combined treatment as compared to 26.79% using insulin alone [18]. Incidence of neonatal jaundice (13.6 vs. 33.6%, $p<0.000$), in combination therapy, was noted to be low versus when insulin was used alone in another RCT [19]. 10.6% newborns in the metformin group and 23.4% in the insulin group had macrosomia; the p -value of 0.020 indicated statistically significant differences in the occurrence of macrosomia between comparison groups. Another trial has supported our findings in which 3 groups were compared, i.e., diet, metformin, and insulin groups, and it was observed that compared to the diet (29.5%) and insulin (21.7%) groups, fewer macrosomic newborns were seen in the metformin group (12.5%) [19]. In contrast to what we and this study experienced, the proportion of LGA babies in the metformin (8.2%) vs insulin (14.3%) groups did not differ significantly from each other in the MiG9 experiment, $p>0.05$. It might be because the metformin group in the aforementioned research received more insulin. Similar findings to ours were reported in the Gandhi *et al.* investigation [19]. In group A, hypoglycaemia occurred in 19.2%, but in group B, it was noted to be high, 33%, p -value of 0.031 indicated statistically significant differences. According to earlier research, the metformin group experienced a lower rate of newborn hypoglycaemia than the insulin group. There was no difference in infant morbidity between the groups receiving oral treatment and those receiving insulin; moreover, the oral treatment groups did not exhibit any occurrences of severe hypoglycaemia or jaundice [20, 21]. One study discovered that preterm births and glyburide use for gestational diabetes mellitus increased the incidence of hypoglycaemia in neonates. There was no discernible difference in risk of neonatal hypoglycaemia between pregnancies that were insulin-dependent and those that were controlled only with dietary changes. This study has also emphasized how crucial it is to check all newborns for hypoglycaemia during pregnancies involving GDM. Even those who were regarded as "lower risk" had a rather high chance of newborn hypoglycaemia, with hypoglycaemia seen in 39% of GDM-affected women's neonates, 35% of whom had hypoglycaemia treated with diet alone, and 33%

of whom had it treated with medication [22]. 9.6% newborns in the metformin group and 20.2% in the insulin group had the incidence of RDS, p -value of 0.041 indicated statistically significant variances among comparison groups. The pooled OR calculated was 1.47 for the relationship between maternal DM and risk of newborn RDS. For both GDM and pre-gestational diabetes mellitus, the pooled OR for the risk of newborn RDS was 1.57 and 2.66, respectively. So, it means GDM is a cause of RDS, not the treatment modalities [23]. It was concluded in one study that, when compared to insulin treatment for GDM, metformin may lower the risk of certain outcomes for mothers and newborns [24]. Insulin has several drawbacks, including daily injections, the possibility of hypoglycaemia, and weight gain in mothers. On the other hand, metformin is less expensive, safe, and has no appreciable effects on the mother or newborn, making it more acceptable to women with GDM [25]. More iatrogenic preterm births would occur if metformin had any unforeseen negative effects on fetal development or well-being. Furthermore, compared to insulin, metformin therapy produced better glycaemic control and better outcomes for newborns [2]. It was evaluated that the long-term effects of metformin on offspring occur due to its placental crossing. They demonstrated that over the first 18 months of life, growth, motor, and social development of children whose mothers were on metformin did not vary from those of control newborns. Thus, metformin is a good option for GDM, particularly for patients who are overweight but not obese [26].

Although the primary goal of our study was to compare the newborn outcomes using either metformin or insulin, it is essential to recognize that some limitations exist. First off, the relationship between maternal glycaemic management and newborn outcomes was not specifically examined in our study. Although it wasn't expressly included in our study, the effectiveness of metformin and insulin in lowering maternal blood glucose levels may have an impact on the outcomes of newborns. Furthermore, the primary focus of our research was the assessment of short-term newborn outcomes; there was no assessment of long-term neonatal outcomes. Further investigation is necessary to thoroughly assess these connections and the long-term results on the newborn.

CONCLUSIONS

The efficacy of metformin is as high as that of insulin in terms of neonatal outcome (macrosomia, hypoglycaemia, and respiratory distress) in women with gestational diabetes.

Authors' Contribution

Conceptualization: MI

Methodology: MI, MJ

Formal analysis: NA, SC, NA

Writing and Drafting: MI, TA

Review and Editing: MI, MJ, NA, SC, TA, NA

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



Knowledge, Attitude, and Practice of Healthcare Professionals of Pakistan Regarding Consumption of Carbonated Drinks

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ABSTRACT

Carbonated drinks contain acidic ingredients and high amounts of sugar. Such constituents lead to adverse oral and systemic manifestations, such as caries, dental erosion & hypersensitivity, diarrhea, GERD, respiratory, and bone disorders. **Objectives:** To determine the awareness, attitude, and practice of healthcare workers regarding carbonated drinks and to gauge their attitude and consumption habits regarding these drinks. **Methods:** A cross-sectional study was carried out across Pakistan, over eight months from January 2022 to August 2022. There was adequate representation from all provinces, and 1930 MBBS, BDS, and Allied Health Science workers filled out a pre-tested questionnaire. These professionals had different designations in government and private setups. A non-probability convenience sampling was done. Frequency and percentages depicted the data. One-way ANOVA was performed to compare composite knowledge and attitude scores, while Chi-square tests with Cramer's V were used for practice variables. **Results:** 97.5% of the healthcare workers knew about carbonated drinks, but only 85.1% were aware of their composition, whereas 93.1% knew about their side effects. 34.4% consumed carbonated drinks with meals. 87.2% believed that carbonated drinks have harmed teeth, and 60.2% experienced changes in the oral environment. **Conclusions:** Despite an abundance of knowledge regarding the composition and harmful effects of carbonated beverages, their consumption was high among the targeted population.

INTRODUCTION

The carbonated drinks are universally consumed beverages that are enjoyed by every generation. Their consumption has become a trend, which is on the rise [1]. High consumption of these drinks is reported to have significant health concerns, as they contain excessive quantities of sugars and acids [2]. Weight gain and obesity [3], nutritional deficiencies, cardiac diseases, neurological ailments, bone fractures, type II diabetes [4], and multiple metabolic malfunctions are commonly associated

problems [5]. On top of this, these drinkables can also lead to dental ailments, for example, caries [6], dentin sensitivity, gum problems, and tooth loss [7]. Globally, the revenue generated in the soft drinks market has escalated to US\$468.50bn in 2026 [8]. The assimilation of carbonated beverages can induce dental decay in children as well as adolescents [9]. Healthcare professionals can play a vital role in society in promoting oral health and in making people aware of the unfavorable effects of excessive intake



of carbonated drinks. An Indian study analyzed the carbonated drink consumption pattern among medical students. It was deduced that 44.09% participants consumed carbonated drinks and 26.36% experienced adverse effects of soft drinks [10]. There has been an increased consumption of carbonated drinks in Pakistan, as there has been globally [11]. A Pakistani study explored the consumption pattern of carbonated drinks in secondary school students; around 85% of them enjoyed having these beverages [12].

Although studies have explored the level of knowledge and practices of healthcare professionals regarding carbonated drinks, limited research has targeted healthcare workers across all fields and across diverse populations, particularly from multiple provinces. Moreover, the majority of studies have highlighted the general health effects of carbonated drinks, but specific ill effects on dentition have not been properly targeted. Therefore, the study aimed to assess the knowledge, attitudes, and practices of healthcare professionals from all fields across all provinces of Pakistan regarding carbonated drink consumption and its impact on dental health.

METHODS

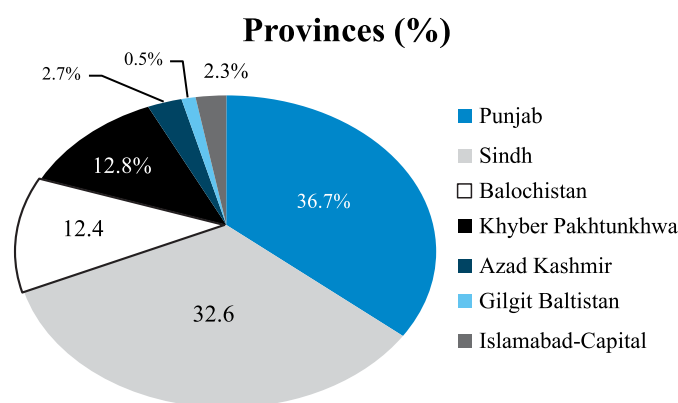
This was a cross-sectional study conducted on healthcare professionals in Pakistan who were approached in their private or government setups and institutes. The study was completed in a period of eight months from January 2022 to August 2022 after receiving an ethical letter from the Ethical Review Board of Combined Military Hospital Lahore Medical College and Institute of Dentistry (Reference No.4412/ERC/CMH/LMC; dated 13th August 2021). It was directed towards MBBS doctors, BDS doctors, and the workers of Allied Health Sciences (psychologists, physiotherapists, biochemists, pharmacists, radiographers, sonographers, nutritionists, homeopathic and neuropathic doctors, and speech therapists). The healthcare workers from Punjab, Sindh, Baluchistan, KPK, Azad Kashmir, Gilgit Baltistan, and Islamabad, the capital, were approached. The doctors who fall under the age bracket of 20-60 and above were targeted. This study excludes nurses, technicians, assistants, and other supporting staff. Healthcare workers with medical problems known to independently affect the oral cavity, like GERD, vomiting, bulimia, and anorexia, were also excluded from the study to reduce potential confounding and enhance internal validity. Additionally, any non-carbonated drinks, non-sugary drinks, lemon, vinegar, and acidic medicines were also excluded. A sample size was calculated using the WHO formula for cross-sectional studies ($n = Z^2 p (1-p) / d^2$). Assuming an expected prevalence (p) of 50%, with a 95% confidence level ($Z=1.96$) and a

margin of error of 5% ($d=0.05$), the minimum required sample size was 384 participants. To enhance study precision, a total of 2000 participants were approached, of which 35 individuals refused participation, and 35 were excluded due to unreliable responses. The final analyzed sample was composed of 1930 participants, yielding an overall response rate of 96.5%. A non-probability convenience sampling was done. The majority of participants were approached directly in person at their clinics/hospitals and educational institutes by a team of researchers. The participants were briefed about the purpose of this study and the nature and content of the questionnaire. Some of the participants were approached online, and the questionnaire on Google Form was sent to them through professional WhatsApp groups, professional Facebook medical groups, and institutional email accounts. To ensure honest responses, a consent and honesty statement was added in the beginning, stating that responses will be kept anonymous and will be used only for academic purposes. An attention check question was added in the questionnaire to filter out careless and fake responses. A preexisting closed-ended questionnaire was used in this study, whose validity was already confirmed [13]. For the internal reliability of the questionnaire, a pilot survey was conducted among 30 healthcare professionals, and Cronbach's alpha value was found to be 0.865.

Data analysis has been conducted on a sample of 1930 respondents from all the provinces of Pakistan. SPSS software (Statistical Package for Social Sciences, IBM, USA) version 23.0 was used. Statistical tests included frequency analysis and cross-tabulation. One-Way ANOVA was used to assess the composite knowledge and the composite attitude scores. Before ANOVA, the assumptions of normality and homogeneity of variances were assessed using the Shapiro-Wilk test and Levene's test, respectively. Post-hoc pairwise comparisons were performed using Tukey's HSD test. The categorical practice variables were evaluated by the chi-square test. The strength of associations was determined by Cramer's V, where statistical significance was set at $p < 0.05$.

RESULTS

The sample consisted of 56.8% females and 43.2% males who were mainly aged between 20 and 39 years. Moreover, over 50% of the respondents were MBBS, and 34.4% were BDS. The sample consisted of only 10.3% of Allied Health Sciences respondents. It was seen that the majority of respondents (63.7%) belonged to Government hospitals or colleges, and only 36.3% were from private setups. A major chunk of the sample belonged to Punjab (36.7%) and Sindh (32.6%), as these two are the country's largest provinces in terms of population (Figure 1).

**Figure 1:** Responses from Province (n=1930)

The awareness level of carbonated drinks among all three kinds of healthcare professionals was very high (97.5%). Around 85% of healthcare workers knew about the components of carbonated drinks. All healthcare professionals were well aware of the side effects of these beverages (93.1%). The composite knowledge scores did not differ significantly among professional groups (ANOVA $F=0.195$, $p=0.823$). Homogeneity of variances was confirmed by Levene's test ($p=0.498$). Post-hoc Tukey HSD showed no significant differences between MBBS, BDS, and Allied Health Science workers ($p=0.815$) (Table 1).

Table 1: Knowledge of Healthcare Professionals Regarding Carbonated Drinks

Responses	Frequency (%)	MBBS	BDS	Allied Health
Awareness of Carbonated Drink				
Yes	1881 (97.5%)	1040	651	190
No	49 (2.5%)	31	12	6
Awareness of the Composition of Carbonated Drinks				
Yes	1642 (85.1%)	913	571	158
No	288 (14.9%)	158	92	38
Awareness of the Side Effects of Carbonated Drinks				
Yes	1798 (93.1%)	1005	611	182
No	288 (6.8%)	158	92	38
Awareness of Sugar-Free Carbonated Drinks				
Yes	1749 (90.6%)	975	591	183
No	181 (9.4%)	96	72	13

The majority of the respondents preferred Coca-Cola (34.8%), followed by Sprite (19.6%) and Pepsi (10.0%). It was also seen that 9.3% of respondents didn't consume any carbonated drinks. A mixed response was observed when respondents were asked about their future consumption of

carbonated drinks. The composite attitude scores did not differ significantly among professional groups (ANOVA $F=0.186$, $p=0.830$). Homogeneity of variances was confirmed by Levene's test ($p=0.006$). Post-hoc Tukey HSD showed no significant differences between MBBS, BDS, and Allied Health Science workers ($p=0.768$) (Table 2).

Table 2: Attitude of Healthcare Professionals Regarding Carbonated Drinks

Responses	Frequency (%)
Preferred Carbonated Drinks	
Pepsi	193 (10.0%)
Coca Cola	679 (35.2%)
Sprite	379 (19.6%)
Fanta	180 (9.3%)
Dew	94 (4.9%)
Red Bull or Energy Drinks	68 (3.5%)
Sports Drinks	40 (2.1%)
Malt	118 (6.1%)
I Don't Consume	179 (9.3%)
Planning To Stop Consumption of Carbonated Drinks	
Yes	901 (46.7%), (MBBS=519, BDS=296, Allied Health=86)
No	825 (42.7%), (MBBS=456, BDS=284, Allied Health=85)
I Don't Consume/I Have Already Stopped Consumption	204 (10.6%), (MBBS=96, BDS=83, Allied Health=25)
Believing Carbonated Drinks Can Hurt Teeth	
Yes	1682 (87.2%), (MBBS=901, BDS=607, Allied Health=174)
No	236 (12.2%), (MBBS=158, BDS=56, Allied Health=22)
Maybe	12 (0.6%), (MBBS=12, BDS=0, Allied Health=0)

The majority of the respondents consume carbonated drinks once or twice a week (23.7%) or once or twice a month (22.9%). Some of these respondents either always consumed carbonated drinks with their meals (34.4%). 38.9% of respondents suggested that they did not consume carbonated drinks with meals (95% CI: 36.7-41.1%). 60.2% (95% CI: 58.0-62.4) experienced changes in the oral environment. Chi-square values hinted at a strong association between all practice variables and the field of study. Although Cramer's V gave values in lower ranges, it suggested that the consumption practices of MBBS, BDS, and Allied Health workers were quite similar (Table 3).

Table 3: Practice of Healthcare Professionals Regarding Carbonated Drinks

Responses	Frequency (%)	95% CI	MBBS	BDS	Allied Health	Chi-square (p-Value) Cramer's V
Frequency of consuming carbonated drinks						
I Don't Consume	180 (9.3)	—	99	68	23	$\chi^2=63.30$ (<0.001) $V=0.128$
Once or Twice a Day	259 (13.4%)	—	171	58	30	
Thrice or More a Day	122 (6.3%)	—	55	48	19	

Once or Twice a Week	458 (23.7%)	—	275	164	19	
Thrice or More a Week	137 (7.1%)	—	86	39	12	
Once or Twice a Month	442 (22.9%)	—	221	175	46	
Thrice or More a Month	169 (8.8%)	—	95	48	26	
Once or twice, or three times a Year	163 (8.4%)	—	79	63	21	
Prefer to consume carbonated drinks with meals						
Yes	664 (34.4%)	32.3-36.5	381	245	38	x ² =25.29 (<0.001) V=0.081
No	751 (38.9%)	36.7-41.1	424	234	93	
Sometime	515 (26.7%)	24.7-28.7	266	184	65	
Number of years of consumption of carbonated drinks						
I Don't Consume/Stopped	217 (11.2%)	—	117	72	28	x ² =34.31 (<0.001) V=0.094
Less Than a Year	83 (4.3 %)	—	36	37	10	
1-4	104 (5.4%)	—	77	16	11	
5-9	187 (9.7)	—	109	65	13	
10-13	261 (13.5%)	—	137	89	35	
14-15	387 (20.1 %)	—	204	150	33	
More than 15	696 (36.1%)	—	396	354	66	
Experience any change in the oral environment due to the consumption of carbonated drinks						
Yes	1162 (60.2%)	58.0-62.4	642	414	104	x ² =19.03 (0.001) V=0.070
No	278 (14.4%)	12.8-16.0	122	105	36	
Maybe	499 (25.9%)	23.9-27.9	303	143	53	

95% CI=95% Confidence Interval is reported only for primary binary outcome variables

DISCUSSION

97.5% of MBBS, BDS, and Allied Health Science workers were aware of carbonated drinks, 85.1% knew about the composition of carbonated drinks, and 93.1% knew about their adverse effects. As opposed to the Metta *et al.* study, where only 46.1% of dental students knew about the composition of carbonated drinks, and 97.1% knew about the adverse effects of these beverages [14]. Although our study has targeted professional doctors from multiple specialties, Metta *et al.* have targeted only dental students [14]. Coca-Cola was the most consumed beverage by practitioners, as 35.2% of the target population selected it as their most preferred drink, and this was followed by Sprite (19.6%). A KAP study conducted among university students of Malaysia revealed that every week, 52.3% of participants consumed soft drinks and 46% consumed fresh fruit juices [15]. In the present paper, 87.2% healthcare professionals believed that these beverages have harmful effects on teeth, and 0.6% were unsure about their dental effects; as opposed to Metta *et al.* study, where 58.8% were aware of the adverse effects on dentition [14]. 46.7% of our respondents were willing to quit consumption of such harmful beverages. As opposed to the Malaysian study, in which 99.7% undergraduate students showed positive attitudes towards giving up consumption [16]. Overall attitude scores revealed no significant differences among groups (ANOVA $F=0.186$, $p=0.830$). Post-hoc Tukey comparisons revealed consistent consumption among all groups ($p=0.768$). Studies have shown a dose-response association between the frequency of consumption of

carbonated drinks and adverse oral changes [17, 18]. Upon inquiring about the frequency of consumption, 13.4% of healthcare workers consumed once or twice a day, and 6.3% consumed thrice or more a day. This conflicts with Metta *et al.* where 84.3% dental students consumed once daily [14], and with Gedi *et al.* where 30.5% participants consumed daily [19]. The present paper found that 60.2% (95% CI: 58.0-62.4) of healthcare professionals noted damaging effects in their oral cavities. Although the association was statistically significant ($\chi^2=19.30$, $p=0.001$), the very weak effect size (Cramer's $V=0.070$) demonstrated limited practical significance, likely under the influence of a large sample size. Similar self-reported dental complaints have been documented by Niaz *et al.* where 41.7% reported sensitivity and 41.1% reported caries [20].

This study focused on healthcare workers of all age groups, with higher qualifications, work environments, and various professional sectors all over Pakistan. A large sample size provides a strong and generalizable estimate of knowledge, self-reported oral changes, and attitude towards consumption of carbonated drinks. This study has not explored the statistical association between demographic variables and consumption habits of healthcare professionals. Additionally, this study has not provided a detailed clinical assessment of changes in the oral cavity due to the ill effects of carbonated drinks. Future research needs to assess the analytical association between demographic factors and consumption of these beverages. Future research should incorporate a

longitudinal design to study the behavior of healthcare workers over time, and clinical assessment should also be included as part of data collection.

CONCLUSIONS

The majority of healthcare workers demonstrated good knowledge of the adverse effects of carbonated drinks, but their attitudes and consumption practices were moderate. This pattern was consistent across MBBS, BDS, and Allied Health Professionals.

Authors' Contribution

Conceptualization: AS, JS

Methodology: MJ, ZN, JA

Formal analysis: AS, MU, JA

Writing and Drafting: AS, JS, MJ

Review and Editing: JS, MJ, AS, ZN, MU, JA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



The Stone Kidney Size (SKS) Score Breakthrough: A Simple Yet Powerful Tool to Predict Success and Safety Outcomes in Pediatric Mini Percutaneous Nephrolithotomy (PCNL)

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ABSTRACT

Mini percutaneous nephrolithotomy (PCNL) is now considered one of the important treatment modalities for large renal stones or stones that are refractory to other treatments. **Objective:** To evaluate the predictive accuracy of the Stone Kidney Size (SKS) score for the prediction of the success rate of mini PCNL in the pediatric population. **Methods:** A prospective cross-sectional validation study was conducted at Tabba Kidney Hospital for a period of 7 months (from June 2025 to December 2025). A total of 124 children aged 1-14 years with unilateral renal stones were included. SKS score was calculated preoperatively using Ultrasound KUB based on the number of stones and Stone Kidney Index (SKI). Statistical analysis included chi-square test, logistic regression, and ROC curve analysis. **Results:** The mean age of the participants was 6.05 ± 3.32 years, and 67.7% male predominance was observed. Overall, the stone clearance rate was 81.4%. A total of 19% patients experienced postoperative complications, with a higher proportion in patients with a SKS score of ≥ 6 ($P=0.034$). The SKS score was found to be an independent predictor of incomplete stone clearance ($p<0.001$) with good predictive accuracy on ROC analysis. **Conclusions:** The SKS score is a simple, non-invasive, and reproducible tool that could be evaluated preoperatively with the use of Ultrasound KUB. It has good predictive ability for stone clearance and postoperative complications.

INTRODUCTION

Urolithiasis is one of the important clinical pathologies in the pediatric population, and the incidence of renal stones in the pediatric population has been rising with an estimated annual increase of 4-16% [1, 2]. Pakistan reports one of the highest pediatric urolithiasis prevalence rates, reaching 11.7% [3]. Mini percutaneous nephrolithotomy (mini PCNL) is an established treatment for renal stones that are larger than 2 cm or smaller stones that are resistant to extracorporeal shock wave lithotripsy (ESWL)

or ureteroscopic treatment [4]. In children, mini PCNL has a high stone clearance rate and acceptable complication rates, with studies showing an overall stone-free rate of 97%, ranging 91% to 100%, and a complication rate of 19% [5, 6]. In the era of minimally invasive surgery, to reduce complication rates in patients, instruments of smaller size have now been introduced [7, 8]. Studies show that mini PCNL reduces hospital stay, operative time, and postoperative complications [9]. Different scores like



Guy's, Seoul National University Renal Stone Complexity (S-ReSC), and S.T.O.N.E nephrolithometry score are there for preoperative prediction of complete stone clearance and post-operative complications rates [10, 11]. These scores are difficult to apply in children undergoing PCNL, as they require multiple preoperative and postoperative parameters. The Stone Kidney Size (SKS) score was found to be the simplest score that was developed for preoperative prediction of stone clearance rate for mini PCNL in the pediatric population, along with the prediction of perioperative complication rates using less invasive investigation [12]. So, a preoperatively calculated SKS score will be helpful for surgeons for counselling of parents/ guardians regarding the chances of complete stone clearance and perioperative complications [13].

However, its predictive accuracy has not been validated for the Pakistani pediatric population. This study was conducted to evaluate the predictive accuracy of the SKS score for success and complication rates in pediatric PCNL by using preoperative and postoperative ultrasound, KUB, and lab parameters. By using this scoring system, we sought to assess whether or not the SKS score can reliably predict postoperative stone clearance and complications in our pediatric population, so that it can be used as a counselling tool. The objective of this study was to evaluate the predictive accuracy of the SKS score for determining stone clearance and postoperative complications in pediatric patients undergoing mini PCNL. Additionally, this study aimed to assess the utility of the SKS score as a simple preoperative counselling tool in the local pediatric population.

METHODS

This prospective cross-sectional validation study was conducted in the Urology Department of Tabba Kidney Institute (TKI) for a period of 7 months from 1st June 2025 to 31st December 2025. The ethical approval was obtained from Tabba Kidney Institute, Hospital Ethical Committee (TKI-HEC) with ERC NO. TKI-HEC042 approved on 25th May 2025. Sample size was calculated by OpenEpi software, taking the prevalence of stone-free rate 80.6%, sensitivity 62.1%, specificity 78%, precision of 10%, and a confidence interval of 95%. The calculated sample size was 113 [14]. A total of 124 patients were assessed for the outcomes, including both male and female children from ages 1 to 14 years. Children with unilateral single, multiple, or staghorn stones were included in the study, and those with chronic kidney disease, previous same-site open surgical intervention history, or anatomical anomalies were excluded. After approval of the study by the hospital ethical committee, data were collected by using the hospital medical record number. Informed consent in the language of understanding was presented to parents/guardians

before enrollment. Patients meeting the inclusion criteria underwent mini PCNL following EAU guidelines. After consent and enrollment, patients were assessed with Ultrasound KUB and baseline laboratory parameters (CBC, UCE, urine analysis, urine culture, and coagulation profile). Preoperative Ultrasound KUB was used to observe the number of stones and to calculate SKI, which is a ratio of the length of the stone in the longest diameter and the length of the kidney along its longest diameter. In case of multiple stones, the sum of the length of each stone was taken as the longest diameter. These measurements were taken from formal radiologist reports. The SKS score and SKI were calculated using simple formulas based on preoperative ultrasound measurements. The SKI was determined by dividing the length of the stone along its longest axis by the length of the kidney along its longest axis, as measured on Ultrasound KUB. The SKS score was then calculated by adding points assigned for the number of stones and the SKI: a single stone was given 1 point, while more than one stone was given 2 points; similarly, an SKI of less than 0.3 was assigned 1 point, and an SKI greater than 0.3 was assigned 2 points. The sum of these points yielded the SKS score, which could range from 2 to 4 in this study. The SKS score was calculated as the sum of points for the number of stones. 1 point was given for a single renal stone, and 2 points were given for more than one stone. Similarly, 1 point was given to SKI < 0.3, and 2 points were given to SKI > 0.3. By the sum of these points, we obtained three possible SKS scores (2, 3, 4). According to these SKS scores, three groups were made, which were labelled as Group A, B, and C. Group A patients had SKS scores of 2, Group B patients had SKS scores of 3, and Group C patients had SKS scores of 4. Patients of the above-mentioned groups were then compared for perioperative complications and for stone clearance. All PCNLs were performed as mini PCNL technique under GA in the prone position with fluoroscopic guidance. The Amplatz sheath size and nephroscope were selected as per patient age, body habitus, and stone burden. During PCNL, operative time, on-table blood loss, need for intraoperative transfusion, and need for antegrade double J stent (DJS) were documented and compared between the three groups. After mini PCNL, labs were repeated on the 1st postoperative day to document postoperative hemoglobin drop, any increase in total leukocyte count (TLC) to rule out sepsis, and any derangement of renal function tests. Grades of postoperative hematuria, non-hemorrhagic complications (fever, vomiting, and pain), and duration of hospital stay were also compared. 1st Follow-up Ultrasound KUB was done in the 4th postoperative week, and complete stone clearance was documented as no residual stone fragments. After documentation of all preoperative, perioperative, and postoperative data, the three groups (A,

B, C) were compared for stone clearance, either partial or complete, and complications like hemoglobin drop, hematuria, and need for blood transfusion, fever, sepsis, and postoperative pain. Other parameters, like need for DJS and inpatient hospital stay, were also assessed. For data analysis, Statistical Package for the Social Sciences (SPSS) version 23.0 was used to enter, sort, and analyze the data. Continuous variables were analyzed as mean and standard deviation, while categorical variables were analyzed as frequencies and percentages. Continuous variables were age, operative time, and stone site, and stone size, number of stones, postoperative pain, in-hospital stay, and hemoglobin drop. Categorical variables were fever, hematuria, flank pain, vomiting, sepsis, need for transfusion, and DJ placement. The primary outcome variable was stone clearance (categorized as complete or partial clearance) at the 4th postoperative week follow-up Ultrasound KUB, and it was compared with the prediction based on the preoperatively calculated SKS score. Secondary outcomes were represented as residual stones, hemoglobin drop, need for postoperative transfusion, and DJ stent placement. The chi-square test and Fisher's exact test were used to see associations between categorical variables, and a p-value of <0.05 was considered significant. To identify independent predictors for stone clearance and postoperative outcomes, the predictive accuracy of the SKS score was evaluated via the receiver operating characteristic (ROC) curve analysis. The predictive validity of the SKS score was determined by taking into consideration various statistical methods. Receiver operating characteristic (ROC) curve analysis was used to assess discriminatory ability, and the area under the curve (AUC) was computed to evaluate the sensitivity of SKS score in predicting stone clearance, residual stones, and postoperative complications. The model was calibrated using the comparison of the predicted results with the observed results between SKS categories. Further, binary logistic regression analysis was conducted to assess the independent predictive value of SKS score, which was presented as odds ratios (OR) with 95% confidence intervals. Comparison of continuous variables between SKS groups was done through one-way analysis of variance (ANOVA). A p-value less than 0.05 was taken to be statistically significant.

RESULTS

There were 124 pediatric patients undergoing mini PCNL. Mean age was 6.05 ± 3.32 years. The majority were males (67.7%). Patients had a mean stone size of 2.14 ± 0.88 cm, and 64.5% were found to have many stones. The renal pelvis was the site that had the majority of the stones (64.5%)(Table 1).

Table 1: Baseline and Perioperative Characteristics of Study Population(n=124)

Variables	Values
Age (years)	6.05 ± 3.32
Age range (years)	1.3 – 14
Male	84 (67.7%)
Female	40 (32.3%)
Kidney length (cm)	7.64 ± 1.32
Stone size (cm)	2.14 ± 0.88
Number of stones (mean)	1.92 ± 0.83
Single stone	44 (35.5%)
Multiple stones	80 (64.5%)
Stone location (Renal pelvis)	80 (64.5%)
Renal pelvis + calyces	38 (30.6%)
Other locations	6 (4.9%)
Surgical approach (Subcostal)	124 (100%)
Amplatz sheath (12 Fr)	102 (82.3%)
Nephroscope (8 Fr)	104 (83.9%)
Lithotripsy (Pneumatic)	112 (90.3%)
Operative time (minutes)	121.3 ± 29.3

The overall stone clearance rate was 81.4%. A significant inverse relationship was observed between SKS score and stone clearance, with higher scores associated with lower clearance rates (Table 2).

Table 2: Postoperative Stone Clearance Rate According to Stone Kidney Size (SKS) Score

SKS Score	Groups	Total Patients (n)	Complete Stone Clearance, n (%)	Residual Stones, n (%)	p-value
2	A	42	42 (100%)	0 (0%)	0.002
3	B	48	37 (77.1%)	11 (22.9%)	
4	C	34	22 (64.7%)	12 (35.3%)	
Total		124	101 (81.4%)	23 (18.6%)	

Statistical test: Chi-square test

Interpretation: Stone clearance rate decreased significantly with increasing SKS score ($p \leq 0.05$)

Postoperative complications occurred in 21% of patients, most commonly fever (11.3%). Hematuria requiring transfusion was observed in 16% of patients. Complications increased significantly with higher SKS scores (Table 3).

Table 3: Postoperative Complications According to Stone Kidney Size (SKS) Score

Complications	Group A (SKS 2), n (%)	Group B (SKS 3), n (%)	Group C (SKS 4), n (%)	p-value
Hematuria requiring blood transfusion	2/42 (4.76%)	4/48 (8.33%)	10/34 (29.41%)	0.030
Postoperative fever	1/42 (2.38%)	7/48 (14.58%)	6/34 (17.65%)	0.021
Vomiting	0/42 (0%)	4/48 (8.33%)	1/34 (2.94%)	0.114
Flank pain	0/42 (0%)	3/48 (6.25%)	0/34 (0%)	0.152
Mild postoperative pain	1/42 (2.38%)	2/48 (4.17%)	1/34 (2.94%)	0.780

Statistical test: Fisher's Exact test

Interpretation: Postoperative complications increased

significantly with a higher SKS score

On logistic regression, SKS score was an independent predictor of incomplete stone clearance (OR = 9.16, $p < 0.001$). ROC curve illustrating the predictive validity of the SKS score for postoperative stone clearance, which indicates good discriminative ability (Figure 1).

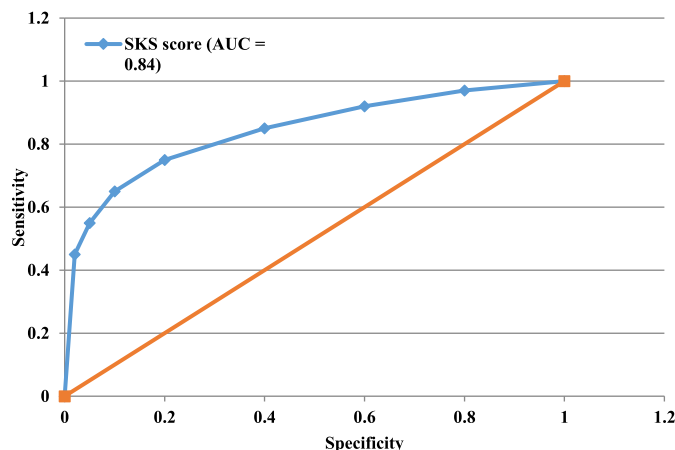


Figure 1: ROC Curve, SKS Predicting Postoperative Stone Clearance

ROC curve that demonstrates the predictive validity of SKS score in the prediction of postoperative complications, which is acceptable to good (Figure 2).

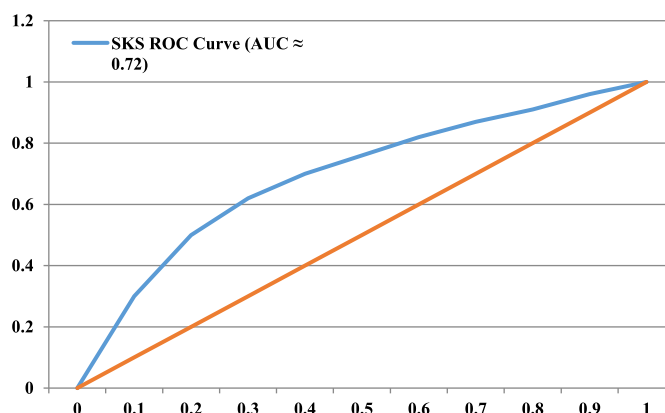


Figure 2: ROC Curve, SKS Predicting Postoperative Complications

In the multivariate logistic regression analysis, SKS score was a significant independent predictor of failed stone clearance, following age, stone size, and count of stones, and the duration of operation. One unit change (SKS) in the correct clearance score had an odds ratio of about nine ($p=0.001$). The other factors that were found to be significantly associated with incomplete clearance were the size of the stones and the number of stones, whereas age and operative time were found to have no statistically significant relationship. The positive correlation with SKS score showed a considerable increase in the operating

time, hemoglobin decrease, and length of stay in the hospital, demonstrating that the SKS score of the patients in the higher groups had more complex procedures and morbidity (Table 4).

Table 4: Multivariable Logistic Regression Analysis and SKS-Based Perioperative Outcomes

Variables	Categories	Group A / Effect	Group B / Effect	Group C / Effect	AOR / Mean $\pm$ SD	95% CI	p-value
Logistic Regression (Predictors of Incomplete Stone Clearance)	SKS score	—	—	—	9.16	3.92 – 21.45	<0.001
	Stone size (cm)	—	—	—	1.78	1.08 – 2.94	0.024
	Number of stones	—	—	—	1.69	1.02 – 2.81	0.041
	Operative time (min)	—	—	—	1.01	0.99 – 1.02	0.176
	Age (years)	—	—	—	0.96	0.87 – 1.06	0.392
	Stone location (pelvis vs calyces)	—	—	—	1.34	0.65 – 2.78	0.423
Perioperative Outcomes across SKS Groups	Operative time (min)	105.2 $\pm$ 18.4	122.6 $\pm$ 25.3	139.8 $\pm$ 30.1	—	—	0.001
	Hemoglobin drop (g/dL)	0.9 $\pm$ 0.4	1.3 $\pm$ 0.6	1.9 $\pm$ 0.8	—	—	<0.001
	Hospital Stay (days)	2.8 $\pm$ 0.9	3.6 $\pm$ 1.2	4.5 $\pm$ 1.5	—	—	—

DISCUSSION

Renal stones in children have become a major problem in the world in the past two decades, with the transformations in eating habits, water consumption, and genetic factors being the reasons behind the rise in their prevalence in children [15]. Although CT KUB is still the most sensitive and specific imaging modality in the diagnosis of renal stones, it is not utilized much in children because of the radiation exposure. Ultrasound KUB is thus a first-line diagnostic modality of choice in the pediatric population because it is non-invasive, safe, and able to identify most clinically important stones without exposing

children to unnecessary radiation [15]. Early and prompt diagnosis is essential in the prevention of complications that could involve obstruction, frequent infections, and renal impairment. Pediatric stone management is based on the size, location, and composition of the kidney stone and patient-specific factors (age and renal structure) [16]. Mini PCNL has proved to be safe and effective in the treatment of large and complex stones with high stone clearance and low complication rates [14, 17]. Mini PCNL in pediatrics should be performed carefully with a lot of planning and consideration to anatomical differences. Reduced calyceal

size, inconsistent renal sizes, and fragile renal parenchyma make them more technically demanding and require a judicious choice of sheath size, nephroscope, and surgery methodology [18]. Surgeons should also be able to predict possible problems during surgery, such as bleeding, inaccessibility of stones, or the necessity of auxiliary procedures. Several variables, such as stone burden, count of stones, position of stones, and anatomy of the patients, have been found to influence stone clearance and postoperative safety outcomes in children undergoing mini PCNL [19]. Nevertheless, they tend to be complicated systems that need several imaging and intraoperative parameters, which restrict their practical implementation in the pediatric population [12]. The SKS score was formed as a simplified assessment tool designed to be used with children and is based on the preoperative measurements of Ultrasound KUB. The purpose of our research was to confirm the SKS score among Pakistani pediatric patients and determine its predictive capability regarding the stone clearance and post-operative complications. Multiple scoring systems have been created to help adults preoperatively predict stone clearance and perioperative complications to guide surgical planning and counseling purposes [19, 20]. The present study showed that patients with a higher SKS score will have more chances of residual stone, need for DJS, secondary procedure, and need for transfusion, similar to the results of the parent article [21]. Specifically, we have shown that the lower the SKS score, the lower the chance of clearance, and the more stone burden affected the surgical outcome, i.e., all patients with a SKS score of 2 showed complete clearance, while those with scores of 3 and 4 showed decreased chances of clearance, and more stone burden was observed in patients with 3 and 4 [22, 23]. These results can be compared to those of other researchers who find that the preoperative stone features observed have a significant impact on the success of the procedure. The SKS score has a number of advantages in practice. It can be easily calculated during the preoperative period, and only a non-invasive ultrasound assessment is needed to give valuable prognostic data to both the surgeon and family. The presence of higher SKS scores can warn the surgeon about possible complications, and he or she may take precautionary actions, including preparing blood products, negative or treated urine cultures, optimizing perioperative care, and intensive postoperative monitoring. The score can also be used as a counseling instrument among parents or guardians, and it offers realistic expectations towards stone clearance, possible complications, and the possibility of secondary interventions. Finally, the SKS score is one of the simplest, most reliable, and non-invasive instruments to predict stone clearance rates and perioperative complications of

mini PCNL in children. Integrating it into standard preoperative evaluation, surgeons can enhance surgical preparation, patient safety, and counseling. Research in the future should focus on determining the validity of the SKS score in larger multicenter cohorts, determining the usability of the SKS score with newer imaging methods, and determining long-term outcomes such as stone recurrence and renal functioning.

Although this study has shown the predictive power of the SKS score in pediatric mini PCNL, it is associated with several limitations. This was carried out in one tertiary care center with a rather small sample size, which can make the application of the results to other populations questionable. The researchers used Ultrasound KUB as the only measurement technique during preoperative examination, which is not invasive but might not be as accurate as CT-based examinations. Moreover, no long-term follow-up was conducted after the fourth week after the operation was conducted; thus, no postoperative complications in the late period or stone recurrence could be evaluated. Future studies must be based on multicenter studies involving larger, more diverse pediatric cohorts, use more sophisticated imaging techniques to calculate the SKS score, and determine long-term outcomes in order to further confirm the usefulness of the SKS score in predicting both stone clearance and perioperative complications. While SKS offers practical prognostic value, it should be used alongside a comprehensive clinical assessment. Further studies in larger, multicenter settings are warranted to validate and refine its predictive accuracy in diverse pediatric populations.

CONCLUSIONS

The Stone Kidney Size (SKS) score is a simple, noninvasive, and reliable preoperative tool for predicting stone clearance and perioperative complications in children undergoing mini PCNL. It allows surgeons to provide clear, individualized counseling to parents and guardians regarding the likelihood of complete stone removal and potential risks.

Authors' Contribution

Conceptualization: YF

Methodology: YF, AM

Formal analysis: SSQ, AM, SAS, HAK

Writing and Drafting: JS, UR

Review and Editing: YF, SSQ, JS, UR, AM, SAS, HAK

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency and Precipitating Factors of Hyperglycemic and Hypoglycemic Emergencies in Diabetic Patients Presenting at Tertiary Care Hospital, Islamabad

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ABSTRACT

Diabetes mellitus (DM) is a highly widespread chronic metabolic condition and one of the major challenges to the health care system because of its acute and chronic complications.

Objective: To determine the frequency and precipitating factors of hyperglycemic and hypoglycemic emergencies among diabetic patients presenting to a tertiary care hospital in Islamabad. **Methods:** A cross-sectional study at the Department of Medicine, Pakistan Institute of Medical Sciences, Islamabad, between 5th April 2025 and 5th October, 2025. The enrolled sample size was 150 diabetic patients with altered consciousness (GCS $\leq$ 13) between the ages of 30 and 80 years using non-probability consecutive sampling. A structured pre-tested proforma was used to gather socio-demographic and clinical information such as type and duration of diabetes, modality of treatment, comorbidity, and past glycemic emergency. The Chi-square test, t-test, and the Mann-Whitney U test was applied, and a p-value of less than 0.005 was considered statistically significant. **Results:** Hyperglycemic emergencies were found to be 64.0%, and hypoglycemic emergencies were found to be 36.0%. The predictors of hyperglycemia that had significant values were missed insulin/medication (AOR = 4.21, $p < 0.001$), infection (AOR = 3.67, $p = 0.001$), and poor dietary adherence (AOR = 1.92, $p = 0.045$). Hypoglycemia was independently predicted by excess levels of insulin/OHA (AOR = 5.62, $p < 0.001$). **Conclusion:** Hyper and hypoglycemic crises are frequently observed in diabetic patients, and they are mostly caused by modifiable factors, including missed medications, infections, noncompliance with diets, overdosing, and missed meals. By focusing on these particular factors, it is possible to minimize morbidity and enhance the outcome.

INTRODUCTION

Diabetes mellitus (DM) is a highly widespread chronic metabolic condition and one of the major challenges to the health care system because of its acute and chronic complications [1, 2]. Among them, hyperglycemic and hypoglycemic crises are life-threatening acute complications that often result in emergency department visits and hospitalization [3]. Hyperglycemic emergencies

encompass diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS), compared to hypoglycemia, which involves mild cases of signs and symptoms, and in severe cases, this can be accompanied by coma, seizures, and death [4]. Diabetes has become a significant global problem in the past decades, especially in the low- and middle-income countries, where healthcare facilities are



scarce, and patient education is very poor [5]. A recent systematic review indicated that DKA, HHS, and severe hypoglycemia are among the most frequent acute diabetic crises, and the scope and predictors of those complications are not well defined in developing nations [6]. DKA and HHS are hyperglycemic crises that are usually precipitated by factors that can be identified [7]. Furthermore, the burden of hyperglycemic crises in the resource-constrained context is also subject to socio-economic barriers, low access to healthcare, and late presentation [8]. Various risk factors have been identified in studies, such as high doses of insulin, skipped meals, kidney failure, past cases of hypoglycemic events, and old age [9]. In 2024, a cross-sectional study stated that missing meals and hypoglycemic drugs were some of the most prevalent triggers of hypoglycemic events, and lifestyle behavior and treatment adherence were crucial [10]. Recognition of precipitating factors is essential to formulate specific interventions like patient education, structured follow-up, and protocol-driven management strategies in emergency departments. Early detection of high-risk persons and risk factors that can be managed will reduce hospitalization, enhance glycemic control, and reduce mortality related to diabetic crisis considerably. Additionally, tertiary care hospitals are referral hospitals, where acutely ill patients arrive and allow an analysis of the burden and trends related to such emergencies in a real-world clinical environment. This research seeks to offer evidence-based information to inform preventive measures, enhance clinical management guidelines, and minimize the cost of acute diabetic complications in Pakistan by determining the prevalent antecedents and patient factors linked to these emergencies.

The current study hypothesized that the primary causes of hyperglycemic crises would be missed medications, infections, and non-adherence to diet, whereas hyperglycemic crises would be related to excessive drug intake, lack of meals, and advanced age. The current study aimed to determine the frequency and the precipitating factors of hyperglycemic and hypoglycemic emergencies in diabetic patients presenting to a tertiary care hospital in Islamabad.

METHODS

It was a cross-sectional research study carried out in the Department of Medicine, Pakistan Institute of Medical Sciences (PIMS), Islamabad. The research was conducted and conducted in 6 months, from 5th April 2025 to 5th October, 2025. The Institutional Review and Ethics Board (IREB) of PIMS gave ethical approval (Approval No: F-5-2/2024(ERRC)/PIMS; dated 11th November 2024). The calculation of the sample size was determined based on the WHO sample size calculation software. Using a prevalence

rate of 46.6%, an error margin of 8%, and a confidence level of 95%, it was estimated that 150 patients were required [11]. The sampling technique used was a non-probability consecutive sampling method. Adults aged 30–80 years with a known diagnosis of type 1 or type 2 diabetes mellitus presenting to the Emergency Department of PIMS with altered consciousness (Glasgow Coma Scale ≤ 13) were recruited. Eligible participants included those with clinical and laboratory evidence of hyperglycemic crises or hypoglycemic crises. Patients were excluded if they had conditions that could independently affect glucose metabolism, including thyroid disorders, pregnancy, other endocrinopathies, or a history of malignancy or chemotherapy. After identifying the eligible patients, the patient gave informed consent or, in case the patient could not do it because of an altered mental status, an attendant or a legally authorized representative. Clinical and socio-demographic data, such as age, gender, residence, education, presentation symptoms, Glasgow Coma Scale [12], vital signs, and physical examination, were gathered prospectively during the presentation using a structured and pre-tested data collection pro forma. Routine diagnostic investigations, including random and fasting blood glucose, HbA1c, serum ketones, arterial blood gases, serum electrolytes, renal function test, and serum osmolality, were also documented at the presentation. These clinical and laboratory findings were then used to classify the patients as hyperglycemic or hypoglycemic emergencies. The factors that precipitated were determined via direct interviews with patients or their attendants.

The results were analyzed with the Statistical Package of Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to test the normality of continuous variables. Continuous variables that were normally distributed were described in terms of mean and standard deviation (SD), and non-normally distributed variables were described in terms of median and interquartile range (IQR). Frequencies and percentages were used to describe categorical variables. The frequency of hyperglycemic and hypoglycemic emergencies was the primary outcome variable. Proportions representing the prevalence of each type of emergency were computed as 95% intervals. The Chi-square test was used to compare categorical variables. To compare the continuous variables, an independent samples t-test was applied to compare normally distributed data, whereas a Mann-Whitney U test was applied to compare non-normally distributed data. Binary logistic regression analysis was conducted to determine independent variables that were related to hyperglycemic and hypoglycemic crises. The data of variables whose p-value was less than 0.20 in the univariate analysis were included in the multivariate

logistic regression model. To identify the strength of association between precipitating factors and glycemic emergencies, adjusted odds ratios (AORs) and 95% confidence intervals were reported. Variance inflation factor (VIF) was used to test multicollinearity, and the Hosmer-Lemeshow goodness-of-fit test was used to test model fitness. All analyses were taken to be statistically significant at a p-value of less than 0.005.

RESULTS

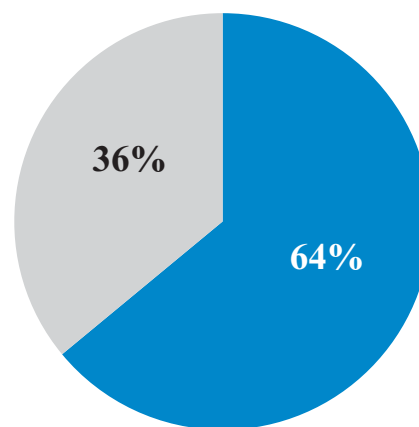
The study included 150 diabetic patients with glycemic emergencies, with a mean age of 57.4 ± 11.2 years and a slight male predominance. Most participants were urban residents and had type 2 diabetes, with a disease duration commonly between 5 and 10 years. Insulin was the most frequently used treatment, and a substantial proportion had prior glycemic emergencies and comorbid conditions, particularly hypertension (Table 1).

Table 1: Socio-Demographic and Clinical Characteristics of Study Participants (n=150)

Variables	Category	n (%) / Mean $\pm$ SD
Age (Years)	Mean $\pm$ SD	57.4 $\pm$ 11.2
Gender	Male	82 (54.7%)
	Female	68 (45.3%)
Residence	Urban	97 (64.7%)
	Rural	53 (35.3%)
Education Status	Illiterate	46 (30.7%)
	Primary	41 (27.3%)
	Secondary	38 (25.3%)
	Graduate & above	25 (16.7%)
Type of Diabetes	Type 1	38 (25.3%)
	Type 2	112 (74.7%)
Duration of Diabetes	<5 Years	44 (29.3%)
	5–10 Years	61 (40.7%)
	>10 Years	45 (30.0%)
Treatment Modality	Insulin	72 (48.0%)
	Oral Hypoglycemics	53 (35.3%)
	Combination therapy	25 (16.7%)
Previous Glycemic Emergency	Yes	59 (39.3%)
	No	91 (60.7%)
Comorbidities	Hypertension	98 (65.3%)
	Cardiovascular Disease	41 (27.3%)
	Chronic Kidney Disease	29 (19.3%)

There were 64.0% hyperglycemic crises, e.g., diabetic ketoacidosis and hyperosmolar hyperglycemic state, and 36.0% hypoglycemic crises. The 95% confidence interval of hyperglycemic emergencies was 54.4% to 73.6%, and the 95% confidence interval of hypoglycemic emergencies was 26.4% to 45.6% (Figure 1).

Frequency of Glycemic Emergencies



■ Hyperglycemic Emergencies (DKA/HHS) ■ Hypoglycemic Emergencies

Figure 1: Frequency of Glycemic Emergencies (n=150)

Hyperglycemic patients were generally younger with a shorter duration of diabetes but showed poorer long-term glycemic control, along with higher BMI, systolic blood pressure, and serum potassium levels. In contrast, hypoglycemic patients were older with longer disease duration and had relatively higher serum creatinine levels, indicating a possible association with impaired renal function. These findings highlight distinct clinical and metabolic profiles between the two groups (Table 2).

Table 2: Comparison of Continuous Variables by Emergency Type (n=150)

Variables	Hyperglycemic (n=96), Mean $\pm$ SD	Hypoglycemic (n=54), Mean $\pm$ SD	p-value
Age (years)	55.5 $\pm$ 11.0	60.0 $\pm$ 11.5	0.021*
Duration of Diabetes (years)	7 (4–10)	9 (5–13)	0.033*
Random Blood Glucose (mg/dL)	485 $\pm$ 130	52 $\pm$ 14	<0.001*
HbA1c (%)	10.9 $\pm$ 2.1	8.1 $\pm$ 1.7	<0.001*
BMI (kg/m ²)	28.1 $\pm$ 3.4	26.5 $\pm$ 3.1	0.012*
Systolic BP (mmHg)	138 $\pm$ 16	132 $\pm$ 15	0.045*
Diastolic BP (mmHg)	85 $\pm$ 10	82 $\pm$ 9	0.078
Serum Creatinine (mg/dL)	1.2 (0.9–1.5)	1.4 (1.1–1.8)	0.022*
Serum Potassium (mmol/L)	4.2 $\pm$ 0.5	3.7 $\pm$ 0.4	<0.001*

Missed medications, infections, and dietary noncompliance were significantly associated with hyperglycemic emergencies, whereas excessive medication intake and missed meals were the main triggers for hypoglycemia ($p < 0.005$). No significant differences were observed between the groups regarding cardiovascular events, recent surgery or trauma, or alcohol intake. These findings highlight distinct precipitating factors for each type of glycemic emergency (Table 3).

Table 3: Precipitating Factors of Glycemic Emergencies

Precipitating Factors	Hyperglycemic, n (%)	Hypoglycemic, n (%)	χ^2 Test	p-value
Missed Insulin/Medication	61 (63.5%)	12 (22.2)	26.4	<0.001*
Infection	52 (54.2%)	8 (14.8%)	23.7	<0.001*
Dietary Noncompliance	39 (40.6%)	11 (20.4%)	6.7	0.010*
Excess Insulin/OHA	4 (4.2%)	31 (57.4%)	56.3	<0.001*
Missed Meals	9 (9.4%)	29 (53.7%)	44.1	<0.001*
Cardiovascular Event	12 (12.5%)	6 (11.1%)	0.06	0.800
Surgery/Trauma	8 (8.3%)	3 (5.6%)	0.38	0.530
Alcohol Intake	6 (6.3%)	7 (13.0%)	1.9	0.170

Multivariate analysis identified non-adherence to medication, infections, and poor dietary compliance as key independent predictors of hyperglycemic emergencies. In contrast, excessive medication use, missed meals, and older age were strongly associated with hypoglycemic events. These findings highlight distinct risk profiles, emphasizing the need for targeted prevention and patient-specific management strategies (Table 4).

Table 4: Binary Logistic Regression Analysis of Factors Associated with Hyperglycemic and Hypoglycemic Emergencies (n=150)

Variables	Hyperglycemia AOR, (95% CI, p-value)	Hypoglycemia AOR, (95% CI, p-value)
Missed Insulin/Medication	4.21 (2.01-8.81), <0.001*	1.12 (0.50-2.52), 0.780
Infection	3.67 (1.74-7.75), 0.001*	1.31 (0.55-3.13), 0.540
Poor Dietary Adherence	1.92 (1.01-3.65), 0.045*	1.48 (0.73-3.02), 0.270
Duration of Diabetes >10 Years	1.88 (0.92-3.84), 0.080	1.21 (0.62-2.36), 0.570
Insulin Therapy	1.31 (0.67-2.56), 0.420	1.05 (0.49-2.23), 0.900
Excess Insulin/OHA Dose	0.87 (0.34-2.20), 0.770	5.62 (2.71-11.63), <0.001*
Missed Meals	0.92 (0.39-2.17), 0.850	4.87 (2.34-10.13), <0.001*
Older Age (>60 Years)	0.78 (0.36-1.66), 0.520	2.11 (1.01-4.42), 0.047*
Chronic Kidney Disease	1.13 (0.52-2.46), 0.760	1.94 (0.89-4.25), 0.090

DISCUSSION

Diabetic emergencies such as hyperglycemic episodes and hypoglycemic episodes are important morbidity and hospitalization causes in any part of the world. Hyperglycemic crises were more prevalent than hypoglycemic ones, as we found that almost two-thirds of the group were affected. The fact that missed insulin or medication doses and infection are the leading precipitating factors to hyperglycemic emergencies in this current study is consistent with the literature on this topic in developing countries, where noncompliance and intercurrent illness are the most common precipitations of severe hyperglycemia [13, 14]. In the same way, a cross-sectional study conducted in Pakistan by Rahak et al. reported that infection was the most frequently occurring precipitant of DKA (68.7%), with missed insulin doses

representing a smaller but significant fraction (12.2%) [15]. This finding is supported by longitudinal analyses indicating that long disease history is a risk factor for metabolic variability and complications. The current finding of longer diabetes history and worse long-term glycemic control (increased HbA1c) in hyperglycemic emergencies supports this finding. Whereas other studies have underlined the necessity of new-onset diabetes to act as a risk factor of DKA, especially within the context of type 1 diabetes, adult cohorts have repeatedly demonstrated chronic dysregulation as a significant predictor of severe hyperglycemia [6, 16]. Hypoglycemic crises were strongly linked to older age (>60 years) in our study, with an odds ratio of over twice that of younger patients (p=0.047). The result is consistent with the prior research, which established old age, kidney comorbidities, and some antidiabetic treatment as independent risk factors of inpatient hypoglycemia. Despite the important risk factor studies in hospitalized patients like that of Alghamdi et al. before 2021 which emphasized insulin regimen, infection and nutritional status as the determinants of inpatient hypoglycemia, modern cross-sectional studies in St. John's Medical College Hospital in India, observed older age, lower education, renal comorbidities, and the use of sulfonylureas as the independent risk factors of inpatient hypoglycemic episodes [17, 18]. This is in accordance with our results that the odds of hypoglycemia were more than twice when age >60 years (p=0.047). Comparative international studies reinforce both similarities and differences. The multicenter retrospective observational study on infections in DKA and HHS highlighted respiratory and urinary infections as frequent triggers, echoing our data, where infections substantially raised the risk of hyperglycemic emergencies [19]. Additionally, research examining outcomes in diabetic emergencies among acute care settings in North India identified DKA as the most frequent endocrine emergency, with advanced age and comorbidities correlating with severity and adverse outcomes, aligning with our findings on age and prolonged disease duration contributing to emergency risk [20].

This study provides important insights into the frequency and precipitating factors of diabetic emergencies, but several limitations should be acknowledged. It was conducted at a single tertiary hospital, limiting generalizability, and its cross-sectional design prevents causal inference. Reliance on patient recall for medication adherence, diet, and missed meals may introduce bias, while incomplete laboratory data restricts comprehensive biochemical assessment. A prevalence of 46.6% of the population in Italy was used to calculate the sample size, which might not be the best representation of a local Pakistani setting because of the demographic and healthcare systems differences. This dependency on

foreign data may influence the external validity of the results and must be taken into account during the interpretation of the results. Despite these limitations, the findings identify key modifiable risk factors that can inform targeted interventions to prevent acute glycemic crises. Further studies in Pakistan and other South Asian communities should focus on larger multicenter studies that can confirm the prevalence and precipitating factors of glycemic emergencies. Structured medication adherence programs, dietary counseling, and personalized antidiabetic therapy for older adults should be evaluated by interventional studies. Also, implementing predictive risk tools in emergency departments could help identify individuals at high risk early and reduce the number and severity of hyperglycemic and hypoglycemic crises.

CONCLUSIONS

Hyperglycemic and hypoglycemic crises continue to be a major burden on diabetic patients and have unique precipitating factors. Hyperglycemic crises can be mainly linked to missed medications, infections, and lack of adherence to a healthy diet, and hypoglycemic emergencies are more susceptible in older patients. They are provoked by an overdose of medications and missed food.

Authors' Contribution

Conceptualization: MAA

Methodology: JH, SW, MH

Formal analysis: JH

Writing and Drafting: JH, MAA, MH, AK, MS

Review and Editing: JH, MAA, SW, MH, AK, MS

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

Conflict of Interest

All the authors declare no conflict of interest.

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Original Article

Microbial Profiles and Antibiotic Resistance Patterns in Neonatal Sepsis:
A Frequency AnalysisImran Qaisar¹, Ishfaq Ahmed², Arif Hussain³, Irfan Ullah³, Aummara Rafique⁴ and Saba Afzal Sheikh³¹Department of Pediatrics, Quaid-e-Azam Medical College, Bahawalpur, Pakistan²Department of Pediatrics, Bahawal Victoria Hospital, Bahawalpur, Pakistan³Department of Pediatrics, Akthar Saeed Medical College, Rawalpindi, Pakistan⁴Department of Pediatrics, Akbar Niazi Teaching Hospital, Lahore, Pakistan

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ABSTRACT

Neonatal sepsis remains an important cause of neonatal morbidity, mortality, and prolonged hospitalization, and the spectrum of causative organisms and their antibiotic susceptibility varies across settings. Updated local microbiological data are therefore essential for appropriate empirical therapy and antimicrobial stewardship. **Objective:** To determine the frequency of different microorganisms and their antibiotic susceptibility pattern in neonatal sepsis. **Methods:** This descriptive cross-sectional study was conducted in the Pediatric Ward of Bahawal Victoria Hospital, Bahawalpur, from 09-02-2024 to 08-08-2024. A total of 119 term neonates with clinical features of sepsis were included. Blood cultures were processed by standard microbiological methods, and antibiotic susceptibility was assessed against commonly used antibiotics. Data were analyzed using SPSS version 25.0. Post-stratification Chi-square test was applied, and $p \leq 0.05$ was considered statistically significant. **Results:** *Escherichia coli* was the most frequent isolate, identified in 41 (34.45%) cases, followed by *Staphylococcus aureus* in 24 (20.17%) and *Klebsiella* species in 19 (15.97%). Overall, gram-negative organisms predominated. Amikacin showed the highest sensitivity, 111 (93.28%), followed by gentamicin, 107 (89.92%), whereas relatively lower sensitivity was observed for ceftazidime, 85 (71.43%), cefotaxime, 86 (72.27%), and tobramycin, 91 (76.47%). Stratification by age and gender showed no statistically significant differences in microorganism distribution or antibiotic susceptibility (all $p > 0.05$). **Conclusions:** *Escherichia coli* was the leading pathogen in neonatal sepsis in this cohort. The comparatively higher sensitivity to amikacin and gentamicin, together with lower sensitivity to some cephalosporins and tobramycin, supports the need for hospital-specific empirical antibiotic policies, regular antibiogram updates, and antimicrobial stewardship.

INTRODUCTION

Neonatal sepsis remains a major global cause of neonatal morbidity and mortality, especially in low- and middle-income countries where the burden of severe neonatal infection continues to be disproportionately high [1]. Recent evidence indicates that neonatal sepsis contributes substantially to preventable neonatal deaths, prolonged hospitalization, increased healthcare costs, and greater antibiotic exposure during the neonatal period [2]. Because the clinical presentation may be subtle or nonspecific, delayed recognition can rapidly worsen outcomes in affected newborns [1, 3]. Another important

challenge in neonatal sepsis is the evolving microbiological pattern across different hospitals, countries, and clinical settings. Contemporary studies have shown that the spectrum of pathogens is not uniform, with some units reporting a predominance of gram-positive organisms, while others continue to report a high burden of gram-negative pathogens such as *Escherichia coli* and *Klebsiella* species [3, 4]. Recent reports have also suggested an increasing importance of *Escherichia coli* in early-onset neonatal sepsis, while other centers continue to observe significant roles for coagulase-negative staphylococci,



Staphylococcus aureus, and other opportunistic organisms [3, 4]. These geographic and temporal variations make it unsafe to depend on older epidemiological data when selecting empirical antibiotics. Antimicrobial resistance has further complicated the management of neonatal sepsis. Recent studies have highlighted the growing resistance of neonatal pathogens to commonly used first-line antibiotics, creating difficulty in choosing effective empirical regimens and increasing the risk of treatment failure [4-6]. At the same time, overuse of broad-spectrum antibiotics in neonatal units may itself accelerate resistance, emphasizing the need for careful stewardship and unit-specific treatment protocols [5-7]. Systematic reviews have shown that surveillance of antimicrobial susceptibility and implementation of stewardship programs can reduce unnecessary antibiotic exposure without worsening neonatal outcomes [6-8]. Recent hospital-based studies from different regions continue to report marked variation in both pathogen frequency and susceptibility patterns [8-10].

Such differences underline the importance of local data when framing empirical therapy and infection-control strategies. In our setting, limited recent local literature is available on the current microbial profile and antibiotic sensitivity pattern in neonatal sepsis. Therefore, the study aimed to determine the frequency of different microorganisms isolated in neonatal sepsis and to evaluate their antibiotic susceptibility pattern so that local treatment decisions may be better aligned with current microbiological evidence.

METHODS

This descriptive cross-sectional study was carried out in the Pediatric Ward of Bahawal Victoria Hospital, Bahawalpur, from February 2024 to August 2024 (letter No. 2359/DME/QAMC, Bahawalpur; dated 9th February 2024). The sample size was calculated by the formula $n = Z^2 P(1-P)/d^2$ using a 95% confidence level, anticipated *Escherichia coli* frequency of 9.1% from a recent neonatal sepsis study [11], and an absolute precision of 5.2%, yielding a required sample of approximately 119 neonates. Non-probability consecutive sampling was used. Eligible participants were term neonates aged 0-28 days of either gender presenting with clinical features suggestive of sepsis for ≤ 24 hours. Neonates born preterm, those who had already received antibiotics before presentation, those with previous surgery, and those whose parents/guardians did not provide consent were excluded. After ethical approval and informed consent, 3-5 mL blood samples were collected aseptically using sterile syringes and inoculated into blood culture bottles. Blood cultures were processed by the BACTEC method and monitored for bacterial growth over 24-48 hours. Positive cultures were

identified by standard microbiological techniques, including Gram staining and routine organism identification procedures. Antibiotic susceptibility testing was performed for ampicillin, amoxicillin-clavulanate, gentamicin, amikacin, tobramycin, cefotaxime, and ceftazidime using routine laboratory protocols, with interpretation based on standard quality-controlled laboratory practice.

Data were entered and analyzed using IBM SPSS Statistics version 25.0. Age was expressed as mean $\pm$ standard deviation. Gender, isolated microorganisms, and antibiotic susceptibility results were presented as frequencies and percentages. Stratification was performed with respect to age and gender. Post-stratification Chi-square test was applied, and $p \leq 0.05$ was considered statistically significant.

RESULTS

A total of 119 neonates were included in the study, with a mean age of 7.82 ± 5.41 days. Overall, *Escherichia coli* was the most frequent microorganism isolated, followed by *Staphylococcus aureus* and *Klebsiella* species. In antibiotic susceptibility testing, amikacin and gentamicin showed the highest sensitivity, while ceftazidime, cefotaxime, and tobramycin showed comparatively lower sensitivity (Table 1).

Table 1: Frequency of Different Microorganisms and Antibiotic Susceptibility in Neonatal Sepsis

Microorganisms	Frequencies	Sensitive, n (%)	Resistant, n (%)
Microorganism Susceptibility			
<i>Escherichia coli</i>	41 (34.45%)	—	—
<i>Klebsiella species</i>	19 (15.97%)	—	—
<i>Staphylococcus aureus</i>	24 (20.17%)	—	—
<i>Acinetobacter species</i>	12 (10.08%)	—	—
<i>Staphylococcus epidermidis</i>	10 (8.40%)	—	—
<i>Enterobacter cloacae</i>	7 (5.88%)	—	—
<i>Moraxella species</i>	6 (5.04%)	—	—
Antibiotic Susceptibility			
Ampicillin (10 µg)	—	99 (83.19%)	20 (16.81%)
Amoxicillin-clavulanate (20/10 µg)	—	101 (84.87%)	18 (15.13%)
Gentamicin (10 µg)	—	107 (89.92%)	12 (10.08%)
Amikacin (30 µg)	—	111 (93.28%)	8 (6.72%)
Tobramycin	—	91 (76.47%)	28 (23.53%)
Cefotaxime	—	86 (72.27%)	33 (27.73%)
Ceftazidime	—	85 (71.43%)	34 (28.57%)

Across age groups, *Escherichia coli* and *Klebsiella* species were numerically more frequent in the 0-14-day group than in the 15-28-day group, but none of the age-based differences reached statistical significance (Table 2).

Table 2: Stratification of Different Microorganisms with Respect to Age

Microorganisms	Status	0–14 days (n=100)	15–28 days (n=19)	p-value
<i>Escherichia coli</i>	Yes	38 (38.0%)	3 (15.79%)	0.062
	No	62 (62.0%)	16 (84.21%)	
<i>Klebsiella species</i>	Yes	18 (18.0%)	1 (5.26%)	0.165
	No	82 (82.0%)	18 (94.74%)	
<i>Staphylococcus aureus</i>	Yes	21 (21.0%)	3 (15.79%)	0.604
	No	79 (79.0%)	16 (84.21%)	
<i>Acinetobacter species</i>	Yes	9 (9.0%)	3 (15.79%)	0.368
	No	91 (91.0%)	16 (84.21%)	
<i>Staphylococcus epidermidis</i>	Yes	9 (9.0%)	1 (5.26%)	0.590
	No	91 (91.0%)	18 (94.74%)	
<i>Enterobacter cloacae</i>	Yes	6 (6.0%)	1 (5.26%)	0.900
	No	94 (94.0%)	18 (94.74%)	
<i>Moraxella species</i>	Yes	5 (5.0%)	1 (5.26%)	0.962
	No	95 (95.0%)	18 (94.74%)	

With respect to gender, *Escherichia coli* was numerically more common in female neonates, whereas *Klebsiella* species and *Moraxella* species were more frequent in male neonates. However, these differences were not statistically significant (Table 3).

Table 3: Stratification of Different Microorganisms with Respect to Gender

Microorganisms	Status	Male (n=79)	Female (n=40)	p-value
<i>Escherichia coli</i>	Yes	24 (30.38%)	17 (42.50%)	0.189
	No	55 (69.62%)	23 (57.50%)	
<i>Klebsiella species</i>	Yes	16 (20.25%)	3 (7.50%)	0.073
	No	63 (79.75%)	37 (92.50%)	
<i>Staphylococcus aureus</i>	Yes	15 (18.99%)	9 (22.50%)	0.652
	No	64 (81.01%)	31 (77.50%)	
<i>Acinetobacter species</i>	Yes	8 (10.13%)	4 (10.0%)	0.983
	No	71 (89.87%)	36 (90.0%)	
<i>Staphylococcus epidermidis</i>	Yes	5 (6.33%)	5 (12.50%)	0.252
	No	74 (93.67%)	35 (87.50%)	
<i>Enterobacter cloacae</i>	Yes	5 (6.33%)	2 (5.0%)	0.771
	No	74 (93.67%)	38 (95.0%)	
<i>Moraxella species</i>	Yes	6 (7.59%)	0 (0.0%)	0.074
	No	73 (92.41%)	40 (100.0%)	

Antibiotic susceptibility by age group showed some numerical variation, but none of the differences between the 0–14-day and 15–28-day groups were statistically significant (Table 4).

Table 4: Stratification of Antibiotic Susceptibility with Respect to Age

Antibiotics	Status	0–14 days (n=100)	15–28 days (n=19)	p-value
Ampicillin (10 µg)	Sensitive	84 (84.0%)	15 (78.95%)	0.589
	Resistant	16 (16.0%)	4 (21.05%)	
Amoxicillin-clavulanate (20/10 µg)	Sensitive	85 (85.0%)	16 (84.21%)	0.929
	Resistant	15 (15.0%)	3 (15.79%)	

Gentamicin (10 µg)	Sensitive	90 (90.0%)	17 (89.47%)	0.944
	Resistant	10 (10.0%)	2 (10.53%)	
Amikacin (30 µg)	Sensitive	95 (95.0%)	16 (84.21%)	0.085
	Resistant	5 (5.0%)	3 (15.79%)	
Tobramycin	Sensitive	78 (78.0%)	13 (68.42%)	0.367
	Resistant	22 (22.0%)	6 (31.58%)	
Cefotaxime	Sensitive	72 (72.0%)	14 (73.68%)	0.881
	Resistant	28 (28.0%)	5 (26.32%)	
Ceftazidime	Sensitive	70 (70.0%)	15 (78.95%)	0.429
	Resistant	30 (30.0%)	4 (21.05%)	

Likewise, antibiotic susceptibility by gender did not show statistically significant differences (Table 5).

Table 5: Stratification of Antibiotic Susceptibility with Respect to Gender

Antibiotics	Status	Male (n=79)	Female (n=40)	p-value
Ampicillin (10 µg)	Sensitive	65 (82.28%)	34 (85.0%)	0.708
	Resistant	14 (17.72%)	6 (15.0%)	
Amoxicillin-clavulanate (20/10 µg)	Sensitive	68 (86.08%)	33 (82.50%)	0.607
	Resistant	11 (13.92%)	7 (17.50%)	
Gentamicin (10 µg)	Sensitive	71 (89.87%)	36 (90.0%)	0.983
	Resistant	8 (10.13%)	4 (10.0%)	
Amikacin (30 µg)	Sensitive	74 (93.67%)	37 (92.50%)	0.809
	Resistant	5 (6.33%)	3 (7.50%)	
Tobramycin	Sensitive	59 (74.68%)	32 (80.0%)	0.518
	Resistant	20 (25.32%)	8 (20.0%)	
Cefotaxime	Sensitive	57 (72.15%)	29 (72.50%)	0.968
	Resistant	22 (27.85%)	11 (27.50%)	
Ceftazidime	Sensitive	58 (73.42%)	27 (67.50%)	0.499
	Resistant	21 (26.58%)	13 (32.50%)	

DISCUSSION

In the present study, *Escherichia coli* was the most frequent isolate, followed by *Staphylococcus aureus* and *Klebsiella* species, with an overall predominance of gram-negative organisms. This pattern is partly comparable to recent studies showing that pathogen distribution in neonatal sepsis is highly variable across centers. Majigo et al. reported that gram-positive bacteria predominated in their Tanzanian cohort, but *Escherichia coli* remained the leading gram-negative isolate, and amikacin showed comparatively lower resistance among gram-negative pathogens [11]. The difference from our findings may reflect variation in case mix, neonatal unit practices, and local epidemiology. Our findings also differ from those of Karimi et al. reported *Klebsiella pneumoniae* and coagulase-negative staphylococci as the most frequent isolates in culture-positive neonatal sepsis, highlighting substantial regional diversity in pathogen prevalence [12]. Similarly, Siwakoti et al. reported a different bacteriological profile in Nepal, again emphasizing that empirical therapy for neonatal sepsis should be guided by local microbiological data rather than borrowed directly from

other institutions [13]. These differences support the reviewer's concern that the discussion should be contextualized using recent regional and global literature. The numerical predominance of *Escherichia coli* in the 0–14-day age group in our study may carry practical implications even though the difference did not reach statistical significance. Early neonatal predominance of gram-negative organisms may justify maintaining adequate gram-negative empirical coverage in clinically suspected cases, while also reinforcing maternal screening, aseptic delivery practices, and early neonatal infection-prevention measures. This interpretation is consistent with recent reports describing evolving early-onset and late-onset pathogen trends in neonatal sepsis [14, 15]. We also observed some gender-based numerical variation in microorganism distribution, with *Escherichia coli* more common among female neonates and *Klebsiella* species more common among male neonates, but these differences were not statistically significant. Such variation may simply reflect limited subgroup sizes, random variation, or unmeasured exposure-related factors rather than a true biological sex-based difference. Therefore, our data do not support gender-specific empirical antibiotic protocols. Recent hospital-based studies likewise emphasize the importance of unit-level epidemiology over subgroup assumptions [15, 16]. Regarding antibiotic susceptibility, amikacin and gentamicin showed the highest activity in our study, whereas relatively lower sensitivity was observed for ceftazidime, cefotaxime, and tobramycin. This has important therapeutic implications. Lower susceptibility to ceftazidime and tobramycin suggests that these agents may be less reliable as stand-alone empirical choices in our setting, particularly when gram-negative organisms predominate. Recent studies have similarly highlighted changing susceptibility patterns, rising multidrug resistance, and the need for regular surveillance-driven empirical policy revision [14–17]. Yang *et al.* further demonstrated that epidemiological shifts may occur over time even within the same institution, which reinforces the need for ongoing monitoring rather than one-time antibiogram review [17]. Our findings are also consistent with broader recent evidence showing the continuing burden of gram-negative neonatal sepsis and the importance of choosing effective empirical therapy early. Utomo *et al.* reported a predominance of gram-negative organisms in culture-proven neonatal sepsis, while Solomon *et al.* documented very high resistance to commonly used first-line agents among gram-negative bloodstream infections, with amikacin retaining comparatively lower resistance [18, 19]. These observations align with our results, where amikacin remained the most active antibiotic. In addition, Lee *et al.*

reported that contemporary neonatal sepsis management remains challenging due to evolving microbial patterns and the need to optimize antimicrobial use in neonatal units [20].

The fact that no statistically significant differences were found in antibiotic susceptibility across age and gender strata in our study has practical value. It suggests that, at present, a unit-level empirical antibiotic policy may be more appropriate than subgroup-specific protocols in this setting. However, these nonsignificant findings should not be interpreted as proof of the absence of clinically meaningful variation; rather, they point to the need for larger multicenter studies with sufficient power to detect subgroup differences. Meanwhile, hospital infection-control policies should focus on hand hygiene, aseptic blood culture sampling, rational antibiotic prescribing, and periodic antibiogram review. This study has some limitations. It was conducted at a single center, included a modest sample size, and was restricted to term neonates, which may limit generalizability. In addition, advanced molecular resistance characterization was not performed. Nevertheless, the study provides locally relevant microbiological and susceptibility data that may help guide empirical therapy and support antimicrobial stewardship in our setting.

CONCLUSIONS

Escherichia coli was the most frequent pathogen isolated in neonatal sepsis in this study, followed by *Staphylococcus aureus* and *Klebsiella* species, with overall predominance of gram-negative organisms. Amikacin and gentamicin showed the highest sensitivity, whereas relatively lower sensitivity was observed for ceftazidime, cefotaxime, and tobramycin. These findings support the use of periodic local microbiological surveillance, regular antibiogram-based revision of empirical antibiotic policies, and strengthened antimicrobial stewardship and infection-control practices in neonatal care.

Authors' Contribution

Conceptualization: IQ

Methodology: IQ

Formal analysis: IA, AR, SAS

Writing and Drafting: IQ, IA

Review and Editing: IQ, IA, IU

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

Conflict of Interest

All the authors declare no conflict of interest.

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Original Article



Bacteriology of Lower Respiratory Tract Samples with Antibiotic Susceptibility Patterns at a Tertiary Care Hospital in Karachi

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ABSTRACT

Lower respiratory tract infections are widespread in Pakistan. Determining sensitivity is crucial to combat increasing antimicrobial resistance. **Objectives:** To ascertain the prevalence of bacterial pathogens isolated in lower respiratory tract samples and the antimicrobial susceptibility patterns of these pathogens in one of the tertiary care hospitals in Karachi.

Methods: This study was a prospective observational study that took place for six months. Three hundred and thirty-five positive respiratory samples of patients with clinical LRTIs were collected. Identification of the bacteria was conducted by the standard microbiological procedures, and the determination of antimicrobial resistance was conducted by the Kirby-Bauer disk diffusion test according to the guidelines of CLSI 2025. SPSS version 26.0 was used to analyze data. The chi-square test was applied, and a p-value <0.050 was deemed significant.

Results: The study examined 335 culture-positive patient isolates, revealing Gram-negative rods (GNR) as the predominant pathogens (n=275), mainly *Klebsiella* spp., *Acinetobacter* spp., and *Pseudomonas aeruginosa*. Gram-positive cocci (GPC) (n=38) included *Staphylococcus aureus* and *Streptococcus pneumoniae*, while *Nocardia* was identified among gram-positive rods (n=22). Organism type significantly influenced resistance patterns (p<0.001), but specimen type did not (p=0.401). **Conclusions:** The most common LRTI pathogens were *Klebsiella* spp., *Acinetobacter* spp., and *Pseudomonas aeruginosa* that exhibited a wide spectrum of multidrug resistance. Stringent antibiotic stewardship plays a crucial role in preventing further increases in resistance.

INTRODUCTION

Lower respiratory tract infections (LRTIs) are among the common causes of morbidity and mortality and have a significant impact on the overall burden of disease in the world, as they affect people of all ages. [1]. The Global Burden of Disease (GBD) study also reveals pneumonia as the major contributor to death in the low and middle-income countries [2]. Bacterial pathogens, like *Streptococcus pneumoniae*, *Staphylococcus aureus*,

Pseudomonas aeruginosa, *Klebsiella* spp., and *Acinetobacter* spp. still dominate, but their treatment has become complicated with the emergence of antimicrobial resistance (AMR) [3]. The development of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria is a real concern to clinicians and health officials in general [4]. Alarming trends are reported in the global surveillance of resistance: the Global Antimicrobial



Resistance and Use Surveillance System (GLASS) of WHO has reported resistance rates of more than 50% in third-generation cephalosporin in *Klebsiella* spp. isolates in some parts of the world [5], with carbapenem resistance reported to be more than 60% in some regions of Asia and the Middle East [6]. According to reports made by the European Centre for Disease Prevention and Control (ECDC), resistance to the major antibiotics like fluoroquinolones, carbapenems, and aminoglycosides against *Pseudomonas aeruginosa* and *Klebsiella* spp. is on the rise [7]. Worldwide, antimicrobial resistance is already causing an estimated 700,000 deaths per year, and it is projected that this figure may increase unless there is a change in this situation. Hospitals, due to high levels of antibiotic utilization and high density of ill individuals, are the best breeding grounds for these formidable pathogens [8]. Pakistan is no exception, as the situation resembles these global trends with a concerning increase in the resistance of respiratory pathogens. The studies done in Karachi have established that more than 60% of the bacterial isolates on samples of lower respiratory tracts are MDR, with resistance rates among isolates of the ICUs being highly disproportionate, highlighting the critical care environments in the spread of resistant organisms [9]. A growing percentage of XDR strains is being reported. To make treatment decisions, stop the transmission of resistant strains, and reduce the load on the health sector, regular monitoring of AMR trends of respiratory pathogens is essential [4]. High disease burden and increased resistance highlight the necessity of local surveillance data. The trends on bacterial prevalence and susceptibility are usually dependent upon the geographical location, health care facility, and the patient. Thus, the current data should be used to make empirical antibiotic decisions, which should be based on the regionally specific data itself and not just on the international guidelines. Systematic surveillance of respiratory pathogens and antimicrobial profiles in the Karachi context is essential, given the high population density and healthcare needs, as it can improve patient outcomes and provide valuable information on hospital antibiotic stewardship initiatives.

Pakistan lacks multicenter surveillance data on LRTI bacteriology and antimicrobial resistance patterns, with most studies limited to single tertiary care hospitals in Karachi. No national standardized protocol exists for monitoring MDR and XDR respiratory pathogens across different regions. The current research seeks to determine the prevalence of bacterial pathogens sampled in the lower respiratory tract in a tertiary care hospital in Karachi and to determine the pattern of antibiotic susceptibility of bacteria. In addition, the study aims to determine the burden of MDR and XDR organisms among these isolates, thereby contributing crucial evidence to local and national

AMR surveillance efforts.

METHODS

This prospective observational study was conducted in the Department of Microbiology, Sindh Institute of Urology and Transplant, a tertiary care center in Karachi, Pakistan, from June 2025 to November 2025. The study protocol was reviewed by the Institutional Review Board (approval No. SIUT-ERC-2025/A-568; dated 3rd June 2025), and written approval was obtained before data collection. Patient confidentiality was maintained throughout the study after obtaining consent. Positive respiratory cultures, including sputum, bronchoalveolar lavage (BAL), and endotracheal aspirates (ETT), were obtained from patients of all ages and both sexes who presented with clinical features of LRTI, such as cough, fever, dyspnea, or purulent sputum. A non-probability, consecutive sampling technique was employed. Specimens that were improperly labeled, collected in compromised containers, or that showed fungal growth or *Mycobacterium tuberculosis* bacteria were excluded. Samples from transplant recipients were also excluded to avoid confounding immunosuppression. Using the WHO sample size calculator, the required sample size was determined. Based on the previous minimum estimation of *Staphylococcus aureus* isolation, found in 8.88% of samples, with a 3% margin of error and a 95% confidence level, a total of 335 positive respiratory cultures will be required for this study [3]. All specimens were collected under strict aseptic conditions. The specimen's quality was evaluated using Bartlett's scoring system, and specimens with a score of less than 1 were rejected. Specimens were processed in the microbiology laboratory without delay. All the samples were inoculated on Blood agar (Oxoid), MacConkey agar (Oxoid), and Chocolate agar (Oxoid) and incubated at 35–37°C for 18–24 hours. Identification of bacterial isolates was done using standard microbiological tests, such as Gram staining, colony morphology, and standard biochemical analyses (e.g., oxidase, catalase, indole, citrate utilization, urease, etc.) [10]. The Kirby-Bauer disk diffusion test was used to perform antimicrobial susceptibility testing on Mueller-Hinton agar as recommended by Clinical and Laboratory Standards Institute (CLSI) 2025 guidelines [11]. The antibiotic panel included β -lactams (ampicillin, amoxicillin-clavulanate, ceftriaxone, cefepime, ceftazidime), carbapenems (imipenem, meropenem), fluoroquinolones (ciprofloxacin, levofloxacin), aminoglycosides (amikacin, gentamicin, tobramycin), and other agents such as piperacillin-tazobactam and colistin for GNR, as well as vancomycin and linezolid for GPC when indicated. Vancomycin E test strips were used to measure minimum inhibitory concentrations (MICs) of MRSA. The standard ATCC reference strains were used to control

quality: *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *Staphylococcus aureus* ATCC 25923. All procedures adhered to CLSI quality control guidelines. CDC follows Magiorakos criteria for MDR and XDR bacteria. MDR Bacteria are strains that are non-susceptible to at least 1 in 3 antimicrobial categories, while XDR Bacteria are strains non-susceptible to at least 1 agent in all but 1 or 2 antimicrobial categories. Enzymes (New Delhi metallo-beta-lactamases NDM) identified in Carbapenem-resistant respiratory pathogens using the EDTA disk synergy test. Aztreonam Combination with Ceftazidime Avibactam on Carbapenem Resistant pathogens was synergetic observable in the case of double disc synergy [11].

Demographic information about the patients, the type of specimen, isolated organisms, and the antibiotic susceptibility outcomes were entered into a predesigned proforma and examined with SPSS software (version 26.0, IBM Corp., Armonk, NY). The frequencies and percentages were calculated by means of descriptive statistics. Chi-square test evaluated the associations between bacteria species and patterns of antibiotic resistance ($p < 0.005$ as statistically significant and $p < 0.001$ reported for highly significant associations) and a confidence interval 95%. No correction for multiple testing was applied, as the analysis was exploratory in nature.

RESULTS

Out of a total of 335 positive cultures of patients, 187 (55.8%) were from males, and 148 (44.1%) were from females. The mean age of the study population was 42.85 ± 19.50 years (mean $\pm$ SD), and the participants represented a wide age range. Among these, Gram-negative rods (GNR)

were the predominant group, accounting for 275 isolates (82%), while Gram-positive cocci (GPC) represented 38 isolates (11.34%). Within the GNR organisms, the most frequently isolated species was *Klebsiella* spp., found in 119 cases (43.22%), followed by *Acinetobacter* spp. in 62 cases (22.5%), and *Pseudomonas aeruginosa* in 57 cases (20.7%). Among the GPC, *Staphylococcus aureus* was the most common isolate, detected in 21 cases (55.3%), followed by *Streptococcus pneumoniae*, identified in 17 cases (44.7%). 22 cases of *Nocardia* were seen as gram-negative branching rods (Table 1).

Table 1: Distribution of Respiratory Pathogens in Different Sample Types

Organisms (n)	Sputum, n (%)	Tracheal Aspirate, n (%)	BAL, n (%)
Gram Negative Rods (n=275)			
<i>Klebsiella</i> spp. (119)	62 (52.1%)	53 (44.53%)	4 (3.36%)
<i>Actinobacter</i> spp. (62)	31 (50%)	29 (46.7%)	2 (3.22%)
<i>Pseudomonas aeruginosa</i> (57)	35 (61.4%)	19 (33.3%)	3 (5.26%)
<i>Haemophilus influenzae</i> (16)	16 (100%)	0	0
<i>Stenotrophomonas</i> (9)	8 (88.1%)	0	1 (11.1%)
<i>Moraxella</i> (3)	2 (66.6%)	1 (33.3%)	0
<i>Pseudomonas species</i> (3)	1 (33.3%)	2 (66.6%)	0
<i>E. Coli</i> (3)	1 (33.3%)	2 (66.6%)	0
<i>Elizabeth meningoseptica</i> (2)	1 (50%)	1 (50%)	0
<i>Morganella</i> (1)	0	1 (100%)	0
Gram Positive Cocci (n= 38)			
<i>Staphylococcus aureus</i> (21)	8 (38.09%)	12 (57.1%)	1 (4.7%)
<i>Streptococcus pneumoniae</i> (17)	15 (88.23%)	2 (11.7%)	0
Gram Positive Rods (n=22)			
<i>Nocardia</i> (22)	15 (68.1%)	3 (13.6%)	4 (18.1%)

Most of the respiratory pathogens were isolated from cultures of the patients falling in the age group 35- 55 years, especially *Klebsiella* spp. and *Pseudomonas aeruginosa*. *Acinetobacter* spp. was more commonly seen in the age group 15-24 years (Table 2).

Table 2: Distribution of Respiratory Pathogens in Different Age Groups and Gender

Variables	<i>Klebsiella</i> spp, n (%)	<i>Acinetobacter</i> spp, n (%)	<i>Pseudomonas Aeruginosa</i> , n (%)	<i>Staphylococcus Aureus</i> , n (%)	<i>Streptococcus pneumoniae</i> , n (%)	<i>Nocardia</i> , n (%)
Age Groups (Years)						
5-14	5 (4%)	4 (6%)	4 (7%)	2 (9%)	1 (5.8%)	0
15-24	14 (11.7%)	17 (27.4%)	6 (10.5%)	5 (23.8%)	3 (17%)	3 (13.6%)
25-34	20 (16.8%)	9 (14.5%)	5 (8.7%)	—	1 (5.8%)	5 (22.7%)
35-44	18 (15.1%)	10 (16.1%)	6 (10.5%)	5 (23.8%)	1 (5.8%)	2 (9.1%)
45-54	25 (21%)	7 (11.2%)	16 (28.1%)	4 (19.0%)	6 (35.2%)	6 (27.2%)
55-64	15 (12.6%)	9 (14.5%)	12 (21%)	4 (19.0%)	3 (17.6%)	6 (27.2%)
Above 65	22 (18.4%)	6 (9.6%)	8 (14%)	1 (4.7%)	2 (11.7%)	0
Total (100)	119 (100%)	62 (100%)	57 (100%)	21 (100%)	17 (100%)	22 (100%)
Gender						
Male	64 (53.7%)	32 (51.6%)	38 (66.6%)	16 (76.1%)	1 (64.7%)	14 (63.6%)
Female	55 (46.2%)	30 (48.3%)	19 (33.3%)	5 (23.8%)	16 (35.2%)	8 (36.3%)

The antimicrobial susceptibility analysis demonstrated significant variability across both Gram-negative and Gram-positive respiratory isolates, with multiple comparisons showing statistical significance ($p < 0.050$). Among Gram-negative

organisms, *Klebsiella* spp. and *Acinetobacter* spp. exhibited low susceptibility to β -lactams, including ceftriaxone (~21–22%) and cefepime (~25–33%), with statistically significant differences across organisms ($p < 0.001$). Carbapenem activity was moderate, particularly reduced in *Acinetobacter* spp. (imipenem 50%), indicating emerging resistance, although interspecies differences were not significant for some agents ($p = 0.978$). Aminoglycosides such as amikacin showed comparatively higher efficacy, especially against *Pseudomonas aeruginosa* (84.2%; $p = 0.005$). The sensitivity pattern for *Hemophilus influenzae* is shown. Fluoroquinolone susceptibility was low overall, particularly in *Acinetobacter* spp. (ciprofloxacin 4.8%), reflecting substantial resistance. In contrast, last-line agents polymyxin and tigecycline demonstrated consistently high susceptibility (>90%) across major Gram-negative isolates, with strong statistical significance ($p < 0.001$). Among Gram-positive organisms, *Streptococcus pneumoniae* remained highly susceptible to β -lactams (amoxicillin and ceftriaxone ~94%; $p < 0.001$). However, *Staphylococcus aureus* showed marked resistance, with low ceftazidime susceptibility (14.2%), indicating a high prevalence of MRSA. Vancomycin and linezolid demonstrated universal efficacy (100%), with no significant variation between organisms ($p = 0.735$), suggesting consistent activity. The results show susceptibility patterns of GNR and GPC in respiratory samples. Among Carbapenem-resistant Gram-negative rods ($n = 135$), NDM was seen in 75.9% of *Klebsiella* spp. isolates, 76.1% of *Acinetobacter* spp. isolates and 33.3% of *Pseudomonas aeruginosa* isolates. Ceftazidime, Avibactam, and Aztreonam showed limited activity against NDM-producing isolates separately. However, in vitro synergy between Ceftazidime – Avibactam and Aztreonam was 82% in our study. Susceptibility to agents such as colistin, doxycycline, and minocycline was variable (Table 3).

Table 3: Susceptibility Pattern of Gram-Negative Rods Isolated from Respiratory Samples

Antibiotics	<i>Klebsiella</i> spp, n (%)	<i>Acinetobacter</i> spp, n (%)	<i>Pseudomonas Aeruginosa</i> , n (%)	<i>Haemophilus influenza</i> , n (%)	<i>Stenotrophomonas</i> spp, n (%)	p-value
Amoxicillin clavulanate (30ug)	—	—	—	13 (81%)	—	<0.001
Ceftriaxone (30ug)	25 (21%)	14 (22.5%)	—	15 (93.7%)	—	<0.001
Cefepime (30ug)	30 (25.2%)	21 (33.8%)	43 (75.4%)	—	—	—
Piperacillin tazobactam	35 (29.4%)	19 (30.6%)	43 (75.4%)	—	—	<0.001
Cefoperazone	34 (28.5%)	19 (30.6%)	43 (75.4%)	—	—	0.978
Amikacin (30ug)	42 (35.2%)	17 (27.4%)	48 (84.2%)	—	—	0.005
Cotrimoxazole	30 (25.2%)	18 (29.0%)	—	7 (43.7%)	9 (100%)	<0.001
Imipenem	43 (36.1%)	31 (50%)	46 (80.7%)	—	—	0.978
Gentamicin (10ug)	52 (43.6%)	18 (29%)	—	—	—	0.868
Levofloxacin (30ug)	26 (21.8%)	5 (8.0%)	41 (71.9%)	11 (68.7%)	9 (100%)	0.963
Doxycycline	57 (47.8%)	33 (53%)	—	—	—	<0.001
Minocycline	65 (54.1%)	35 (56.4%)	—	—	9 (100%)	<0.001
Fosfomycin	61 (51.2%)	—	—	—	—	0.012
Ceftazidime-avibactam	43 (51.2%)	—	45 (78.9%)	—	—	0.087
Aztreonam	40 (33.6%)	—	47 (82.4%)	—	—	0.708
Tigecycline	105 (88.8%)	57 (91.9)	—	—	—	<0.001
Azithromycin	—	—	—	12 (75%)	—	—
Polymyxin	109 (91.6%)	58 (93.5%)	55 (96.4%)	—	—	<0.001

The results show susceptibility patterns of GPC in respiratory samples (Table 4).

Table 4: Susceptibility Pattern of Gram-Positive Organisms Isolated from Respiratory Samples

Antibiotics	<i>Streptococcus Pneumoniae</i> , n (%)	<i>Staphylococcus Aureus</i> , n (%)	<i>Nocardia</i> , n (%)	p-value
Ampicillin	15 (88.2%)	—	—	<0.001
Ceftriaxone	16 (94.1%)	—	6 (27.3%)	<0.001
Cotrimoxazole	9 (52.9%)	13 (61.9%)	22 (100%)	<0.001
Ciprofloxacin	10 (58.8%)	8 (38%)	5 (22.7%)	0.151
Clindamycin	—	12 (57.1%)	—	<0.001
Erythromycin	7 (41.1%)	8 (38.09%)	—	<0.001
Ceftazidime	—	3 (14.2%)	—	<0.001
Azithromycin	7 (41.1%)	—	—	<0.001

Linezolid	17 (100%)	21 (100%)	22 (100%)	0.735
Doxycycline	—	—	16 (72.7%)	<0.001

Acinetobacter spp. showed the highest percentages of MDR and XDR pathogens among GNRs, whereas *Staphylococcus aureus* was found to be the most common MDR pathogen among GPCs. ETT showed a greater frequency of MDR and XDR while sputum and BAL showed comparable patterns (Figure 1).

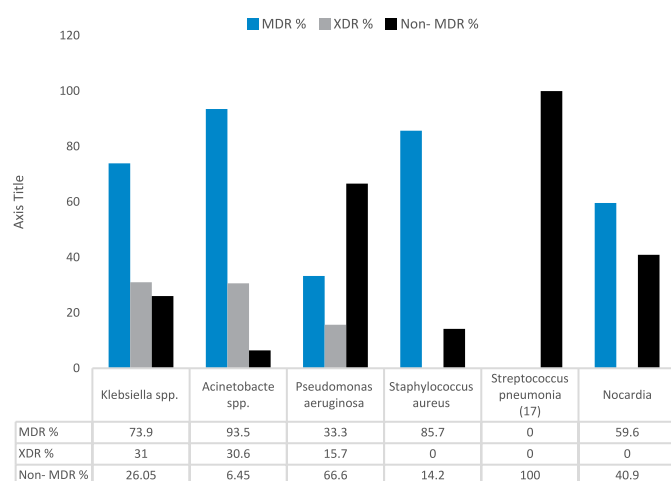


Figure 1: Frequency (%) of MDR, XDR, and Non – MDR in Respiratory Pathogens

DISCUSSION

This study assessed the bacteriological spectrum and antibiotic resistance patterns in LRTIs among patients at a tertiary care hospital in Karachi. The data revealed a predominant presence of Gram-negative bacteria GNRs, particularly *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Acinetobacter* spp. While Gram-positive bacteria GPCs primarily *Staphylococcus aureus* and *Streptococcus pneumoniae*, were less frequent but can lead to severe infections and emerging resistance trends. Gram-negative bacteria cause LRTIs globally, particularly in hospital and ICU settings [12]. An Indonesian study indicated *Klebsiella* spp. as the commonest isolate, followed by *Pseudomonas aeruginosa*, and *Acinetobacter* spp. exhibiting substantial resistance to β lactam, cephalosporins, and fluoroquinolones, and semipermeable to carbapenems and aminoglycosides, results which are in agreement with our study [13]. Within Pakistan, similar trends have been observed. A systematic review by Bilal et al. reported *Klebsiella* spp. as the leading respiratory pathogen, followed by *Pseudomonas* spp. and *Acinetobacter* spp., with high resistance to cephalosporins and quinolones [14]. In contrast, *Streptococcus pneumoniae* and *Hemophilus influenzae* remain the predominant respiratory pathogens in Europe and North America, reflecting differences in healthcare settings, antibiotic usage, and patient profiles [15]. In this current research, the lower frequency of *S. pneumoniae* is probably an indication of the large numbers of hospital-acquired and ventilator-associated respiratory samples, as opposed to community-based cases. The observation that most respiratory pathogens were isolated in the 35–55 year age group, particularly *Klebsiella* spp. and *Pseudomonas aeruginosa*, is consistent with regional case series demonstrating higher GNR infection rates in middle-aged and elderly cohorts because of increased comorbidity and healthcare exposure [16]. Conversely,

Acinetobacter spp. was more common in younger patients (15–24 years), a pattern less frequently reported in the literature and potentially reflective of localized outbreaks or demographic healthcare utilization in the current setting. Other reports have also identified substantial *Acinetobacter* isolation among young hospitalized patients, particularly in ICUs where invasive devices and prolonged stays may contribute to risk [17]. A prospective study from Egypt reported that ETT and BAL samples yielded fundamentally more resistant Gram-negative bacteria than expectorated sputum, suggesting that invasive sampling is more likely to capture hospital-adapted, drug-resistant flora [18]. Third-generation cephalosporins retained strong activity against *Haemophilus influenzae* and *Moraxella catarrhalis*, supported by data from the CHINET 2024 antimicrobial resistance surveillance network report that *H. influenzae* exhibits minimal non-susceptibility ($\leq 0.5\%$) to ceftriaxone in hospital isolates, and *M. catarrhalis* continues to show high overall susceptibility profiles in respiratory samples [19]. Conversely, resistance among *Enterobacterales* to third-generation cephalosporins remains high in the nosocomial context, with resistance levels frequently exceeding 50%, and ESBL prevalence is substantial among hospital-associated isolates [20]. Carbapenem susceptibility was low among *Klebsiella* spp. and *Acinetobacter* spp. in the current study, reflecting the expanded dissemination of carbapenems such as NDM and OXA-type enzymes in tertiary hospitals. Molecular surveillance studies of carbapenem-resistant Gram-negative clinical isolates have repeatedly documented widespread carriage of genes that confer high-level resistance to carbapenems in these isolates from healthcare settings [21]. *Pseudomonas aeruginosa* was relatively more susceptible to anti-pseudomonal cephalosporins and carbapenems, with a similar trend observed in other tertiary settings, as a European surveillance study showed *Pseudomonas aeruginosa* exhibiting greater susceptibility to ceftazidime and cefepime relative to carbapenem-resistant *Enterobacterales* and non-fermenters. However, the resistance rates can be changed but heavily depend on local antibiotic use and infection control practices [22, 23]. Aminoglycosides such as amikacin and tobramycin are fairly active against Gram-negative isolates, consistent with established literature, which positions these agents as important components of combination therapy for severe Gram-negative pneumonia [24]. Among Gram-positive organisms, *Staphylococcus aureus* exhibited high rates of multidrug resistance, aligning with regional and international reports where MRSA remains a frequent MDR isolate in respiratory samples [26]. *Streptococcus pneumoniae* showed high susceptibility to ampicillin and

amoxicillin, which parallels some community pneumonia data, though rising macrolide resistance has been documented globally, with azithromycin susceptibility now <60% in many regions [26], which is also consistent with our study findings. The predominance of MDR and XDR among *Acinetobacter* spp. in this study reflects their well-recognized propensity for accumulating resistance. Extensive resistance in *Acinetobacter* spp. has been reported in multiple ICU surveillance series, often associated with prolonged ventilation and invasive device use [18]. The high prevalence of NDM among carbapenem-resistant *Klebsiella* spp. and *Acinetobacter* spp. isolates in our study are consistent with molecular epidemiology studies from the Indian subcontinent, where NDM has effectively displaced other carbapenamases in many tertiary hospitals [6]. Both ceftazidime avibactam and aztreonam showed limited standalone activity against NDM producers and emphasized the need for combination strategies [27]. Although synergy between ceftazidime avibactam and aztreonam has been detected in selective studies, the high synergism rate (82%) observed in this study suggests that the combination of Ceftazidime avibactam and Aztreonam may provide a reliable treatment option for severe infections caused by NDM-producing organisms [28].

This prospective observational study provides a snapshot of resistance patterns and does not include full genotypic profiling, clinical outcomes, or prior antibiotic exposure. Despite these constraints, it offers valuable local data to guide empirical therapy and stewardship. Overall, the statistically significant differences observed for most antibiotics highlight distinct resistance patterns among organisms, emphasizing the need for targeted therapy. It is high time to make stringent policies for combating antibiotic resistance; otherwise, the clinical implications of AMR will take over, leading to treatment failure, limited therapeutic options, longer hospital stays, higher healthcare costs, and unmanageable infections.

CONCLUSIONS

This study highlights the predominance of respiratory pathogens like *Klebsiella* spp., *Acinetobacter* spp., *Pseudomonas Aeruginosa*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*. The high prevalence of MDR and XDR isolates highlights the importance of effective antimicrobial stewardship.

Authors' Contribution

Conceptualization: AJ

Methodology: AJ, SJ, YP

Formal analysis: MM

Writing and Drafting: AJ, SJ, YP, MM, MA

Review and Editing: AJ, SJ, YP, MM, MA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Risk Factors for the Onset of Aspiration Pneumonia in Stroke Patients

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ABSTRACT

The third causes disability and is the second most common cause of death in the world. It is an interruption in the flow of blood to the brain and denies the brain tissues oxygen and other vital nutrients, thus causing ischemic damage. **Objective:** To determine the risk factors associated with the onset of aspiration pneumonia in stroke patients. **Methods:** A cross-sectional study was carried out from December 2, 2023, to May 1, 2024, at the Department of Medicine, Khyber Teaching Hospital. Participants included 149 patients aged ≥ 18 years who had been diagnosed with aspiration pneumonia complicating a stroke. The following risk variables for aspiration pneumonia were investigated: diabetes, smoking, age over 65, stroke type, Glasgow Coma Scale (GCS) < 8 , and nasogastric (NG) feeding. Data analysis was done with SPSS version 25.0. **Results:** The patients' average age was 61.77 ± 9.58 years. The most frequent risk factor seen in 101 individuals (71.8%) was the kind of ischemic stroke, which was followed by the lack of NG feeding in 95 patients (63.8%). The least prevalent factor was diabetes mellitus ($n=66$, 44.3%). **Conclusions:** Aspiration pneumonia is a dreadful complication in stroke patients. It is more frequent in patients with advanced age, with a GCS less than 8, and without NG feeding.

INTRODUCTION

Stroke is the third leading cause of disability and ranks as the second most frequent cause of death worldwide. It occurs when blood flow to the brain is interrupted, depriving brain tissue of oxygen and essential nutrients, which leads to ischemic damage [1, 2]. Data on stroke prevalence in Pakistan are limited, but estimates suggest an incidence of around 250 cases per 100,000 population, corresponding to approximately 350,000 new cases each year [3]. The hallmark symptom of stroke is sudden weakness or numbness affecting the face, arm, or leg, typically on one side of the body, known as a focal neurological deficit. Other manifestations may include confusion, difficulty with speech or comprehension, visual disturbances in one or both eyes, problems with walking,

dizziness, loss of balance or coordination, severe unexplained headaches, fainting, or loss of consciousness [4, 5]. Risk factors for stroke are classified as modifiable or non-modifiable. Modifiable factors include lifestyle choices such as tobacco and alcohol use, physical inactivity, obesity, high blood pressure, atrial fibrillation, elevated cholesterol, diabetes, and atherosclerosis. Non-modifiable factors encompass age, sex, ethnicity, family history, and previous episodes of stroke or transient ischemic attacks [4, 5]. One of the most common side effects for stroke patients admitted to hospitals is aspiration pneumonia [6]. After being admitted to the hospital for one to two days, stroke patients experience it. A common aspiration among patients who are



incapacitated, such as those who have had a stroke, is food aspiration, which puts the patient at risk for aspiration pneumonia. Apart from aspirating food, other bodily fluids and any type of gastrointestinal material can also enter the lungs and result in aspiration pneumonia. Patient morbidity and death are rising even with the many preventive and therapeutic strategies used in healthcare facilities for patients with post-stroke aspiration pneumonia [7]. According to a study, aspiration pneumonia was associated with the following risk factors: Glasgow Coma Scale (GCS) ≤ 8 in 82.9%, use of nasogastric feeding in 64.4%, age over 65 in 44.6%, smoking in 62.08%, diabetes in 57.4%, hemorrhagic stroke in 62.7% [8]. The aspiration pneumonia risk variables in one study included age over 65, smoking, diabetes, hemorrhagic stroke, GCS ≤ 8 , and nasogastric feeding usage [8].

In Pakistan, there is limited local information regarding risk factors of aspiration pneumonia in stroke patients. There are inconsistent results in the existing international literature, and there is no recent in-depth study that has been carried out in Khyber Pakhtunkhwa. This gap becomes an obstacle to prevention strategies that are evidence-based. This paper determines the important risk factors that can be changed to inform clinical practice. In order to identify and prevent these risk factors, the purpose of this study is to ascertain the frequency with which aspiration pneumonia occurs in stroke patients. This study contributes to improved stroke patient management and a decrease in the morbidity and death of stroke victims. My goal in doing this study is to identify and prevent key risk factors that could further increase the morbidity of stroke patients. This study aimed to determine the risk factors for the onset of aspiration pneumonia in stroke patients.

METHODS

A cross-sectional study was conducted at the Department of Medicine, Khyber Teaching Hospital, from December 2, 2023, to May 1, 2024. The sampling technique used was non-probability consecutive sampling. Ethical approval was obtained from the Review Board of Khyber Medical College (Ref No: 02/DME/KMC; dated 2nd January 2023). The sample size for this study was calculated using the WHO sample size calculator [9], with a 95% confidence interval, 8% absolute precision, and an expected prevalence of aspiration pneumonia of 44.6% in patients aged over 65 years [8], resulting in a total of 149 participants. The study included patients aged 18 years and above who had experienced a stroke and developed aspiration pneumonia, regardless of gender. Patients with congenital anomalies such as cleft palate were excluded. Following ethical approval, eligible inpatients at KTH were approached, and the objectives of the study were explained before obtaining informed consent. Demographic

information collected included age, gender, stroke type, body mass index (BMI), residence, socioeconomic status, education level, occupation, and presence of comorbidities such as diabetes and hypertension, as well as duration of symptoms. A detailed history and physical examination were performed for each participant. The level of consciousness was assessed at admission using the Glasgow Coma Scale (GCS). As part of standard clinical management, initial laboratory evaluations were performed. Patients were subsequently observed in the intensive care unit for the development of aspiration pneumonia. Risk factors for aspiration pneumonia were identified according to the operational definition, and all data were systematically recorded using a structured proforma.

Data analysis was conducted using SPSS version 22.0. Continuous variables were expressed as mean $\pm$ standard deviation, whereas categorical variables were summarized using frequencies and percentages. To account for potential effect modifiers, the data were stratified by variables including age, gender, and duration of stroke. Post-stratification analysis was performed using the chi-square test. A p-value of ≤ 0.05 was considered indicative of statistical significance.

RESULTS

The age of the patients ranged from 40 to 80 years. The mean age of the patients was 61.77 ± 9.58 years. The mean BMI of patients was 23.04 ± 2.922 . 90 (60.4%) were male, and 83 (55.7%) patients had a BMI more than 24.0. Most of the patients had an education below matric, 78 (52.3%), as shown in table 1.

Table 1: Study Participants' Demographic Characteristics

Parameters		Frequency (%)
Age in Years	≤ 65	72 (48.30%)
	> 65	77 (51.70%)
Gender	Male	90 (60.40%)
	Female	59 (39.60%)
BMI (kg/m ²)	24.0 or below	66 (44.30%)
	More Than 24.0	83 (55.70%)
Residence	Rural	77 (51.70%)
	Urban	72 (48.30%)
Education	Matric or below	78 (52.30%)
	Above Matric	71 (47.70%)
Profession	Salaried	42 (28.20%)
	Business	59 (39.60%)
Socioeconomic (SE) Status	Yes	78 (52.30%)
	No	71 (47.70%)
Stroke Duration (days)	5 or below	83 (55.70%)
	More Than 5	66 (44.30%)
Hypertension	Yes	57 (38.30%)
	No	92 (61.70%)

Ischemic stroke type was the most consistent risk factor observed in 101 participants (71.8%), followed by the absence of NG feeding in 95 patients (63.8%). Diabetes mellitus was the least common factor (n=66, 44.3%). The frequency of risk factors for aspiration pneumonia in patients with stroke is shown in table 2.

Table 2: Frequency of Risk Factors for Aspiration Pneumonia in Patients with Stroke

Risk Factors		n (%)
Age > 65 Years	Yes	77 (51.70%)
	No	72 (48.30%)
DM	Yes	66 (44.30%)
	No	83 (55.70%)

Smoking	Yes	71 (47.70%)
	No	78 (52.30%)
Glasgow ComaScale (GCS) <8	Yes	89 (59.70%)
	No	60 (40.30%)
Nasogastric (NG) Feeding	Yes	54 (36.20%)
	No	95 (63.80%)
Stroke Type	Ischemic	107 (71.80%)
	Hemorrhagic	42 (28.20%)

Risk factor for aspiration pneumonia is stratified by gender and duration of stroke. After stratification by gender and duration of stroke, the age, type of stroke, and state of consciousness were associated significantly ($p < 0.05$), as shown in table 3.

Table 3: Stratification of Risk Factors for Aspiration Pneumonia with Gender and Duration of Stroke

Risk Factors		Gender			Stroke Duration (Days)		
		Male, n (%)	Female, n (%)	p-value	≤5, n (%)	>5, n (%)	p-value
Age > 65 Years	Yes	36 (46.80%)	41 (53.20%)	<0.001*	30 (41.70%)	42 (58.30%)	0.001*
	No	54 (75.00%)	18 (25.00%)		53 (68.80%)	24 (31.20%)	
Diabetes	Yes	36 (54.50%)	30 (45.50%)	0.192	42 (63.60%)	24 (36.40%)	0.082
	No	54 (65.10%)	29 (34.90%)		41 (49.40%)	42 (50.60%)	
Ischemic Stroke	Yes	54 (50.50%)	53 (49.50%)	<0.001*	65 (60.70%)	42 (39.30%)	0.048*
	No	36 (85.70%)	6 (14.30%)		18 (42.90%)	24 (57.10%)	
Smoking	Yes	42 (59.20%)	29 (40.80%)	0.766	41 (57.70%)	30 (42.30%)	0.632
	No	48 (61.50%)	30 (38.50%)		42 (53.80%)	36 (46.20%)	
GCS <8	Yes	66 (74.20%)	23 (25.80%)	<0.001*	41 (46.10%)	48 (53.90%)	0.004*
	No	24 (40.00%)	36 (60.00%)		42 (70.00%)	18 (30.00%)	
NG Feeding	Yes	36 (66.70%)	18 (33.30%)	0.239	36 (66.70%)	18 (33.30%)	0.042*
	No	54 (56.80%)	41 (43.20%)		47 (49.50%)	48 (50.50%)	

* Shows p-value < 0.05

DISCUSSION

The higher risk of aspirating gastric content is common in patients with stroke for several reasons. For instance, aspiration is more likely to occur in stroke patients who have neurological damage because their swallowing reflexes are compromised. Additionally, because mechanical ventilation via an endotracheal tube can hinder common aspiration defense mechanisms like coughing, individuals who need this are more vulnerable to aspiration [10]. The mean BMI of patients was 23.04 ± 2.922 . 90 (60.40%) were male, and 83 (55.7%) patients had a BMI of more than 24.0. Most of the patients had an education below matric, 78 (52.30%). The most frequent risk factor seen in 101 participants (71.80%) was the kind of ischemic stroke, which was followed by the absence of NG feeding in 95 patients (63.80%). Diabetes mellitus was the least common factor. Aspiration was more common in males compared to females (60.40% versus 39.60%). Males compared to females exhibited a significantly higher risk of developing aspiration pneumonia, aligning with the findings of Lidetu et al. [6]. Additionally, the findings of research carried out in China and the United Kingdom

support this trend [11, 12]. A higher GCS level is more protective in stroke patients against aspiration pneumonia. In this study, aspiration was common in those with a GCS below 8 (59.70% versus 40.30%). These findings were consistent with studies from Ethiopia and Nigeria [10, 13]. Impaired consciousness or low Glasgow Coma Scale (GCS) score, reduced airway reflexes are diminished, increasing susceptibility to aspiration. When these defense mechanisms are compromised, the likelihood of aspirating oropharyngeal or gastric contents rises, potentially leading to aspiration pneumonia [6]. Dysphagia is a common complication following stroke and represents a major risk factor for aspiration pneumonia, contributing significantly to higher rates of mortality and long-term disability [3]. Studies estimate that approximately 50–67% of individuals experience swallowing difficulties after a stroke [4, 5]. Prompt evaluation of swallowing function is therefore essential, as it assists in determining appropriate nutritional strategies and may reduce the risk of stroke-associated pneumonia (SAP) [6, 7]. Evidence indicates that patients with post-stroke dysphagia have a substantially

greater risk of developing pneumonia (22.9%) compared to those without swallowing impairment (1.1%), largely due to aspiration events [8]. Furthermore, the probability of pneumonia may increase incrementally by approximately 1% per day when dysphagia remains undetected or untreated [10]. Stroke frequently results in dysphagia, which raises the possibility of aspiration pneumonia, which has been linked to increased mortality and disability rates [14]. Poststroke dysphagia affects between 50% to 67% of stroke victims [15]. Decisions about nutritional treatment and the potential reduction of stroke-associated pneumonia (SAP) problems are informed by early assessment of swallowing ability in stroke patients [16]. Compared to those without dysphagia (1.1%), patients with dysphagia (poststroke) have a higher incidence of pneumonia (22.90%), which is most likely caused by aspiration [17]. This study observed aspiration in stroke patient were more common in patients aged 65 years of age (51.70% versus 48.3%). Progressive neurological deficits, swallowing difficulties, weakened immunity, and a higher prevalence of comorbidities are all associated with advanced age. Together, these variables increase the incidence of post-stroke aspiration pneumonia in elderly individuals, which is in line with research from several other nations [18, 19]. Aspiration occurred more often in individuals with ischemic stroke than hemorrhagic stroke in the current study (71.8% vs. 28.2%). These results are in line with those of Khalid et al. who found that 35% of their study sample experienced hemorrhagic stroke and 65% had ischemic stroke [20]. Other research, however, has shown contrasting findings, suggesting that people who have had an ischemic stroke may be less likely than those who have had a hemorrhagic stroke to get aspiration pneumonia [6]. The variation between our findings and previous research could be attributed to differences in study design and patient selection. Our study specifically included only stroke patients who developed aspiration pneumonia and did not compare them with stroke patients without aspiration, which may have influenced the distribution. A comparable methodology was adopted in the study conducted by Khalid et al. [20]. This study's findings demonstrated that a greater proportion of patients who developed post-stroke aspiration pneumonia were receiving oral feeding (63.8%) compared to those fed via a nasogastric (NG) tube (36.2%). These results differ from those reported by Nigus et al. who found that stroke patients receiving NG tube feeding were 10.58 times more likely to develop aspiration pneumonia [10]. Additional studies have similarly suggested that NG tube feeding carries a higher risk of aspiration than oral feeding [21, 22]. The elevated risk associated with NG tube feeding may be explained by factors such as excessive feeding volumes, improper patient positioning, particularly feeding in the

supine posture, or incorrect placement of the NG tube. Furthermore, Lin et al. found that patients with oropharyngeal dysphagia were more likely to aspirate when receiving NG tube feeding [23], while it was unclear if the study group was limited to stroke patients. Existing literature indicates that the incidence and determinants of pneumonia during the subacute phase of stroke have not been thoroughly investigated. Moreover, pneumonia developing in the subacute period may follow a different clinical course compared to pneumonia occurring in the acute phase [8]. A notable strength of the present study is the incorporation of admission imaging findings alongside established clinical predictors in the evaluation of pneumonia. This approach may represent a relatively underexplored factor in pneumonia development and could provide a valuable direction for future research.

The small sample size (n=149), no control group, and single-center cross-sectional design limit the generalizability of the findings, as the study was not conducted to determine causality, but only to identify associations; it was also not followed up over the long term, which increases the risk of recall bias. Multicenter prospective cohort designs, control groups, larger samples, prolonged follow-up, dysphagia screening systems, early NG feeding, and designing a local risk score to prevent aspiration pneumonia in stroke patients.

CONCLUSIONS

In conclusion, patients with ischemic stroke with a Glasgow Coma Scale score of less than 8 having no nasogastric feeding were most frequently observed with aspiration pneumonia. Patients with stroke should be evaluated for aspiration at the time of presentation.

Authors' Contribution

Conceptualization: SU, NUH

Methodology: SU, NUH

Formal analysis: IU

Writing and Drafting: SU, NUH, IU, MH, AS, EK, OAK

Review and Editing: SU, NUH, IU, MH, AS, EK, OAK

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

Conflict of Interest

All the authors declare no conflict of interest.

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Original Article

Frequency and Association of Distal Interphalangeal Joint Enthesitis with Nail Psoriasis in Patients with Psoriasis and Psoriatic Arthritis Presenting at a Tertiary Care Hospital in Karachi

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ABSTRACT

Psoriasis is an autoimmune inflammatory disease that has a chronic disease or chronic illness nature, and that is commonly presented in the form of psoriatic arthritis. **Objectives:** To estimate the frequency and association of DIP joint enthesitis with nail psoriasis in patients with psoriasis and psoriatic arthritis presenting at a tertiary care hospital in Karachi. **Methods:** This cross-sectional analytical study was conducted in the Department of Dermatology and Rheumatology, Civil Hospital Karachi, six months following the ethical consent. The enrolment was done through non-probability consecutive sampling among 96 patients aged 18-65 years old with or without psoriatic arthritis, having psoriasis. This data was analyzed in SPSS version 27.0, and the correlation between nail psoriasis and DIP joint enthesitis was discovered with the assistance of chi-square or Fisher's exact test, and a p-value under 0.005 was considered to be statistically significant. **Results:** Nail psoriasis was found in 64.6% of the patients, and ultrasound-verified DIP joint enthesitis was observed in 37.5% of the 96 patients in this cohort. A statistically significant association was found between nail psoriasis and DIP enthesitis confirmed with ultrasound ($p=0.003$). Moreover, the multivariate logistic regression analysis showed that nail psoriasis was independently related to DIP joint enthesitis following the adjustment of age, sex, psoriasis duration, and occurrence of psoriatic arthritis (adjusted OR 3.52; 95% CI 1.289.67; $p=0.014$). **Conclusion:** Nail psoriasis has a strong correlation with distal interphalangeal joint enthesitis in patients with psoriasis and psoriatic arthritis.

INTRODUCTION

Psoriasis is a long-term immune-mediated inflammatory disease, which mostly attacks the skin but often nails and the musculoskeletal system. Pitting, onycholysis, and subungual hyperkeratosis are typical nail changes that could indicate inflammation of the structures most proximate to the distal interphalangeal joint, including nail apparatus and enthesitis of the extensor tendon [1]. According to recent findings, the nail involvement is often correlated with higher disease activity and functional burden in patients with psoriatic arthritis, which suggests

that the nail unit could be a valuable clinical predictor of musculoskeletal disease involvement [2]. This engagement has been further investigated by imaging in order to identify structural and vascular changes in the nail unit and adjacent entheses using high-resolution ultrasonography. Ultrasonographic parameters such as nail plate thickness, nail bed change, and power Doppler signal have been utilized to describe inflammatory variation in patients with psoriasis and psoriatic arthritis, but it has not been easy to differentiate between the two



disorders using solely nail image [3]. Studies have found that nail changes were more prevalent in patients who have concomitant joint disease than those without arthritis [4]. Additionally, international rheumatology standard practices state that nail and distal interphalangeal joint clinical and imaging features can be early indicators of psoriatic arthritis and that these structures require careful consideration in psoriatic arthritis-affected patients [5]. Nail involvement has also been suggested as a possible risk predictor of musculoskeletal manifestation in psoriasis by predictive modeling and observational analyses, but such observations are mostly extrapolated on cross-sectional or observational data that do not determine temporal relationships [6]. On the same note, epidemiologic studies of various groups of patients have demonstrated the presence of relationships between nail disease and various psoriatic arthritis in different populations and within different study designs, with varying strengths and reliability [7]. Dermatologic and dermoscopic studies also indicate that the severity of nail disease can be largely dependent on overall psoriasis in general and serve as support to the notion that nail pathology is a reflection of underlying inflammatory process as opposed to being a predictor of joint involvement on its own [8]. More recently, imaging modalities such as optical coherence tomography and high-frequency ultrasound have been used to assess structural changes in the psoriatic nail unit, enhancing the capacity to detect subclinical alterations that would otherwise be undetected on routine clinical examination [9]. Regardless of such technological advances, the clinical and diagnostic implications of nail and enthesitis abnormalities as detected by imaging are still unclear. The reviews on nail ultrasonography highlight that the existing evidence on nail ultrasonography and distal interphalangeal joint enthesitis has shown association, but most of the evidence available is cross-sectional and, as such, cannot show causation or progression to psoriatic arthritis [10]. The existing literature, therefore, mostly indicates the existence of associative relationships between nail psoriasis and distal interphalangeal joint enthesitis. Numerous investigations of this association have already been performed using ultrasound; most of these studies have been performed in European and other foreign populations, implying that the novelty of further studies is constrained unless they provide information on underrepresented populations or other clinical settings. Published information that assesses the relation between nail psoriasis and distal interphalangeal joint enthesitis is limited in areas like South Asia, and especially in Pakistan. Since it is cross-sectional, the research assessed the associations only at the time, and it cannot determine the relationship and predictive causality between nail psoriasis and distal interphalangeal joint enthesitis over time. Local

statistics can be used to describe patterns of disease manifestation unique to the population, as well as give comparative data to studies in other parts of the world. This study aimed to find the prevalence of distal interphalangeal joint enthesitis and its correlation with nail psoriasis in patients with psoriasis and psoriatic arthritis who went to a tertiary care hospital in Karachi. The research is expected to add regional epidemiologic information to the available international literature.

METHODS

This cross-sectional analytical research was carried out at the Department of Dermatology and Rheumatology, Civil Hospital Karachi, for six months between April 2025 and September 2025, with the approval of the Institutional Ethical Review Committee (Approval No. IRB-3721/DUHS/Approval/2024/101; dated 5th March 2025). The population under study was patients referred to the dermatology and rheumatology clinic outpatient and inpatient services, with a diagnosis of psoriasis and or psoriatic arthritis. A non-probability consecutive sampling technique was used to recruit eligible participants. The calculation of the required sample size was based on the formula of a prevalence study, where the prevalence enthesitis of the distal interphalangeal joint was assumed to be 50% in patients with nail psoriasis. This is a conservative estimate that was taken because of the variation that has been reported in past studies [11]. A 95% confidence level ($Z = 1.96$) and a margin of error of 10% were used, which gave a calculated sample size of 96 participants. Psoriatic arthritis diagnosis was done through clinical examination and meeting the Classification Criteria of Psoriatic Arthritis (CASPAR). The inclusion criteria were patients between the ages of 18 and 65 years old who had a confirmed diagnosis of psoriasis with or without psoriatic arthritis who signed written informed consent. Patients with other inflammatory rheumatologic diseases like rheumatoid arthritis or systemic lupus erythematosus, traumatic nail disorders, onychomycosis, or patients who had undergone biologic therapy in the past six months were ruled out. Any patient who was not willing to participate did not take part in the study. The participants received informed consent and were interviewed on the basis of a structured questionnaire to provide demographic and clinical data such as age, sex, disease duration, and treatment history. The same day, an assessment was carried out through clinical examinations. A dermatologist was used to assess nail psoriasis in terms of the Nail Psoriasis Severity Index (NAPSI). The involvement of the nails was considered a NAPSI score of more than zero. Physical examination of clinical enthesitis of the distal interphalangeal joint was determined according to tenderness or swelling at the

tendon of extensor insertion. Each of the participants was then subjected to high-frequency musculoskeletal ultrasound of the distal interphalangeal joint extensor tendon enthesis. Ultrasound analysis adhered to outlined musculoskeletal imaging measures and criteria along with the definitions of enthesitis in the Outcome Measures in Rheumatology (OMERACT) definitions. The detection of typical features that included hypoechogenicity at the tendon insertion, enthesophyte formation, or hyper-vascularity observed on power Doppler imaging, defined ultrasound-confirmed enthesitis. The radiologist who performed the ultrasound examination was blinded to the findings of the clinical nail assessment to minimize detection bias. Clinical enthesitis detected in physical examination was entered in different categories compared to ultrasound-detected enthesitis, and both of these two variables were analyzed independently. All ultrasound studies were carried out by one radiologist who was skilled in musculoskeletal imaging. To improve methodological rigor, a random sample of the scans (10 percent of examinations) was re-evaluated after two weeks in order to test intra-observer reliability, which was determined with the Cohen kappa coefficient. Presence or absence of psoriatic arthritis was also noted, and the patients with psoriasis alone and with psoriatic arthritis were compared individually and with mixed models to eliminate possible confounding. Possible confounding factors were age, sex, Psoriasis duration, psoriatic arthritis, and previous treatment.

Statistical Package of the Social Sciences (SPSS) version 27.0 was used to analyze the data. Continuous variables (age and disease duration) were used with the mean $\pm$ SD, and frequencies and percentages were used in order to show the categorical variables (sex, nail psoriasis, psoriatic arthritis status, and distal interphalangeal joint enthesitis). The chi-square test or Fisher's exact test, where necessary, was first used to determine the primary relationship between nail psoriasis and ultrasound-detected distal interphalangeal joint enthesitis. Multivariate logistic regression analysis was then done to consider the possible confounding factors. The correlation between nail psoriasis and distal interphalangeal joint enthesitis adjusted by age, sex, disease duration, and psoriatic arthritis was determined, and the adjusted odds ratios (ORs) and 95 percent confidence intervals (CIs) were obtained. Stratified analyses were done to determine whether the association varied based on age group, sex, disease duration, or presence of psoriatic arthritis. Post-stratification comparisons were taken with care since numerous subgroup analyses may lead to the possibility of type I error. The p-value of less than 0.05 was taken to be statistically significant.

RESULTS

A total of 96 patients with psoriasis, with or without psoriatic arthritis, were included in the final analysis. The demographic profile and baseline clinical characteristics are summarized. The mean age of participants was 38.7 ± 11.4 years, with a slight male predominance (54.2%) (Table 1).

Table 1: Demographic and Baseline Clinical Characteristics (n=96)

Variables	n (%) / Mean $\pm$ SD
Mean Age (Years)	38.7 $\pm$ 11.4
Male	52 (54.2%)
Female	44 (45.8%)
Mean Duration of Psoriasis (Years)	6.2 $\pm$ 3.8
History of Joint Pain	58 (60.4%)
Mean Duration of Joint Symptoms (Years)	3.4 $\pm$ 2.6
Positive Family History of Psoriasis/PsA	29 (30.2%)

Nail psoriasis was observed in 62 patients (64.6%). The findings demonstrate extensive erythematous plaques over the trunk and abdomen, consistent with chronic plaque psoriasis. The lesions appear well-demarcated with diffuse scaling, reflecting active cutaneous disease involvement (Figure 1).



Figure 1: Clinical Features of Plaque Psoriasis

The results illustrate typical nail psoriasis changes, including onycholysis, subungual hyperkeratosis, and dystrophic nail plate changes. (a) Fingernail showing onycholysis (arrowhead), characterized by separation of the nail plate from the nail bed. (b) Fingernail demonstrating subungual hyperkeratosis (arrow) with accumulation of keratotic debris beneath the nail plate. (c) Bilateral hand nails showing dystrophic nail plate changes (asterisk), including discoloration, thickening, surface irregularity, and nail deformity consistent with psoriatic nail involvement (Figure 2).



Figure 2: Nail Changes in Nail Psoriasis (a-c)

The most common nail changes were nail pitting (45.8%), followed by onycholysis (32.3%) and subungual hyperkeratosis (27.1%). The mean NAPS score among patients with nail involvement was 14.6 ± 6.9 (Table 2).

Table 2: Nail Examination Findings (n=96)

Nail Parameters	n (%) / Mean $\pm$ SD
Presence of Nail Psoriasis	62 (64.6%)
Nail Pitting	44 (45.8%)
Onycholysis	31 (32.3%)
Subungual Hyperkeratosis	26 (27.1%)
Nail Crumbling	18 (18.8%)
Mean NAPS Score	14.6 ± 6.9

A representative ultrasound image of the DIP joint demonstrating the region of the extensor tendon insertion evaluated for enthesitis is represented. (a) Clinical photograph showing swelling of the affected digit (arrow), (b) Clinical examination image demonstrating the site of tenderness over the involved distal interphalangeal region (arrowhead), (c) Ultrasound image showing features suggestive of enthesitis (asterisk), including thickening/hypo-echogenicity at the tendon insertion with surrounding inflammatory changes (Figure 3).

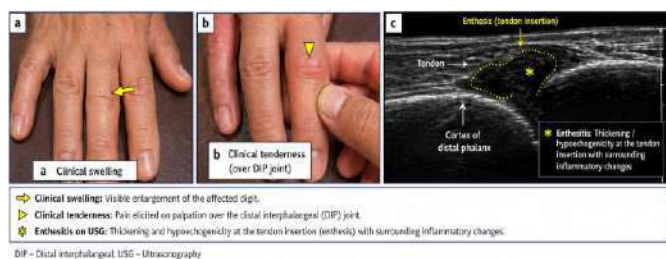


Figure 3: Ultrasound Features of DIP Joint Enthesitis Showing Clinical Tenderness, Clinical Swelling, and Enthesitis

Clinical tenderness was observed in 42.7%, and swelling in 30.2% of DIP joints, whereas ultrasound-confirmed enthesitis was detected in 37.5% of cases (Table 3).

Table 3: DIP Joint Clinical and Ultrasound Findings (n=96)

DIP Joint Findings	n (%)
Clinical Tenderness	41 (42.7%)
Clinical Swelling	29 (30.2%)
Ultrasound-Confirmed Enthesitis	36 (37.5%)

A statistically significant association was observed between nail psoriasis and ultrasound-confirmed DIP joint enthesitis ($p=0.003$, Chi-square test). Enthesitis was

present in 48.4% (30/62) of patients with nail psoriasis compared to 17.6% (6/34) without nail involvement (Table 4).

Table 4: Association Between Nail Psoriasis and DIP Enthesitis (n=96)

Nail Psoriasis	Enthesitis Present	Enthesitis Absent	Total	p-value
Present	30	32	62	0.003*
Absent	6	28	34	
Total	36	60	96	

Chi-square test; $p < 0.005$ considered statistically significant

On multivariable logistic regression analysis, nail psoriasis remained an independent predictor of ultrasound-confirmed DIP enthesitis (OR = 3.52, $p=0.014$). Additionally, the presence of psoriatic arthritis (OR = 2.41, $p=0.047$) and increasing NAPS score (OR = 1.08 per unit increase, $p=0.009$) were significantly associated with enthesitis. Age, sex, and duration of psoriasis were not statistically significant predictors. Correlation analysis demonstrated a statistically significant positive association between NAPS score and ultrasound-confirmed DIP joint enthesitis, indicating that greater nail disease severity increases the likelihood of enthesal involvement (Table 5).

Table 5: Multivariable Logistic Regression Analysis (n=96)

Variables	Adjusted OR	95% CI	p-value
Nail Psoriasis (Present vs Absent)	3.52	1.28 - 9.67	0.014
Age (Per Year Increase)	1.02	0.98 - 1.06	0.301
Male Sex vs Female	1.21	0.52 - 2.83	0.648
Duration of Psoriasis (Years)	1.07	0.96 - 1.19	0.214
Presence of Psoriatic Arthritis	2.41	1.01 - 5.74	0.047
NAPS Score (Per Unit Increase)	1.08	1.02 - 1.15	0.009

Adjusted for age, sex, duration of psoriasis, and psoriatic arthritis

DISCUSSION

A close anatomical and inflammatory relationship between the nail unit and DIP joint enthesitis has been proposed in previous studies. Elliott *et al.* noted that the nail disease was linked to systemic enthesal inflammation among patients with psoriatic arthritis and that nail pathology could indicate inflammation at other enthesal locations [12]. The current research results can be explained by this idea, where patients who had nail psoriasis exhibited a greater rate of ultrasound-detected DIP enthesitis than those whose nails were not involved. Ruscitti *et al.* compared nail and enthesitis involvement with high-frequency ultrasonography in patients with psoriatic disease and demonstrated a high correlation between nail abnormalities and enthesal inflammation [11]. The level of ultrasound-detected DIP enthesitis that was observed in the current study is widely consistent with those that have been demonstrated by imaging studies in the same context of cross-sectional research. Nail psoriasis is also explored

as another possible clinical manifestation of musculoskeletal involvement of psoriasis. Liu *et al.* provided a predictive nomogram to predict the risk of psoriatic arthritis among patients who had plaque psoriasis, and nail involvement was found to be a significant clinical factor that has a higher risk of musculoskeletal disease [13]. The positive correlation of nail psoriasis and ultrasound-confirmed DIP enthesitis in our study during multivariate analysis is consistent with these results. Epidemiological reports have indicated a great difference in the prevalence of psoriatic arthritis amongst patients with psoriasis in various regions. Kang *et al.* provided a worldwide epidemiological study, and they found that there were great regional disparities in the prevalence and burden of psoriatic arthritis [14]. The percentage of patients who experienced joint symptoms among the population of our study remains stable on average, with the trends provided in the epidemiological studies conducted around the world. Psoriatic arthritis is an uncommon, yet clinically important, inflammatory arthropathy related to psoriasis. Recent statistics have shown that psoriatic arthritis is present in about 112/100,000 adults in the world (0.11%). Geographically, there are significant differences in the prevalence, with the lower estimates in Asia (about 37–48 per 100,000) as opposed to Europe and North America. There is little Pakistani data on psoriatic arthritis, but regional studies on the topic in hospitals indicate that psoriatic arthritis is present in a significant percentage of psoriasis patients, with documented prevalence rates of about one-third of cases in the local community [15]. These epidemiological data reveal the need to assess musculoskeletal manifestations in patients with psoriasis, including enthesal. Clinical rheumatology sources have also highlighted the relationship between nail psoriasis and the DIP joint pathology. The prognostic value of nail involvement in psoriatic arthritis and the relationship between nail matrix and the endosteum of the distal phalanx extensor tendon have been mentioned by Queiro *et al.* [16]. This anatomical and pathological correlation is in line with the much greater incidence of ultrasound-confirmed DIP enthesitis in patients with nail psoriasis in the current study. Even though the current study did not examine ultrasound nail imaging, the clinical nail examination, the mean NAPSI score of patients with nail psoriasis was found to be very high, which suggests a significant nail disease burden among this population group. [17]. Bonfiglioli *et al.* examined the place of ultrasonography in the diagnostics and the follow-up of peripheral psoriatic arthritis and highlighted the sensitivity of ultrasonography to detect early enthesal inflammation [18]. In the current research, ultrasound-identified DIP enthesitis was observed in various patients that have failed to show cases of overt

clinical swelling. Nail psoriasis is known to be a typical manifestation of psoriatic disease as far as dermatology is concerned. According to Ji *et al.* nail involvement was a common clinical feature that could be a manifestation of underlying inflammatory activity in psoriasis [19]. The fact that nail psoriasis has a high prevalence in our cohort is in line with the dermatological literature, indicating nail involvement as a frequent occurrence of the disease. It was also reported that clinical studies have found that nail psoriasis can also exhibit several distinct morphological patterns. According to Canal-Garcia *et al.* nail pitting, onycholysis, and subungual hyperkeratosis are typical symptoms of nail psoriasis that occur due to inflammatory processes on the nail matrix and nail bed [20]. The patterns of nail findings in the current study, specifically nail pitting and onycholysis are similar to those earlier reported clinical patterns.

The study supports the claim that nail psoriasis is closely connected with the ultrasound identification of DIP joint enthesitis in psoriasis patients. The study has limitations such as a small sample size, a single-centre study, non-probability sampling, and a cross-sectional evaluation without a mechanistic evaluation. Multicenter longitudinal studies that involve the use of more sophisticated imaging and biomarkers are required to gain a deeper insight into the nail-enthesitis relationship and its clinical implications.

CONCLUSIONS

To summarize, this paper shows that nail psoriasis and enthesitis of the DIP joint have a strong association and that nail inspection and early screening of musculoskeletal ultrasound in psoriasis patients are very crucial. The timely diagnosis of psoriatic arthritis and subsequent good patient outcomes are achievable through early detection of enthesal involvement.

Authors' Contribution

Conceptualization: E

Methodology: E, HT, PK, FN, AR

Formal analysis: E, FN

Writing and Drafting: E, HT, PM, AR

Review and Editing: E, HT, PM, FN, AR

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

Conflict of Interest

All the authors declare no conflict of interest.

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Original Article



Frequency of Hyponatremic Dehydration in Children (6-59 Months) Presenting with Acute Gastroenteritis in a Tertiary Care Facility

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ABSTRACT

Acute gastroenteritis (AGE) is one of the primary morbid and mortal causes among children under five years old, especially in low- and middle-income countries (LMICs). **Objective:** To determine the frequency of hyponatremic dehydration in children aged 6 to 59 months with acute gastroenteritis. **Methods:** The cross-sectional design was employed in the Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad. Non-probability consecutive sampling of children aged 6-59 months of both genders with acute gastroenteritis over six months, from 1st August 2025 to 31st January, 2026, was used to enroll the children. The exclusion criteria were chronic diarrhea, previous administration of intravenous fluids, septic shock, severe malnutrition, chronic illness (CKD, CHD, RTA, CAH), or use of diuretic/steroids. SPSS version 25.0 was used to analyze data. The relationship between hyponatremia and clinical/sociodemographic variables was evaluated using a chi-square test, with $p \leq 0.005$ considered significant. **Results:** Among the 113 children who participated in the study, hyponatremic dehydration was identified in 14.2% (95% CI: 8.1%-21.8%). The prevalence of hyponatremia was more common in children with severe dehydration, underweight nutritional condition, frequent stool frequency, incomplete rotavirus vaccination, and low socioeconomic status ($p < 0.005$). **Conclusions:** Hyponatremic dehydration is a significant, yet not very widespread, complication in children with acute gastroenteritis. Morbidity needs to be reduced through preventive steps, such as rotavirus vaccination and education of caregivers.

INTRODUCTION

Acute gastroenteritis (AGE) is one of the primary morbid and mortal causes among children under five years old, especially in low- and middle-income countries (LMICs) [1]. Recent global estimates suggest that diarrheal diseases account for approximately 1.3 billion episodes and nearly 443,000 deaths annually among children under five years of age, with the greatest burden reported in South Asia and sub-Saharan Africa [2]. The burden of AGE has continued to be a significant challenge to the population, and it continues to be one of the deadliest causes of under-five death worldwide despite significant efforts in preventive

measures, including oral rehydration therapy (ORT), zinc supplementation, and rotavirus vaccination [3]. AGE is mediated by a plethora of viral, bacterial, and parasitic pathogens, with viral pathogens (rotavirus and norovirus) being the most commonly implicated etiologies of hospitalized children [4, 5]. The clinical features of AGE are mild watery diarrhea to severe dehydration, shock, and multisystem complications. These complications also include dehydration and electrolyte imbalances, but the main factors that define the severity and mortality of diseases are these complications. The loss of



gastrointestinal fluids, improper fluid replacement, and hormonal reactions to the disease can lead to electrolyte imbalances, making their early diagnosis and treatment one of the most important in the pediatric practice. Hyponatremia, with a serum sodium level less than 135 mEq/L, is among the most frequent and dangerous electrolyte disorders in children with AGE. Hypotonic fluid loss, excessive free water, or inappropriate antidiuretic hormone secretion during acute illness may result in hyponatremic dehydration. The condition may result in seizures, an altered mental state, cerebral edema, and a risk if it is not diagnosed and treated in time. Recent research has pointed out that dysnatremia is a common observation of children admitted to hospitals with gastroenteritis, with hyponatremia being more common than hypernatremia, especially in children having moderate to severe dehydration [6, 7]. Recently, the epidemiology and clinical implications of hyponatremia in acute illnesses have been a growing topic of pediatric research, with the understanding that this electrolyte imbalance is not inherent to gastrointestinal illnesses but can be found in other acute conditions of childhood. Hyponatremic dehydration is common in children, particularly those with acute diarrhea, occurring in 50% of cases [8]. A multicentric pediatric trial indicated that dysnatremia is not only present in a substantial percentage of children with acute gastroenteritis but that the severity of dehydration and the co-occurrence of vomiting and diarrhea were found to be important predictors of hyponatremia [9]. AGE is one of the significant causes of hyponatremia in children, and it is widespread in LMICs, where the delay in presentation and improper utilization of fluids is typical [10]. Pakistan is one of the countries that has a high burden of childhood diarrheal diseases and related complications. An observational study by Kinasha et al. showed that electrolyte abnormalities (hyponatremia) were common among children with acute gastroenteritis admitted to hospitals and were strongly linked to adverse clinical outcomes, emphasizing the role of early biochemical testing [10]. Recent research has further underscored the fact that electrolyte disturbances in acute gastroenteritis amongst children are high. Khan et al. carried out a study in Pakistan, indicating that electrolyte imbalances, especially hyponatremia, are frequent in children with acute gastroenteritis and strongly related to the degree of dehydration and patient outcomes [11].

Although international guidelines on the management of fluids in pediatric AGE are available, there is scant local evidence to inform clinicians of the burden and trend of hyponatremic dehydration among Pakistani children. The variations in feeding patterns, socioeconomic status, access to healthcare, and clinical management guidelines can also impact the prevalence and severity of

hyponatremia, and thus, it is necessary to produce context-sensitive data. Moreover, electrolyte abnormalities detected at the tertiary care facilities can be optimally treated to eliminate neurological complications related to the improper correction of serum sodium levels. The research helps clinicians make decisions by determining the burden of hyponatremia in this population, which will be presented as evidence to support the use of fluid resuscitation and electrolyte monitoring measures. The results of the current research are likely to lead to the enhancement of clinical practice in pediatrics, institutional guidelines, and preventive measures of morbidity and mortality in children related to acute gastroenteritis and complications. This study aimed to identify the frequency of hyponatremic dehydration in children who attended the tertiary care center with the diagnosis of acute gastroenteritis.

METHODS

The current research was designed as a cross-sectional study at the Department of Pediatrics, Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad, where the study was carried out during six months between 1st August 2025 and 31st January 2026. The Institutional Review Board of PAEC General Hospital, Islamabad (Approval No. PGHI-IRB(DMe)-RCD-06-090, Dated: 11-06-2024) provided the ethical approval. The sample size was determined by considering the WHO sample size calculator with 95% confidence interval, 8% margin of error, and an estimated prevalence rate of hyponatremic dehydration of 12% in children from previous literature [7]. According to these parameters, the sample size calculated was 113 children. Participants who presented to the pediatric department within the period of the study were selected through non-probability consecutive sampling. The study included children aged between 6 and 59 months of age who exhibited acute gastroenteritis according to the operational definition. Both female and male patients were included. Acute gastroenteritis was considered a diarrhea that lasted ≤ 4 days with more than two loose stools per day. The children whose diarrhea lasted >14 days were not included. Patients with previous intravenous fluid administration, who had developed septic shock, severe malnutrition, chronic medical conditions including chronic kidney disease, congestive heart disease, renal tubular acidosis, or congestive adrenal hyperplasia, and patients undergoing diuretics or steroid treatment were also excluded to reduce confounding variables in the determination of serum sodium levels. Children meeting the inclusion criteria were recruited, and written informed consent was obtained from the parents or legal guardians. The principal investigator entered demographic and clinical data on a structured proforma specially made to

capture the information of each child in the study on a list of enrolled children. Demographic factors were age, sex, place of living, the level of maternal education, and the socioeconomic status of the family. The parents or guardians provided the clinical history about the period of diarrhea, whether they had vomited, whether they had taken food orally, and vaccinated against rotavirus. Through a comprehensive physical examination, the extent of dehydration according to World Health Organization clinical guidelines was evaluated, and children were classified as having no dehydration, some dehydration, or severe dehydration [12]. The trained nursing staff or a qualified phlebotomist collected about 2 mL of venous blood from each participant under strict aseptic conditions. The specimen of the blood was taken in a plain vacutainer and taken directly to the hospital laboratory to be subjected to biochemical analysis. The concentration of serum sodium was determined by an automated electrolyte analyzer as per the protocols of the laboratory. A serum sodium level below 135mEq/L was considered hyponatremia. The researcher made sure that the clinical management was not affected by the study participation. Each participant had records taken of the presence or absence of hyponatremic dehydration. The records were kept safely, and only the research team had access to them. The acute gastroenteritis was graded as either grade 3 or grade 4 on the Bristol stool chart, based on the history provided by the parents or guardians [13]. The clinical evaluation of dehydration was conducted: cases of severe dehydration among children were defined as those that exhibited at least two out of the following features: lethargy or unconsciousness, inability to drink, sunken eyes, or sluggish recoil of skin pinch. Children were defined to have some dehydration by having two or more of the following signs: being irritable, eager to drink, sunken eyes, or delayed skin pinch recoil.

Statistical Package of Social Sciences (SPSS) version 25.0 was used to enter and analyze data. Continuous variables, which include age, illness duration, and serum sodium, were summarized using mean and standard deviation when normally distributed. The Shapiro-Wilk test was used to test the normality of quantitative variables, and in case of non-normality, the median and interquartile range (IQR) were used. Categorical variables such as gender, degree of dehydration, rotavirus vaccination status, place of residence, maternal education level, socioeconomic status, and presence of hyponatremia were presented in the form of frequencies and percentages. The number of cases of hyponatremic dehydration was determined as the main outcome variable. The chi-square test was used to determine the association between hyponatremia and the extent of dehydration. The possible effect modifiers were age, gender, rotavirus vaccination status, residence,

maternal education level, socioeconomic status, and duration of disease, which were addressed using stratification. Chi-square tests after stratification were used to establish how these variables affected the outcome. A p-value ≤ 0.005 was taken to be statistically significant. A binary logistic regression model was applied to identify independent predictors of hyponatremia, and variables with $p \leq 0.005$ in univariate analysis were entered into the model.

RESULTS

The study included 113 children aged between 6 and 59 months who arrived in the hospital with an acute gastroenteritis diagnosis. Most of the participants were aged 13 to 36 months, of age and males slightly outmatched the females. The majority of the children were urbanized, and a good percentage of the mothers received primary or no formal education. Almost one-third of households were of the low socioeconomic group. In the aspect of clinical features, 34.5% of children had diarrhea that lasted 3 days or less, 45.1% had between 4 and 7 days of diarrhea, and 20.4% had diarrhea longer than 7 days. The frequency of stool was 3-5 times a day in 40.7%, 6-10 times a day in 43.4%, and greater than 10 times a day in 15.9%. There was vomiting in 62.8% of the children, and fever in 51.3%. As per the feeding habits, 23.9% of children were exclusively breastfed, 38.9% mixed fed, and 37.2% formula fed. Oral rehydration therapy was used before in 58.4% of the cases, and 41.6% had not received ORT at home. In terms of nutritional and hydration status, one-third were underweight, and two-thirds were severely underweight. In most cases, some dehydration was identified, and more than a third of them had severe dehydration. Severely dehydrated children showed clinical signs of sunken eyes, increased capillary refill time, and decreased skin turgor more than 2 secs with tenting (Table 1).

Table 1: Demographic and Socioeconomic Characteristics of Children with Acute Gastroenteritis, Clinical Presentation and Feeding Practices, Nutritional and Hydration Status (n=113)

Variables	Category	n (%)
Demographic and Socioeconomic Characteristics		
Age Group (Months)	6-12	32 (28.3%)
	13-36	47 (41.6%)
	37-59	34 (30.1%)
Gender	Male	61 (54.0%)
	Female	52 (46.0%)
Residence	Urban	68 (60.2%)
	Rural	45 (39.8%)
Maternal Education Level	Illiterate	29 (25.7%)
	Primary	31 (27.4%)
	Secondary	28 (24.8%)
	Matric and above	25 (22.1%)

Socioeconomic Status	Low (< PKR 30,000/Month)	41 (36.3%)
	Middle (PKR 30,000–100,000)	46 (40.7%)
	High (> PKR 100,000/Month)	26 (23.0%)
Clinical Presentation and Feeding Practices		
Duration of Diarrhea	≤3 Days	39 (34.5%)
	4–7 Days	51 (45.1%)
	>7 Days	23 (20.4%)
Stool Frequency (per day)	3–5 Stools	46 (40.7%)
	6–10 Stools	49 (43.4%)
	>10 Stools	18 (15.9%)
Vomiting	Present	71 (62.8%)
	Absent	42 (37.2%)
Fever	Present	58 (51.3%)
	Absent	55 (48.7%)
Feeding Status	Exclusively Breastfed	27 (23.9%)
	Mixed Feeding	44 (38.9%)
	Formula-Fed	42 (37.2%)
Prior ORT Use at Home	Yes	66 (58.4%)
	No	47 (41.6%)
Nutritional and Hydration Status		
Weight-for-Age Status	Normal	67 (59.3%)
	Underweight	34 (30.1%)
	Severely Underweight	12 (10.6%)
Degree of Dehydration	Some Dehydration	71 (62.8%)
	Severe Dehydration	42 (37.2%)
Clinical Signs	Capillary Refill Time >2 Sec	39 (34.5%)
	Sunken Eyes	64 (56.6%)
	Reduced Skin Turgor >2 Sec with Tenting	47 (41.6%)

The average serum sodium was 132.8/6.4 mEq/L. Hyponatremia was identified in 14.2% (95% CI: 8.1% – 21.8%). of children, and mild hyponatremia was the most common. Moderate and severe hyponatremia were rarer but clinically important (Table 2).

Table 2: Serum Sodium Levels and Frequency of Hyponatremia (n=113)

Parameters	Mean ± SD / n (%)
Serum Sodium (Mean ± SD)	136.2 ± 4.1 mEq/L
Normal Sodium (≥135 mEq/L)	97 (85.8%)
Hyponatremia (<135 mEq/L)	16 (14.2%)
Mild Hyponatremia (130–134 mEq/L)	9 (8.0%)
Moderate Hyponatremia (125–129 mEq/L)	5 (4.4%)
Severe Hyponatremia (<125 mEq/L)	2 (1.8%)

The level of dehydration was statistically significantly associated with hyponatremia. The prevalence of hyponatremia was also significantly higher in children with severe dehydration as compared to children with some dehydration ($p=0.003$). Vomiting ($p=0.041$), stool frequency of more than 10 per day ($p=0.028$), and underweight nutritional status ($p=0.033$) were also significantly related to hyponatremia, which showed that both the severity of the disease and the nutritional factors played a role in creating electrolyte imbalances (Table 3).

Table 3: Association between Hyponatremia and Clinical Variables

Variables	Hyponatremia, n (%)	Normal Sodium, n (%)	χ^2	df	p-value
Degree of Dehydration					
Some Dehydration	6 (8.5%)	65 (91.5%)	8.92	1	0.003
Severe Dehydration	10 (23.8%)	32 (76.2%)			
Vomiting					
Present	12 (16.9%)	59 (83.1%)	4.17	1	0.041
Absent	4 (9.5%)	38 (90.5%)			
Stool Frequency >10/day					
Yes	5 (27.8%)	13 (72.2%)	4.86	1	0.028
No	11 (11.6%)	84 (88.4%)			
Underweight Status					
Underweight/Severely Underweight	9 (19.6%)	37 (80.4%)	4.54	1	0.033
Normal Weight	7 (10.4%)	60 (89.6%)			

χ^2 = Chi-square test value; df = degrees of freedom; p = probability value. $p < 0.001$ is considered highly significant

Stratified analysis showed that hyponatremia was significantly related to younger age ($p=0.044$), rural residence ($p=0.026$), low maternal education ($p=0.019$), and low socioeconomic status ($p=0.012$). There was also a significant association based on rotavirus vaccination status with greater prevalence of hyponatremia in the partially vaccinated or nonvaccinated children ($p=0.031$). Hyponatremia was not significantly related to gender ($p=0.381$) (Table 4).

Table 4: Stratified Analysis of Sociodemographic Effect Modifiers (n=113)

Variables	Hyponatremia, n (%)	Normal Sodium, n (%)	χ^2	df	p-value
Age Group					
6–12 Months	7 (21.9%)	25 (78.1%)	6.24	2	0.044
13–36 Months	5 (10.6%)	42 (89.4%)			
37–59 Months	4 (11.8%)	30 (88.2%)			
Gender					
Male	9 (14.8%)	52 (85.2%)	0.75	1	0.381
Female	7 (13.5%)	45 (86.5%)			
Residence					
Urban	6 (8.8%)	62 (91.2%)	4.95	1	0.026
Rural	10 (22.2%)	35 (77.8%)			
Maternal Education					
Illiterate/Primary	11 (18.3%)	49 (81.7%)	5.46	1	0.019
Secondary/Matric+	5 (9.4%)	48 (90.6%)			
Socioeconomic Status					
Low	9 (22.0%)	32 (78.0%)	6.32	1	0.012
Middle/High	7 (9.7%)	65 (90.3%)			
Rotavirus Vaccination					
Fully Vaccinated	4 (9.1%)	40 (90.9%)	4.64	1	0.031
Partial/Unvaccinated	12 (17.4%)	57 (82.6%)			

χ^2 = Chi-square test value; df = degrees of freedom; p = probability value. $p < 0.001$ is considered highly significant

The binary logistic regression model was used to determine independent predictors of hyponatremia. Significant variables in the univariate analysis were included in the model. Following adjustment, serious dehydration, excessive frequency of stool (>10/day), and underweight nutritional condition were independent predictors of hyponatremia. The positive trend of younger age and low socioeconomic status was not statistically significant after adjustment. The model showed reasonable fit and minimization of confounding in comparison to stratified analysis (Table 5).

Table 5: Multivariable Logistic Regression Analysis for Predictors of Hyponatremia

Variables	Adjusted OR (AOR)	95% CI	p-value
Severe Dehydration	3.2	1.1 – 9.1	0.031
Vomiting	1.8	0.7 – 4.5	0.214
Stool Frequency >10/Day	4.1	1.3 – 12.8	0.016
Underweight Status	2.7	1.0 – 7.2	0.048
Age (6-12 Months)	1.6	0.6 – 4.2	0.310
Low Socioeconomic Status	2.0	0.8 – 5.3	0.142
Partial/No Rotavirus Vaccine	1.9	0.7 – 5.0	0.198

DISCUSSION

The current study reveals that hyponatremic dehydration is a significant, but not very common, complication of acute gastroenteritis in children aged 6-59 months, especially in socioeconomically disadvantaged groups. The frequency reflected overall in this study was relatively low, but the condition is clinically relevant as it has the possibility of neurological consequences, such as seizures and altered sensorium, that should not be promptly identified and treated. The incidence of hyponatremia in this case is also consistent with the results of the hospital-based research done in the same resource-restrained environment. A recent cross-sectional study by Khan et al. in Dera Ismail Khan, Pakistan, and Harvey et al. has indicated high levels of electrolyte imbalance, including sodium abnormalities, which are closely linked with the severity of dehydration in children with acute gastroenteritis, which supports the relevance of biochemical monitoring in this condition [11, 13]. The differences in the reported prevalence of the electrolyte abnormalities among epidemiological studies could be attributed to differences in the population of the study, nutritional condition, and access to health care, time of onset, and fluid management strategies. Indicatively, a prospective study by Tombakan et al. at Dr. Soetomo General Academic Hospital in Indonesia found hyponatremia, in many cases with hypokalemia and hyperchloremia, in about one-third of children with diarrhea, the interaction of gastrointestinal fluid losses, vomiting, and renal compensatory responses [14]. Despite the variation in the percentage of children who are affected

in various studies, the consistent finding of sodium imbalance shows that it is a clinically relevant factor in diarrheal illness. Similar issues have been mentioned with other studies in Pakistan. A study by Shah et al. showed that children with acute diarrhea and dehydration have reported high rates of hyponatremia and hypokalemia, and a good correlation between electrolyte imbalance and severity of dehydration underpins the claim that electrolyte measurement needs to be included in the measurement of children with moderate to severe dehydration [15]. The prevalence in the current study was smaller, but findings confirmed that there were strong connections between electrolyte imbalance and the severity of dehydration. This is especially so in places where malnutrition, delayed seeking health care, and partial immunization could predispose an individual to complications. The relationship between hyponatremia and severe dehydration has been observed in the present study and is in line with international evidence that has revealed that an increase in fluid losses is strongly correlated with dysnatremia. Studies by Gupta et al. and Dabek et al. showed that moderate to severe dehydration has been found in situations where sodium imbalance predicts the presentation of acute illness, especially in children who are experiencing both vomiting and diarrhea [16, 17]. This has been physiologically reasonable as hyponatremia may be triggered by increased antidiuretic hormone release relative to free water loss, and this is relevant when the free water loss in relation to sodium loss is disproportionate. Even though most of the literature is devoted to sodium disturbances, the electrolyte imbalance in acute gastroenteritis in pediatrics is not limited to hyponatremia. It has been reported to cause concurrent hypokalemia, metabolic acidosis, and other acid-base imbalances, which are related to a deteriorated clinical condition and extended hospital stay. A study by Hamzah et al. on hospitalized children has shown that various biochemical abnormalities tend to co-occur in diarrheal disease, and that extensive metabolic testing is more valuable than single sodium analysis [18]. Furthermore, studies by Zieg et al. Poe et al. and Adroque et al. emphasized that an electrolyte emergency, either hyponatremia or hypernatremia, can result in neurological and cardiac adverse effects unless it is timely identified and addressed [19-21]. Even though the vast majority of the literature is devoted to sodium disorders, electrolyte imbalance in pediatric acute gastroenteritis is not limited to hyponatremia. It has been reported in studies that hypokalemia is concurrent with metabolic acidosis and other acid-base imbalances that may cause clinical deterioration and extended hospitalization. Long-term studies of electrolyte patterns in admitted children have shown that numerous electrolyte imbalances often co-

exist with diarrheal disease, highlighting the necessity of more comprehensive clinical and chemical analysis, even in patients with a lower rate of hyponatremia [13]. Although hyponatremia appears in a smaller percentage of patients, the presence of other electrolyte derangements should be carefully considered in clinical and laboratory surveillance in severely dehydrated children [13]. Although a smaller percentage of the patients had hyponatremia, several other electrolyte abnormalities were present and, therefore, needed to be closely assessed through clinical and laboratory methods. Clinical implications of the findings of this study are significant. Even though the prevalence rate of hyponatremia was not very large, its strong correlation with serious dehydration and risky sociodemographic factors indicates that selective electrolyte surveillance is recommended in high-risk children. Clinical dehydration scoring is only relied on and may fail to identify underlying biochemical imbalances. Prompt diagnosis of sodium disturbance enables suitable correction of rehydration treatment and minimizes the risk of adverse development of complications associated with incorrect fluid replacement. In the view of public health, enhancing routine rotavirus immunization, enhancing the education of the caregiver, and ensuring prompt administration of oral rehydration salts can be used to ease the degree of dehydration, and thus, reduce the prevalence of electrolyte disorders in children with acute gastroenteritis.

The present study has its limitations, which can be taken into account when analyzing the results. As a cross-sectional study with a single-center setting, it is not possible to draw causal relationships, and the findings might not be applicable to other settings. Also, other electrolytes like potassium, chloride, and bicarbonate were not systematically studied, which would have given a better idea of the metabolic imbalances of acute gastroenteritis. This would be better supported by future multicenter prospective randomized controlled studies that use a broader array of biochemical markers and clinically relevant outcomes, including duration of hospitalization and neurological complications, to support optimal management.

CONCLUSIONS

Hyponatremic dehydration is an important adverse effect of acute gastroenteritis in children, and it should be carefully considered in clinical practice. In the current study, several clinical and sociodemographic variables were associated with hyponatremia in the bivariate analysis. Early diagnosis and proper treatment of dehydration and electrolyte imbalance are important in preventing complications.

Authors' Contribution

Conceptualization: AID

Methodology: AID, SA, SGF, NN, TAC

Formal analysis: AID

Writing and Drafting: AID, SA, SGF, NN, TAC, AHS, HA

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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



Linking Clinical Presentation with Coronary Anatomy: A Study of Angina Severity and Its Relationship with Angiographic Findings in Coronary Artery Disease

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ABSTRACT

No intensive studies have been conducted locally or even in broader regions of the country, which results in a crucial knowledge gap in the establishment of the relationship between the severity of angina and the angiographic findings in patients with coronary artery disease (CAD). **Objectives:** To determine the correlation of angina severity with angiographic findings in patients diagnosed with coronary artery disease. **Methods:** This cross-sectional study was carried out at the Department of Cardiology, Lady Reading Hospital, Peshawar. Male and female patients of age 30 to 70 years diagnosed with coronary artery disease were evaluated for angina severity in comparison to angiographic findings. **Results:** Among 304 patients, angina severity demonstrated a strong positive correlation with angiographic findings ($p = 0.875$, $p < 0.001$). Diabetic patients with severe angina had a higher proportion of high angiographic burden (36.8%) compared to non-diabetics (10.2%), while patients with family history of CAD showed a strong correlation ($p = 0.886$) and relatively weak correlation with Type C complex lesions ($p = 0.706$). **Conclusions:** A strong positive correlation was observed between angina severity and angiographic CAD burden, though this relationship was modified by diabetes, family history, and lesion complexity.

INTRODUCTION

Cardiovascular disease is a leading cause of global morbidity and mortality [1]. It is caused by the constriction or obstruction of the coronary arteries that deliver oxygenated blood to the cardiac muscle [2]. Narrowing typically results from plaque formation within the arterial wall, leading to reduced blood and oxygen delivery to the myocardium [3]. With time, the ischemia can damage the myocardium, which is expressed clinically as chest pain or discomfort, and can eventually cause a heart attack, heart failure, or sudden cardiac demise [4]. Diagnosis as well as the management of CAD is based largely on the degree and

level of arterial blockage, usually measured by coronary angiography, which provides an accurate imaging of the coronary arterial anatomy [5]. Angina pectoris, or angina, is the classic clinical syndrome of myocardial ischemia and is defined by chest pain or discomfort usually resulting from exertion or stress [6]. The condition varies in severity from patient to patient and can be graded with the usual scales like the Seattle Angina Questionnaire (SAQ), from symptoms with heavy exertion to mild discomfort/pain at rest [7, 8]. The gold standard for imaging of coronary arteries and the evaluation for the site, presence, and



degree of arterial stenosis is coronary angiography [9]. The imaging process is achieved by intracoronary delivery of the contrast material, which enables prompt X-ray detection of blood flow and vessel patency [10]. Angiographic findings typically focus on the degree of narrowing of the lumen, distribution of affected vessels, and occurrence of complicated lesions such as calcification and complete occlusion [11]. The relationship between the severity of the angina and the angiographic findings of coronary artery disease is subtle but clinically significant. In most instances, the more intense the angina, the higher the degrees of stenosis and multi-vessel involvement are as seen by angiography [12]. The relationship is nonetheless influenced by a variety of factors including collateral supply, myocardial oxygen demands, and the patient's pain tolerance [13]. Some patients with severely evident angiographic coronary disease are virtually asymptomatic because well-developed collateral pathways provide well-maintained myocardial perfusion [14]. A study conducted by Haider et al. demonstrated a correlation of $r = 0.16$ between symptom severity and angiographic findings [15].

No study has been conducted specifically in the province of Khyber Pakhtunkhwa or even broader regions of the country, which results in a crucial knowledge gap in the establishment of the relationship between the severity of angina and the coronary imaging diagnostics in the population. It is essential to bridge this gap to increase the level of accuracy in the process of diagnosis, management of the patient, and related strategies of treatment under the regional healthcare framework. It is necessary to conduct a study assessing the correlation of angina severity with angiographic findings in coronary artery disease. This study aimed to determine the correlation of angina severity with angiographic findings in patients diagnosed with coronary artery disease.

METHODS

This cross-sectional study was carried out at the Department of Cardiology, Lady Reading Hospital, Peshawar, during the period from 3rd July 2025 to 2nd January 2026 after taking approval from the research review board vide no. 437/LRH/MTI dated 5th November 2024. Male and female patients of age 30 to 70 years diagnosed with coronary artery disease were enrolled. The patients were evaluated for angina severity and compared with angiographic findings. Patients with acute myocardial infarction in the last month, New York Heart Association (NYHA) class IV heart failure, significant valvular heart disease, history of coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), patients with dilated cardiomyopathy, congenital heart disease and severe renal impairment, and patients with

contraindications to coronary angiography were excluded. Coronary artery disease was defined as a luminal diameter narrowing of $\geq 25\%$ in any of the epicardial coronary arteries (left/right) on coronary angiography. Angina severity was assessed using the patient-reported Seattle Angina Questionnaire (SAQ), designed to measure the physical limitations, frequency, stability, and quality of life for patients with coronary artery disease (CAD). The score ranges from 0 (minimum score) to 100 (maximum score). Based on the SAQ score, angina severity was categorized as mild (≤ 50), moderate (score 51-75), and severe (score > 75). Angiographic findings were quantitatively assessed by the percentage of luminal diameter narrowing in the coronary arteries. The severity was scored on a four-point scale [12] (Table 1).

Table 1: Severity Scored on A Four-Point Scale

Stenosis Severity	Percentage of Luminal Narrowing (%)	Score
Normal/No Significant Stenosis	$< 25\%$	1
Mild	$25\% - 49\%$	2
Moderate	$50\% - 70\%$	3
Severe	$> 70\%$	4

The total sample size was 304, calculated using the correlation sample size formula: $N = [(Z\alpha + Z\beta)/C]^2 + 3$, where $\alpha = 0.05$ (two-tailed), $\beta = 0.20$, and expected correlation coefficient $r = 0.16$ [15], with corresponding standard normal deviates $Z\alpha = 1.9600$, $Z\beta = 0.8416$, and $C = 0.1614$. Participants were enrolled using non-probability consecutive sampling. Patients diagnosed with coronary artery disease and meeting the selection criteria were recruited from the Cardiology Department of LRH Peshawar following approval from the Institutional Ethical Review Board. Before participation, all individuals provided informed consent following a detailed briefing on the study's purpose, methods, possible risks, and anticipated benefits. Demographic information such as age, sex, body mass index (BMI), smoking habits, presence of hypertension or diabetes mellitus, family history of coronary artery disease (CAD), and socioeconomic background was gathered through a standardized questionnaire. Each patient underwent a detailed clinical assessment to determine the severity of angina using the Seattle Angina Questionnaire (SAQ), assessed through a standardized interview conducted by the cardiology team. Subsequently, all participants underwent coronary angiography. Angiographic images were reviewed by an experienced interventional cardiologist with more than 3 years of post-fellowship experience who quantified the degree of luminal stenosis in the major coronary arteries. The severity of angiographic findings was recorded according to the four-point quantitative scale based on percentage luminal narrowing ($< 25\%$, $25-49\%$, $50-70\%$,

>70%) as per operational definitions. All relevant data were documented on a pre-designed data collection form specifically developed for this study.

Data were analyzed with a statistical analysis program (SPSS Ver. 26). Frequencies and percentages were computed for categorical variables like gender, smoking status, residential status, hypertension, diabetes, family history of coronary artery disease, and socioeconomic status. Mean $\pm$ SD or median (IQR) was presented for quantitative variables like age, body mass index (BMI), angina severity score, and angiographic findings score (Shapiro-Wilk test was used to check normality). The correlation between angina severity and angiographic findings was assessed using Spearman's correlation coefficient. Post-stratification correlation analysis was performed for subgroups such as age, gender, diabetes, hypertension, family history of coronary artery disease, and socioeconomic status. A p -value ≤ 0.05 was considered statistically significant.

RESULTS

Out of the total 304 participants, 215 patients (70.7%) were aged 51–70 years and had an equivalent gender distribution (156 male, 148 female). Cardiovascular risk factors observed included: hypertension (177, 58.2%), diabetes (120, 39.5%), and history of smoking (163, 53.7% current or former). Coronary lesion complexity revealed Type C lesions present in 74 patients (24.3%), while 106 patients (34.9%) had severe angina. Angiographic findings revealed that 152 patients (50.0%) had low disease burden, yet 152 patients (50.0%) demonstrated moderate-to-high severity. All 304 patients were on aspirin, with high adherence to statin (242, 79.6%) and beta-blocker (188, 61.8%) therapy (Table 2).

Table 2: Descriptive Statistics for categorical Variables (n=304)

Variables	Category	n (%)
Age Group	30–50 Years	89 (29.3%)
	51–70 Years	215 (70.7%)
Gender	Male	156 (51.3%)
	Female	148 (48.7%)
Smoking Status	Current	78 (25.7%)
	Former	85 (28.0%)
	Never	141 (46.4%)
Residential Status	Urban	175 (57.6%)
	Rural	129 (42.4%)
Hypertension	Yes	177 (58.2%)
	No	127 (41.8%)
Diabetes	Yes	120 (39.5%)
	No	184 (60.5%)
Family History CAD	Yes	134 (44.1%)
	No	170 (55.9%)
Socioeconomic Status	Low	112 (36.8%)
	Middle	116 (38.2%)

	High	76 (25.0%)
Lesion Type	Type A (Focal)	112 (36.8%)
	Type B (Tubular)	118 (38.8%)
	Type C (Complex)	74 (24.3%)
Angina Severity Score	Mild (≤ 50)	78 (25.7%)
	Moderate (51–75)	120 (39.5%)
	Severe (> 75)	106 (34.9%)
Angiographic Findings Score	Low (≤ 60)	152 (50.0%)
	Moderate (61–80)	106 (34.9%)
	High (> 80)	46 (15.1%)
Medication Aspirin	Yes	304 (100.0%)
	No	0 (0.0%)
Medication Statin	Yes	242 (79.6%)
	No	62 (20.4%)
Medication Beta Blocker	Yes	188 (61.8%)
	No	116 (38.2%)
Medication ACE Inhibitor	Yes	156 (51.3%)
	No	148 (48.7%)

The mean age of the cohort was 58.3 years (SD 10.2). BMI was normally distributed (mean 26.7 kg/m², SD 2.5; Shapiro-Wilk $p=0.089$). In contrast, Angina Severity Score (median 62.0, IQR 44.0–79.0), Angiographic Findings Score (median 68.0, IQR 49.0–85.0), Hemoglobin A1c (median 6.3, IQR 5.6–7.2), creatinine (median 1.0, IQR 0.9–1.2), ejection fraction (median 57.0, IQR 47.0–66.0), and number of stenosed vessels (median 2.0, IQR 1.0–2.0) all demonstrated significant deviation from normality (all $p<0.005$) (Table 3).

Table 3: Descriptive Statistics for Continuous Variables (n=304)

Variables	Mean $\pm$ SD	Median (IQR)	Shapiro-Wilk p-value
Age (years)	58.3 $\pm$ 10.2	58.0 (50.0–67.0)	0.081
BMI (kg/m ²)	26.7 $\pm$ 2.5	26.5 (24.8–28.5)	0.089
Angina Severity Score	61.1 $\pm$ 21.8	62.0 (44.0–79.0)	0.002*
Angiographic Findings Score	66.3 $\pm$ 22.3	68.0 (49.0–85.0)	0.001*
Hemoglobin A1c (%)	6.5 $\pm$ 1.1	6.3 (5.6–7.2)	0.003*
Creatinine (mg/dL)	1.1 $\pm$ 0.3	1.0 (0.9–1.2)	0.001*
Ejection Fraction (%)	55.7 $\pm$ 12.7	57.0 (47.0–66.0)	0.014*
Number of Stenosed Vessels	1.7 $\pm$ 1.0	2.0 (1.0–2.0)	0.001*

*Note: Angina severity scores, angiographic findings scores, HbA1c, creatinine, EF, and vessel count showed non-normal distribution ($p<0.005$)

A strong, statistically significant positive correlation was observed between Angina Severity Score and Angiographic Findings Score ($p = 0.875$, 95% CI 0.844–0.902; $p<0.001$). Among patients with mild angina (≤ 50 , $n=78$), the majority (52, 66.7%) had low angiographic burden (≤ 60), whereas among those with severe angina (> 75 , $n=106$), 54 (50.9%) had low angiographic scores, and 26 (24.5%) had high scores (> 80) (Table 4).

Table 4: Association and Correlation Analysis between Angina Severity Score and Angiographic Findings Score (n=304)

Angina Severity Score	Angiographic Findings Score			Total, n, (%)	χ^2 and p-value	Spearman, ρ Correlation (95% CI)
	Low (≤ 60), n (%)	Moderate (61-80), n (%)	High (> 80), n (%)			
Mild (≤ 50)	52 (66.7%)	22 (28.2%)	4 (5.1%)	78 (100%)	$\chi^2 = 42.6$, p-value < 0.001 $\rho = 0.875$	(95% CI, 0.844-0.902), Strong positive correlation
Moderate (51-75)	46 (38.3%)	58 (48.3%)	16 (13.3%)	120 (100%)		
Severe (> 75)	54 (50.9%)	26 (24.5%)	26 (24.5%)	106 (100%)		
Total	152 (50.0%)	106 (34.9%)	46 (15.1%)	304 (100%)		

Among diabetic patients with severe angina (n=57), 21 (36.8%) had high angiographic scores (> 80), compared to only 5 (10.2%) among non-diabetics with severe angina (n=49). Similarly, among patients with family history of CAD and severe angina (n=54), 20 (37.0%) had high angiographic scores, versus 6 (11.5%) in those without family history (Table 5).

Table 5: Post-Stratification Analysis: Angina Severity vs. Angiographic Findings (n=304)

Subgroup	Category	Angina Severity*	Low (≤ 60), n (%)	Moderate (61-80), n (%)	High (> 80), n (%)	Total	Spearman, ρ value	p-value
Age Group (years)	30-50 (n=89)	Mild	18 (72.0%)	6 (24.0%)	1 (4.0%)	25	0.862	< 0.001
		Moderate	14 (41.2%)	16 (47.1%)	4 (11.8%)	34		
		Severe	12 (40.0%)	10 (33.3%)	8 (26.7%)	30		
	51-70 (n=215)	Mild	34 (64.2%)	16 (30.2%)	3 (5.7%)	53	0.881	< 0.001
		Moderate	32 (37.2%)	42 (48.8%)	12 (14.0%)	86		
		Severe	42 (55.3%)	16 (21.1%)	18 (23.7%)	76		
Gender	Male (n=156)	Mild	28 (68.3%)	11 (26.8%)	2 (4.9%)	41	0.872	< 0.001
		Moderate	24 (38.7%)	30 (48.4%)	8 (12.9%)	62		
		Severe	28 (52.8%)	12 (22.6%)	13 (24.5%)	53		
	Female (n=148)	Mild	24 (64.9%)	11 (29.7%)	2 (5.4%)	37	0.878	< 0.001
		Moderate	22 (37.9%)	28 (48.3%)	8 (13.8%)	58		
		Severe	26 (49.1%)	14 (26.4%)	13 (24.5%)	53		
Diabetes	Yes (n=120)	Mild	14 (58.3%)	8 (33.3%)	2 (8.3%)	24	0.884	< 0.001
		Moderate	12 (30.8%)	20 (51.3%)	7 (17.9%)	39		
		Severe	20 (35.1%)	16 (28.1%)	21 (36.8%)	57		
	No (n=184)	Mild	38 (70.4%)	14 (25.9%)	2 (3.7%)	54	0.868	< 0.001
		Moderate	34 (42.0%)	38 (46.9%)	9 (11.1%)	81		
		Severe	34 (69.4%)	10 (20.4%)	5 (10.2%)	49		
Hypertension	Yes (n=177)	Mild	28 (62.2%)	14 (31.1%)	3 (6.7%)	45	0.880	< 0.001
		Moderate	24 (34.3%)	36 (51.4%)	10 (14.3%)	70		
		Severe	32 (51.6%)	14 (22.6%)	16 (25.8%)	62		
	No (n=127)	Mild	24 (72.7%)	8 (24.2%)	1 (3.0%)	33	0.867	< 0.001
		Moderate	22 (44.0%)	22 (44.0%)	6 (12.0%)	50		
		Severe	22 (50.0%)	12 (27.3%)	10 (22.7%)	44		
Family History CAD	Yes (n=134)	Mild	18 (60.0%)	10 (33.3%)	2 (6.7%)	30	0.886	< 0.001
		Moderate	16 (32.0%)	26 (52.0%)	8 (16.0%)	50		
		Severe	22 (40.7%)	12 (22.2%)	20 (37.0%)	54		
	No (n=170)	Mild	34 (70.8%)	12 (25.0%)	2 (4.2%)	48	0.867	< 0.001
		Moderate	30 (42.9%)	32 (45.7%)	8 (11.4%)	70		
		Severe	32 (61.5%)	14 (26.9%)	6 (11.5%)	52		
Socioeconomic Status	Low (n=112)	Mild	18 (64.3%)	8 (28.6%)	2 (7.1%)	28	0.879	< 0.001
		Moderate	16 (36.4%)	22 (50.0%)	6 (13.6%)	44		
		Severe	20 (50.0%)	10 (25.0%)	10 (25.0%)	40		
	Middle (n=116)	Mild	18 (69.2%)	7 (26.9%)	1 (3.8%)	26	0.873	< 0.001
		Moderate	16 (40.0%)	20 (50.0%)	4 (10.0%)	40		
		Severe	18 (36.0%)	14 (28.0%)	18 (36.0%)	50		
	High (n=76)	Mild	16 (66.7%)	7 (29.2%)	1 (4.2%)	24	0.871	< 0.001
		Moderate	14 (38.9%)	16 (44.4%)	6 (16.7%)	36		
		Severe	16 (100.0%)	0 (0.0%)	0 (0.0%)	16		

Smoking Status	Current (n=78)	Mild	14 (66.7%)	6 (28.6%)	1 (4.8%)	21	0.870	<0.001
		Moderate	12 (37.5%)	16 (50.0%)	4 (12.5%)	32		
		Severe	12 (48.0%)	6 (24.0%)	7 (28.0%)	25		
	Former (n=85)	Mild	14 (63.6%)	7 (31.8%)	1 (4.5%)	22	0.877	<0.001
		Moderate	12 (37.5%)	16 (50.0%)	4 (12.5%)	32		
		Severe	16 (51.6%)	8 (25.8%)	7 (22.6%)	31		
	Never (n=141)	Mild	24 (68.6%)	9 (25.7%)	2 (5.7%)	35	0.875	<0.001
		Moderate	22 (39.3%)	26 (46.4%)	8 (14.3%)	56		
		Severe	26 (52.0%)	12 (24.0%)	12 (24.0%)	50		
Lesion Type	Type A (n=112)	Mild	28 (77.8%)	7 (19.4%)	1 (2.8%)	36	0.764	<0.001
		Moderate	24 (51.1%)	20 (42.6%)	3 (6.4%)	47		
		Severe	18 (62.1%)	8 (27.6%)	3 (10.3%)	29		
	Type B (n=118)	Mild	16 (57.1%)	10 (35.7%)	2 (7.1%)	28	0.792	<0.001
		Moderate	14 (35.0%)	22 (55.0%)	4 (10.0%)	40		
		Severe	20 (40.0%)	14 (28.0%)	16 (32.0%)	50		
	Type C (n=74)	Mild	8 (57.1%)	5 (35.7%)	1 (7.1%)	14	0.706	<0.001
		Moderate	8 (24.2%)	16 (48.5%)	9 (27.3%)	33		
		Severe	16 (59.3%)	4 (14.8%)	7 (25.9%)	27		
Residential Status	Urban (n=175)	Mild	30 (65.2%)	13 (28.3%)	3 (6.5%)	46	0.876	<0.001
		Moderate	26 (37.1%)	34 (48.6%)	10 (14.3%)	70		
		Severe	32 (54.2%)	14 (23.7%)	13 (22.0%)	59		
	Rural (n=129)	Mild	22 (68.8%)	9 (28.1%)	1 (3.1%)	32	0.873	<0.001
		Moderate	20 (40.0%)	24 (48.0%)	6 (12.0%)	50		
		Severe	22 (46.8%)	12 (25.5%)	13 (27.7%)	47		

*Angina severity = mild (≤ 50), moderate (51-75), severe (> 75)

DISCUSSION

The present study demonstrated a statistically significant positive correlation between angina severity and the angiographic burden of coronary artery disease. The pattern of correlation observed in our study is consistent with the broader body of literature examining the relationship between clinical presentation and anatomical disease severity. Patients with classic angina had greater Gensini scores and a higher incidence of multivessel disease than those with unusual presentations. According to Khezri *et al.* substantial correlations exist between symptom attributes and angiographic imaging findings [16]. These conclusions are supported in another study by Al Chaar *et al.* [17]. Lowenstern *et al.* in their analysis involving over 4,000 patients, demonstrated that typical angina was significantly associated with obstructive coronary artery disease on invasive angiography, with a positive predictive value exceeding 70% for patients presenting with classic symptoms [18]. Among the diabetic patients in our cohort, those with severe angina had a markedly higher proportion of high angiographic scores compared to non-diabetic patients with severe angina. This indicates that diabetic patients with severe angina in this cohort had a higher proportion of extensive anatomical disease [19, 20]. The relationship between diabetes and the clinical presentation of coronary artery disease has been extensively characterized [21]. Kawsar *et al.* demonstrated

that diabetic patients undergoing coronary angiography had significantly higher Gensini scores and a greater prevalence of multivessel disease compared to non-diabetic patients [22]. Furthermore, among elderly patients with acute coronary syndrome, diabetes was associated with more extensive angiographic disease, including higher rates of triple vessel disease and left main stem involvement in a study by Wen *et al.* [23]. Diabetes was also found by Aksu and Ahmed to be a strong predictor of higher Gensini scores in angiography patients [24]. Patients with a family history of coronary artery disease also showed a notable pattern. In the research of Lebanese subjects undergoing coronary angiography, Al Chaar *et al.* showed that, regardless of conventional risk variables, a family history of early CAD was substantially linked to higher SYNTAX scores and a greater risk of coronary artery disease [17]. In a similar manner, Aghajani *et al.* found that in comparison to individuals who had advanced CAD, those with early CAD had much greater percentages of positive family history [21]. The finding that family history enhanced both the strength of the correlation and the proportion of severe disease in symptomatic patients supports the incorporation of family history as a key variable in clinical decision-making. An observation was noted regarding lesion complexity. Among patients with Type C complex lesions, the correlation was relatively weak. This finding

may be explained by several mechanisms. Theofilis et al. discussed the complex pathophysiology of acute coronary syndromes, noting that patients with chronic, diffuse atherosclerosis may develop collateral circulation that preserves myocardial perfusion [2]. A study stated that the existence of established collaterals can greatly reduce anginal symptoms [4]. Boerhout et al. emphasized that in individuals without obstructive coronary vessels, the level of epicardial stenosis does not necessarily correspond with the severity of symptoms [8]. Clinical implications of these findings include the necessity for objective evaluation, as patients with known complicated or multivessel CAD may not be able to accurately convey the entire scope of their condition through symptom reporting alone. It is important to consider the connection between morphological findings and symptoms in individuals with non-obstructive coronary arteries. Liu et al. highlighted that emotional distress and physical ischemia both caused a higher symptom load in individuals with angina and without obstructive coronary disease [7]. Wen et al. investigated the trend further and found that the coronary sluggish flow phenomenon, which was linked to inflammatory signals and may account for symptom generation in the absence of substantial stenosis [23]. These results are especially pertinent to our finding that angiographic load was more evenly distributed among patients with severe angina in the high socioeconomic level category. This might be due to the population's increased incidence of non-obstructive coronary artery disease, microvascular abnormalities, or non-cardiac causes of chest pain.

Some limitations warrant recognition. The cross-sectional design makes it impossible to establish a causal relationship between symptom severity and anatomical findings. Subgroup Spearman correlations were compared descriptively; statistical testing for differences between these correlations was not performed. Generalizability to other communities with differing healthcare systems or demographics may be limited by the single-center setting. Even while visual angiographic evaluation is clinically conventional, quantitative techniques like the Gensini score may add observer variability. Furthermore, coronary collaterals were not extensively evaluated in the research. It is recommended that future prospective multicenter studies should incorporate standardized collateral circulation assessment and utilize validated angiographic scoring systems to confirm these findings and objectively prioritize clinical decision-making in this population.

CONCLUSIONS

In individuals with coronary artery disease, angina symptom severity had a significant positive correlation with angiographic disease burden. Severe angiographic

abnormalities were more common in diabetic individuals and those with a family history of CAD. In contrast, patients with Type C complex lesions exhibited a weaker correlation between symptom severity and anatomical disease.

Authors' Contribution

Conceptualization: MAI

Methodology: HU

Formal analysis: HU

Writing and Drafting: HU, MAI, SK, NK, SU

Review and Editing: HU, MAI, SK, NK, SU

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

Efficacy of Spinal Anesthesia Versus General Anesthesia for Single-Level Microdiscectomy at POF Hospital, Wah Cantt

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ABSTRACT

Existing studies show varying results regarding the outcomes of single-level lumbar microdiscectomy under spinal anesthesia and general anesthesia, leaving uncertainty about their relative benefits. **Objective:** To compare the outcomes of spinal anesthesia versus general anesthesia in single-level microdiscectomy. **Methods:** This quasi-experimental study was conducted at the Department of Neurosurgery, POF Hospital, Wah Cantt. A total of 60 male and female patients with lumbar disc herniation with single-level microdiscectomy under spinal and general anesthesia were compared for outcomes in terms of surgery time, post-anesthesia care unit time, intraoperative blood loss, dural tear, post-operative pain, and hospital stay. **Results:** The mean age of the participants was 49.65 ± 7.43 years, and participants aged more than 45 years were 37 (61.7%), while the majority of the patients were female, $n=32$ (53.3%). The mean operative time with spinal anesthesia was 71.0 ± 4.30 minutes versus 88.00 ± 4.21 minutes with GA ($p<0.001$). Mean PACU time spent by patients with spinal and general anesthesia was 1.50 ± 0.63 days and 2.03 ± 0.85 days, respectively ($p=0.008$). Mean hospital stay of patients with spinal was 2.57 ± 0.63 days versus 3.67 ± 0.80 days with general anesthesia ($p<0.001$). Dural tears were observed in patients (3.3%) with spinal versus 02 patients (6.6%) with general anesthesia ($p=0.643$). **Conclusions:** Spinal anesthesia was associated with better perioperative outcomes than general anesthesia in patients who underwent lumbar microdiscectomy when assessed in terms of operative time, PACU time, and hospital stay.

INTRODUCTION

Lumbar spine surgery is one of the most common procedures performed nowadays. Microdiscectomy is done for symptomatic lumbar disc herniation, and there is also a growing trend toward the microendoscopic technique to decrease blood loss, ligamentous structural integrity, decrease operative time, and shorten hospital length of stay [1]. Lumbar spine surgery, such as microdiscectomy, can be performed using various anesthetic techniques. It can be performed under spinal (SA) as well as general anesthesia (GA) [2]. Surgical outcome after lumbar surgery also depends on anesthesia type; therefore, several studies have compared general

versus spinal anesthesia in terms of perioperative complications, hemodynamic parameters, operative time, anesthesia, and recovery time [3]. Anesthesia selection involves a shared decision among the surgeon, the anesthetist, and the patient. General anesthesia is preferred more often due to provider familiarity, patient acceptance for prolonged surgery, and airway security in the prone position [4]. Spinal anesthesia offers benefits over general anesthesia, including rapid onset, reduced intraoperative blood loss, decreased surgical and post-anesthesia care time, fewer thrombotic events, lower pulmonary complications, and diminished post-operative



cognitive decline [3]. Understanding the benefits, drawbacks, level of patient satisfaction, and affordability of SA vs. GA in microdiscectomies is necessary for the best possible surgical use [5]. Numerous studies indicate that spinal anesthesia could be better than general anesthesia, with fewer perioperative problems, improved cardiovascular metrics, economic viability, and shorter operating, anesthesia, and recovery durations [6]. The distinct biophysical characteristics of spinal and general anesthesia have an impact on the outcomes of lumbar microdiscectomy surgery. Although general anesthetics provide stable placement in prone posture, safe airway management, and ideal muscular relaxation, it is linked to greater systemic opioid doses, longer recovery durations, and higher rates of postoperative nausea and vomiting. On the other hand, sympathetic blocking provided by spinal anesthesia maintains hemodynamic stability, minimizes intraoperative blood loss by reducing epidural venous plexus congestion, and permits direct neurological input during nerve root manipulation. However, there are several possible drawbacks to spinal anesthesia, such as the possibility of insufficient surgical anesthesia necessitating conversion, the difficulty of preserving hemodynamic stability during prone placement, and patient concern during awake positioning [3, 4]. In a study, post-operative pain (VAS) between groups was comparable, time of surgery (time to enter in OT to incision) (GA vs. SA; 30.22 ± 8.21 minutes vs. 15.55 ± 7.12 minutes) and average hospital stay (GA vs. SA; 3.05 ± 0.67 days vs. 1.61 ± 0.55 days) were significantly higher among GA group when compared to SA group ($p < 0.05$), while insignificant differences were seen in blood loss (GA vs. SA; 40.23 ± 10.45 ml vs. 30.22 ± 11.21 ml; $p = 0.552$) and dural tear (GA vs. SA; 4% vs. 4%; $p = 1.000$) [1]. In another study, at 24 hours postoperatively, the mean VAS score was 3.24 ± 1.06 in the spinal group and 3.93 ± 1.02 in the general anesthesia group ($p < 0.01$) [7].

Single-level lumbar microdiscectomy is commonly performed under either spinal or general anesthesia, yet existing studies report conflicting outcomes regarding operative time, recovery profile, and complications, leaving uncertainty about the optimal technique. Most available evidence is derived from diverse settings with varying surgical and anesthetic protocols, limiting applicability to routine neurosurgical practice. Additionally, there is a dearth of direct comparable data from regional institutions. In order to close this data gap and promote sensible anesthetic choice, the study compared the perioperative results of spinal and general anesthesia for single-level microdiscectomy.

METHODS

This quasi-experimental study was conducted at the Department of Neurosurgery, POF Hospital, Wah Cantt,

during the period 2nd September 2025 till 1st February 2026, after taking approval from the institutional research review board vide no. IRB/POFH/05-2025/NEURO-SURG/01 on 16th May 2025. Male and female patients aged 18 to 60 years diagnosed with lumbar disc herniation were enrolled. Patients with a prior history of intervention for lumbar disc herniation, blood dyscrasias, immune-compromised patients, and referred patients handled at other centers were excluded. Lumbar disc herniation was diagnosed with an MRI of the lumbar spine showing localized displacement of the disc material beyond the normal margins of the intervertebral disc space. The outcomes were assessed in terms of: 1) Surgery time: The duration in minutes from entry into the operating theatre till completion of skin closure. 2) PACU time: The total time in days the patient spends in the Post Anaesthesia Care Unit (PACU) from arrival after surgery until discharge to the ward. 3) Blood loss intra-operatively (ml): The total volume of blood lost during the surgery, measured in milliliters, calculated from suction canisters (after subtracting irrigation fluid) and estimated swab loss. 4) Dural tear: Any intraoperative accidental breach of the dura mater. 5) Postoperative pain: Measured using the patients' reported Visual Analogue Scale (VAS) that ranges from 0 to 10. 6) Hospital stays: The total duration in days in the hospital from the time a patient is admitted for surgery till discharge. Using Open Epi software, the sample size was determined to be 60 (30 in each group), with a 95% confidence level, 80% power, taking a mean hospital stay (GA vs. SA) of 3.05 ± 0.67 days vs. 1.61 ± 0.55 days [1]. Participants who met the eligibility parameters were recruited after approval from the hospital's ethical and research department. Every patient provided written informed consent. Age, gender, BMI (kg/m^2), pain duration, and comorbidities were noted. Patients were assigned to either the general anesthesia (GA) or spinal anesthesia (SA) group depending on their preferences and the anesthetist's judgment. The anesthesiology staff provided uniform preoperative education to all patients about the advantages and disadvantages of both SA and GA, comprising an overview of the specifics of the procedure, anticipated recovery periods, and possible complications. To ensure procedural uniformity, the same neurosurgeon and team conducted each procedure. All surgeries were performed using the Zeiss OPMI Pentero operative microscope in the prone position on a Wilson frame, and the surgical technique was a typical posterior midline incision. The most often encountered levels were L4-L5, although they varied from L3-L4 to L5-S1. Using OT time logs, the duration of the procedure was recorded from the time the patient arrived in the operating room until the skin repair concluded. Patients were sent to the Post Anaesthesia Care Unit (PACU) following surgery, and the number of days they

spent there until they were discharged was noted. Intraoperative blood loss was calculated by measuring the volume collected in the suction canister after subtracting the irrigation fluid used, and estimating blood soaked in surgical sponges as per standard practice. The occurrence of dural tear during surgery was documented as yes or no based on the operative notes. Postoperative pain was assessed using the Visual Analogue Scale (VAS), measured in centimeters, and recorded at predefined time intervals during the postoperative period. Total hospital stay was calculated in days from the date of admission to the date of discharge after surgery. All data were collected systematically in a structured proforma immediately post-

surgery and during the hospital stay, and later entered into an electronic database for analysis.

All the data were entered and processed by using SPSS version 26.0. Qualitative variables like gender and dural tears were presented as frequencies and percentages. Quantitative variables like age, BMI, surgery time, PACU time, blood loss intra-operatively, post-op pain (VAS), and Hospital stay were presented as Mean $\pm$ S.D. Surgery time, PACU time, Blood loss intra-operatively, post-op pain (VAS), and Hospital stay were compared between groups by t-test, and dural tear by Chi-square test. Data were stratified for gender, age, and BMI. A $p \leq 0.05$ was considered significant.

RESULTS

The mean age of the participants was 49.65 ± 7.43 years. Participants aged more than 45 years were 37 (61.7%), while the majority of the patients were female, $n=32$ (53.3%). A BMI more than 24.0 kg/m^2 was recorded in 32 patients (53.3%). Mean surgery time, hospital stay, and post-operative VAS score were 79.50 ± 9.55 minutes, 3.12 ± 0.90 days, and 3.95 ± 1.03 , respectively. There were no statistically significant differences between the SA and GA groups at baseline. Age ($p=0.275$) and BMI ($p=0.540$) were comparable between the two groups. Similarly, the distribution of gender was nearly identical, with each group comprising 14 males (46.7%) and 16 females (53.3%) ($\chi^2=0.067$, $p=0.796$) (Table 1).

Table 1: Baseline Characteristics and Descriptive Statistics of Study Participants ($n=60$)

Variable	Subgroup	Overall ($n = 60$)	SA ($n = 30$)	GA ($n = 30$)
Age (Years)	Mean $\pm$ SD	49.65 ± 7.44	48.60 ± 7.54	50.70 ± 7.28
	≤ 45 years, n (%)	23 (38.3%)	—	—
	> 45 years, n (%)	37 (61.7%)	—	—
Gender, n (%)	Male	28 (46.7%)	14 (46.7)	14 (46.7)
	Female	32 (53.3%)	16 (53.3)	16 (53.3)
BMI (kg/m^2)	Mean $\pm$ SD	24.30 ± 1.36	24.19 ± 1.36	24.41 ± 1.37
	≤ 24.0 , n (%)	28 (46.7%)	—	—
	> 24.0 , n (%)	32 (53.3%)	—	—
Surgery Time (min)	Mean $\pm$ SD	79.50 ± 9.56	—	—
PACU Time (Days)	Mean $\pm$ SD	1.77 ± 0.79	—	—
Hospital Stays (Days)	Mean $\pm$ SD	3.12 ± 0.90	—	—
Blood Loss (ml)	Mean $\pm$ SD	260.00 ± 23.07	—	—
Postoperative Pain (VAS)	Mean $\pm$ SD	3.95 ± 1.03	—	—

Dural tears were observed in one patient (3.3%) with spinal anesthesia versus 02 patients (6.6%) with general anesthesia (p value 0.643). The mean operative time with spinal anesthesia was 71.0 ± 4.30 minutes versus 88.00 ± 4.21 minutes with general anesthesia ($p < 0.001$). Mean PACU time spent by patients with spinal and general anesthesia was 1.50 ± 0.63 days and 2.03 ± 0.85 days, respectively ($p=0.008$). Mean hospital stay of patients with spinal anesthesia was 2.57 ± 0.62 days versus 3.67 ± 0.80 days with general anesthesia ($p < 0.001$). The p -values for the difference in blood loss and postoperative pain VAS in spinal versus general anesthesia were < 0.001 and < 0.001 , respectively (Table 2).

Table 2: Comparison of Outcomes Between SA and GA ($n=60$)

Outcome Variables	Group ($n=30$)	Mean $\pm$ SD	Mean Difference (95% CI)	Cohen's d	p-value
Surgery Time (min)	SA	71.00 ± 4.30	-17.00 (-19.20 to -14.80)	-3.96	< 0.001
	GA	88.00 ± 4.22			
PACU Time (days)	SA	1.50 ± 0.63	-0.53 (-0.92 to -0.14)	-0.70	0.008
	GA	2.03 ± 0.85			
Hospital Stay (days)	SA	2.57 ± 0.63	-1.10 (-1.47 to -0.73)	-1.51	< 0.001
	GA	3.67 ± 0.80			
Blood Loss (ml)	SA	242.00 ± 11.57	-36.00 (-43.47 to -28.53)	-2.55	< 0.001
	GA	278.00 ± 16.69			
Postoperative Pain (VAS)	SA	3.50 ± 0.82	-0.90 (-1.38 to -0.42)	-0.96	< 0.001
	GA	4.40 ± 1.04			

In the subgroup analysis, surgical time was consistently shorter in the SA group, with the most pronounced

difference observed in patients ≤ 45 years (69.50 ± 3.80 vs 86.20 ± 3.90 minutes, $p < 0.001$). Blood loss was also significantly lower with SA, with the greatest reduction seen in patients with BMI ≤ 24.0 kg/m² (238.00 ± 10.50 vs 273.00 ± 15.20 ml, $p < 0.001$) (Table 3).

Table 3: Stratified Analysis of Surgical Outcomes by Age, Gender, and BMI (n=60)

Stratification Variables	Subgroup	Outcome Variable	SA (Mean $\pm$ SD)	GA (Mean $\pm$ SD)	t-test p-value
Age (Years)	≤ 45 Years (n=23)	Surgery Time (min)	69.50 ± 3.80	86.20 ± 3.90	<0.001
		PACU Time (days)	1.30 ± 0.48	1.80 ± 0.63	0.012
		Hospital Stay (days)	2.30 ± 0.48	3.40 ± 0.70	<0.001
		Blood Loss (ml)	238.00 ± 10.20	272.00 ± 14.5	<0.001
		Postop Pain (VAS)	3.20 ± 0.63	4.10 ± 0.88	0.001
	>45 Years (n=37)	Surgery Time (min)	72.10 ± 4.10	89.20 ± 4.00	<0.001
		PACU Time (days)	1.65 ± 0.67	2.20 ± 0.89	0.015
		Hospital Stay (days)	2.75 ± 0.64	3.85 ± 0.81	<0.001
		Blood Loss (ml)	245.00 ± 11.80	282.00 ± 17.1	<0.001
		Postop Pain (VAS)	3.70 ± 0.80	4.60 ± 1.02	0.001
Gender	Male (n=28)	Surgery Time (min)	70.50 ± 4.10	87.50 ± 4.30	<0.001
		PACU Time (days)	1.45 ± 0.52	2.00 ± 0.82	0.014
		Hospital Stay (days)	2.50 ± 0.52	3.60 ± 0.74	<0.001
		Blood Loss (ml)	245.00 ± 12.30	282.00 ± 17.8	<0.001
		Postop Pain (VAS)	3.40 ± 0.70	4.30 ± 0.95	0.001
	Female (n=32)	Surgery Time (min)	71.40 ± 4.20	88.40 ± 4.10	<0.001
		PACU Time (days)	1.55 ± 0.68	2.06 ± 0.86	0.011
		Hospital Stay (days)	2.63 ± 0.67	3.73 ± 0.82	<0.001
		Blood Loss (ml)	239.00 ± 10.80	275.00 ± 15.9	<0.001
		Postop Pain (VAS)	3.60 ± 0.84	4.50 ± 1.08	0.001
BMI	≤ 24.0 kg/m ² (n=28)	Surgery Time (min)	70.20 ± 4.00	87.80 ± 4.20	<0.001
		PACU Time (days)	1.40 ± 0.52	1.95 ± 0.76	0.009
		Hospital Stay (days)	2.45 ± 0.51	3.55 ± 0.69	<0.001
		Blood Loss (ml)	238.00 ± 10.50	273.00 ± 15.2	<0.001
		Postop Pain (VAS)	3.30 ± 0.67	4.20 ± 0.92	0.001
	>24.0 kg/m ² (n=32)	Surgery Time (min)	71.80 ± 4.30	88.20 ± 4.10	<0.001
		PACU Time (days)	1.60 ± 0.67	2.10 ± 0.88	0.013
		Hospital Stay (days)	2.68 ± 0.68	3.78 ± 0.84	<0.001
		Blood Loss (ml)	246.00 ± 11.90	283.00 ± 17.3	<0.001
		Postop Pain (VAS)	3.70 ± 0.82	4.60 ± 1.05	0.001

In patients ≤ 45 years, dural tear occurred in 0.0% of the SA group versus 8.3% in the GA group ($p = 0.442$), while in those >45 years, rates were 5.0% and 5.6%, respectively ($p = 0.735$). Similarly, no significant differences were observed based on gender or BMI, with dural tear rates ranging from 0.0–6.3% in the SA group and 6.3–7.7% in the GA group (all $p > 0.05$) (Table 4).

Table 4: Stratified Analysis of Dural Tear by Age, Gender, and BMI (n=60)

Stratification Variables	Subgroup	Dural Tear	SA (n, %)	GA (n, %)	Total (n, %)	Test	p-value
Age (years)	≤ 45 (n=23)	Yes	0 (0.0%)	1 (8.3%)	1 (4.3%)	Fisher's Exact	0.442
		No	10 (100%)	11 (91.7%)	21 (95.7%)		
	>45 (n=37)	Yes	1 (5.0%)	1 (5.6%)	2 (5.4%)	Fisher's Exact	0.735
		No	19 (95.0%)	17 (94.4%)	36 (94.6%)		
Gender	Male (n=28)	Yes	0 (0.0%)	1 (7.1%)	1 (3.6%)	Fisher's Exact	0.483
		No	14 (100%)	13 (92.9%)	27 (96.4%)		
	Female (n=32)	Yes	1 (6.3%)	1 (6.3%)	2 (6.3%)	Fisher's Exact	0.763
		No	15 (93.8%)	15 (93.8%)	30 (93.8%)		
BMI (kg/m ²)	≤ 24.0 (n=28)	Yes	0 (0.0%)	1 (7.7%)	1 (3.6%)	Fisher's Exact	0.467
		No	13 (100%)	12 (92.3%)	25 (96.4%)		

	>24.0 (n=32)	Yes	1(5.9%)	1(6.3%)	2(6.3%)	Fisher's Exact	0.751
		No	16(94.1%)	15(93.8%)	31(93.8%)		

DISCUSSION

Spinal anesthesia (SA) offers substantial and statistically noteworthy benefits over general anesthesia (GA) in several postoperative domains, according to the direct comparison carried out in this study. Our results show that SA is the best anesthetic technique suited to this commonly performed neurosurgical procedure since it is linked to a more effective surgical technique, a better post-operative recovery profile, and improved satisfaction for patients. The most striking finding was the significant reduction in operative time with SA (71.0 ± 4.3 min vs. 88.0 ± 4.2 min; $p < 0.001$). Published research on spinal anesthesia for spinal surgery consistently emphasizes its effectiveness. Similar reduced operating room durations for lumbar discectomy under SA were observed in a study, attributing this to the removal of time for GA emergence and airway management [8]. This is further corroborated by a recently published study, which demonstrated the importance of spinal anesthesia in increasing surgical facility throughput by confirming that operational time is consistently decreased in lumbar spine surgeries [9]. Under SA, deep muscle relaxation may facilitate surgical exposure, perhaps reducing the requirement for additional anesthetic medications and cutting down on dissection duration. Beyond operational effectiveness, the SA group's recovery trend was noticeably quicker. Patients under SA had a decrease of an entire day in overall hospital stay and a substantially shorter PACU stay. The rationale for SA in an Enhanced Recovery After Surgery (ERAS) program for spine surgery is based on this finding. Neuraxial anesthesia for lumbar spine procedures was often linked to a shorter hospital stay, according to a review by Liu *et al.* [10]. They cited earlier ambulation, better pain management, and less post-operative nausea and vomiting (PONV) as associated variables. An important benefit is being able to mobilize promptly without experiencing severe dizziness or PONV, which are frequent aftereffects of GA. Early ambulation was attained far more quickly in the SA group, which directly affected discharge readiness, according to research by Jaafarpour *et al.* [11]. Another important advantage of SA is its excellent pain control characteristic. Both statistically and clinically, the SA group's post-operative VAS ratings were considerably lower. This is consistent with the physiological explanation that SA's remnant sensation blocking offers a defensive palliative benefit in the early post-operative phase. A randomized controlled trial by Sekerak *et al.* directly compared SA and GA for lumbar disc surgery and found not only lower early post-operative pain scores in the SA group but also a significantly reduced requirement for rescue opioids [12].

Effective analgesia with less systemic opioid use directly contributes to lower rates of sedation, ileus, and respiratory depression, thereby accelerating recovery. This is corroborated in a study where patients under SA had a significantly lower total morphine consumption in the first 24 hours post-operation [13]. The much lower intraoperative bleeding in the SA group was an intriguing and possibly clinically relevant outcome. Arteriolar dilation occurs in the lower limbs because of sympathetic block triggered by SA; however, Ye *et al.*'s description of the simultaneous decrease in central venous pressure and the formation of a less congested epidural venous plexus probably results in a drier operative area and more accurate hemostatic control [14]. In microdiscectomy, where total disc component removal and nerve root preservation depend heavily on good visibility, this can be especially helpful. Surgeons claimed a better visual field under SA than under GA, according to recent research by Yang *et al.* that used surgical field grading systems to give quantitative measurements [15]. In terms of complications, the SA group had a lower rate of dural tear, but the disparity failed to be statistically significant. Given the small total number of incidents, this is probably a Type II mistake. Importantly, in the case of a nerve root or dural sac proximity, the existence of a conscious patient under SA offers prompt feedback, which may enable the surgeon to modify technique and prevent a complete rupture. It is still a potential advantage of awake spine surgery under SA that needs more research in bigger cohorts, even if our evidence is not strong enough to support it [16]. Additionally, an upward trajectory toward decreased cumulative complication rates with SA was seen in a systematic study by Liu *et al.* but they also demanded more reliable data on surgical problems. Ghaith *et al.* demonstrated a significant shift toward non-GA techniques for lumbar spine surgeries, particularly in outpatient clinics, in a comparative study assessing the changes in anesthetic technique [17, 18]. SA lowers postoperative pain and the requirement for analgesics in the PACU after spinal lumbar surgery, according to a meta-analysis. Without affecting blood pressure, heart rate, or urine output, it is associated with both greater patient satisfaction and a lower incidence of PONV [19]. Kilic *et al.* reported improved perioperative effects, significantly lower anesthetic costs, and a quicker return to work, confirming the economic viability of SA [20]. Due to its observational, single-center methodology, this study has several limitations. Even though the groups were almost equal in size, the non-randomized patient

distribution raises the possibility of selection bias. Although the sample size was acceptable for key continuous outcomes, it was inadequate to make definitive inferences on uncommon surgical issues such as dural tears or neurologic deficits following surgery. The likelihood of residual confounding by unmeasured covariates and biased selection of anesthesia type cannot be completely ruled out, even if stratified analysis was used to account for measured confounders. It is recommended that future large-scale, randomized controlled trials confirm these results and investigate how they affect patient satisfaction and long-term functional outcomes.

CONCLUSIONS

In contrast to general anesthesia, spinal anesthesia was associated with a superior outcome profile in individuals undergoing single-level lumbar microdiscectomy. It enabled the procedure to proceed more quickly, reduced blood loss, offered better analgesia after surgery, and encouraged a much quicker recovery and immediate discharge. These advantages were in coherence with the aims of contemporary ERAS protocols and value-driven neurosurgical treatment. SA should be given serious consideration and made available as the primary anesthetic method for qualified patients, considering this data.

Authors' Contribution

Conceptualization: HA

Methodology: HA

Formal analysis: MA, SA

Writing and Drafting: HA, SA

Review and Editing: HA, MA, SA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Diagnostic Accuracy of Elevated Neutrophil: Lymphocyte Ratio (NLR) and Platelet: Lymphocyte Ratio (PLR) for the Prediction of 28-Day Mortality in Patients Presenting with Acute Exacerbation of COPD at Tertiary Care Hospital, Karachi

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) patients experiencing sudden flare-ups and immediate risk of death, and basic inflammatory indicators may assist in early risk assessment.

Objectives: To assess the diagnostic performance of elevated neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in predicting 28-day mortality among patients presenting with acute exacerbations of chronic obstructive pulmonary disease. **Methods:** The study was a prospective observational cohort study conducted at the Ojha Institute of Chest Diseases, Karachi (June 2025 to November 2025), following ethical approval. 88 AECOPD patients aged 20-70 years were recruited through consecutive sampling. Complete blood counts were used to calculate baseline NLR and PLR, which had predetermined cutoffs (>6.74 and >203.6). Mortality within 28 days was tracked among patients. Data analysis was done using SPSS version 25.0. Sensitivity, specificity, and ROC curves, along with multivariate logistic regression with confounder adjustments, were used to assess prognostic performance. **Results:** Among 88 AECOPD patients, the mean age was 61.16 ± 9.89 years, and 26 (29.5%) died within 28 days. Elevated NLR (84.1%) and PLR (78.4%) were common. The sensitivity of NLR was higher (80.77%), whereas its specificity (14.52%) and prognostic value (AUC 0.58) were lower, and the performance of PLR was poorer (AUC 0.52). Subgroup analysis indicated a better performance among older patients. In general, both biomarkers showed less than optimal prognostic value for 28-day mortality, with NLR being slightly better than PLR. **Conclusions:** While increased NLR and PLR were typical findings in acute COPD exacerbations, they showed poor diagnostic utility for forecasting 28-day mortality.

INTRODUCTION

Chronic obstructive lung disease (COPD) is the most common condition of health outcomes and fatality rates across the globe and is a progressive airflow limitation with frequent acute exacerbations. There exists a high mortality rate in acute exacerbations of COPD (AECOPD), especially in the initial 28 days of hospital-based care, and thus, there is a necessity to identify early and reliable prognostic indicators to inform clinical management [1]. Although treatment progress has been made, determining outcomes in AECOPD is difficult, particularly in limited

healthcare environments. Systemic inflammation is a central component of AECOPD pathophysiology and leads to the further course of the disease, dysfunction of organs, and death. In this regard, inflammatory biomarkers based on routine complete blood counts have received attention because they are simple, available, and cost-effective. As part of inflammatory biomarkers, NLR and PLR have been suggested as useful predictors in acute COPD exacerbations [2]. There is an indication that patients who have high neutrophil-to-lymphocyte ratio (NLR) and



platelet-to-lymphocyte ratio (PLR) are more likely to die in-hospital and early post-admission, which indicates that they may be used as cheap prognostic biomarkers in acute exacerbation of COPD [3]. There is evidence to indicate that the hematological ratios continue to be prognostic even in critically ill patients. NLR and PLR above normal have both been shown to predict ICU mortality risk in affected individuals during AECOPD and should therefore be used in severe cases of the disease [4]. Extensive database studies have also supported the role of inflammatory markers in disease severity and outcome prediction, such as NLR, in predicting in-hospital death in patients with AECOPD who have acute respiratory failure complications [5]. Additionally, Evidence synthesized from a previous study demonstrated that elevated NLR correlates strongly with all-cause mortality among patients with COPD, which justifies its usefulness as a strong prognostic biomarker [6]. This body of evidence has been extended by recent prospective cohort studies that have shown that inflammatory and nutritional markers such as NLR remain independently related to death from any cause in hypercapnic respiratory failure COPD patients [7]. Moreover, high NLR has been aligned with higher inflammatory load, represented by higher levels of C-reactive proteins in cases of acute exacerbation [8]. Moreover, the prognostic significance of a platelet-to-lymphocyte ratio (PLR) is supported by evidence showing that an elevated platelet-to-lymphocyte ratio (PLR) correlates with 90-day mortality in patients with acute exacerbation of COPD, which further supports its prognostic importance. [9]. The relevance of high levels of inflammatory biomarkers in poor clinical outcomes in AECOPD is further supported by studies based on long-term observation [10].

Even though there is growing evidence that inflammatory biomarkers like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are linked to disease severity and mortality during acute exacerbation of COPD (AECOPD), the majority of existing studies have been retrospective, used heterogeneous populations, or assessed only short-term. Furthermore, there are only a few studies by local populations which examine their independent prognostic performance based on standardized cut-off values and multivariate adjustment to predict short-term mortality. Regardless of the accumulating evidence of global data, local information assessing the diagnostic power of NLR and PLR as clarifying indicators of 28-day mortality in patients who present with AECOPD in Pakistan is insufficient. This study aimed to assess the diagnostic performance of NLR and PLR in predicting 28-day mortality in patients with acute exacerbation of COPD at a tertiary care center in Karachi. These easily obtainable biomarkers can be easily

established as prognostic to enable the risk stratification of individuals during an early stage and to enable better clinical decision-making in a resource-constrained environment.

METHODS

It was a prospective observational cohort trial that was to be carried out at the Ojha Institute of Chest Diseases, Karachi, for six months (June 2025 to November 2025) following the approval of the research synopsis. The Institutional Review Board of Dow University of Health Sciences (IRB-3805/DUHS/Approval/2025/213; dated 29th May 2025) provided ethical approval. All participants were informed to sign informed consent before enrolment. The participants were informed of the purpose and procedures of the study, possible risks and benefits, and their confidentiality was assured, and they were even given the right to discontinue participation at any time without it impacting their medical care. Non-probability consecutive sampling was used to sample patients who presented with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Both male and female patients aged 20-70 years who met the operational definition of AECOPD were included. Acute exacerbation was considered a known case of COPD with acute (less than 14 days) worsening of respiratory symptoms, which included increased dyspnea, cough, or production of sputum, and at least two clinical characteristics: tachypnea, tachycardia, fever, hypoxemia, respiratory acidosis, or supportive radiographic evidence. Patients with predispositions to influence inflammatory markers were eliminated, such as vasculitis, connective tissue disorders, seropositive or seronegative arthritis, pregnancy, tuberculosis, asthma, pneumonia, idiopathic pulmonary fibrosis, lung carcinoma, or malignancies. The sample size was computed using a previously reported sensitivity (82.54%) and specificity (71.38%) of the neutrophil-to-lymphocyte ratio (NLR) to predict 28-day mortality under the assumption that the prevalence is 9, the confidence level is 95, and the margin of error is 10 to get the required sample size of 88 patients. Nevertheless, the mortality of the study group was more than expected, and this could affect the accuracy and extrapolation of the estimates. Baseline demographic information, such as gender and age, was taken at the time of admission. Complete blood count was taken, and NLR and platelet-to-lymphocyte ratio (PLR) were determined. NLR above 6.74 and PLR above 203.6 were taken as high, based on earlier defined thresholds. The patients were monitored over 28 days since the time of admission, and deaths within the 28 days were noted.

SPSS version 25.0 was used to perform statistical analysis. Mean + SD or median + interquartile range were used to represent continuous variables based on the distribution

of data, which were evaluated by the Kolmogorov-Smirnov test. Frequencies and percentages were used to show categorical variables. The predictive ability of elevated NLR and PLR as prognostic factors to predict 28-day mortality was first assessed using 2x2 contingency tables, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated. The analysis of the Receiver Operating Characteristic (ROC) curves was carried out to evaluate the accuracy of prediction, and the area under the curve (AUC) was determined. The Youden Index was used to find the optimal cutoff values. To determine the independent relation between elevated NLR and PLR and 28-day mortality, multivariable logistic regression analysis was performed that adjusted the results for the possible confounders such as age, gender, severity of exacerbation, and comorbidities. Adjusted odds ratios, as well as confidence intervals of 95 percent, were provided.

RESULTS

The study included 88 patients who had an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The study gives a summary of the baseline demographic and clinical characteristics of the study population. The average age of the participants was 61.16/9.89 years, and the majority of the participants were males (84.1%). The acute exacerbation period in the median was 10.00 days (IQR: 9.00). The majority of patients were jobless (88.6%), and earned less than 75,000 PKR per month per family (92.0%). The neutrophil-to-lymphocyte ratio (NLR) was 9.00 (IQR: 3.00), and the platelet-to-lymphocyte ratio (PLR) had a mean value of 300.71 ± 188.14 . The patients had a high NLR (>6.74) and high PLR (>203.6) in 84.1% and 78.4% of cases, respectively. After a total of 28 days, the mortality rate was 29.5% (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population (n=88)

Variables	Mean $\pm$ SD / n (%)
Age (Years)	61.16 $\pm$ 9.89
Gender	
Male	74 (84.1%)
Female	14 (15.9%)
Duration of Acute Exacerbation	
Duration (Days)	10.00 (9.00)*
Occupational Status	
Employed	10 (11.4%)
Unemployed	78 (88.6%)
Family Monthly Income	
$>75,000$ PKR	7 (8.0%)
$\leq 75,000$ PKR	81 (92.0%)
Others	
Neutrophil-to-Lymphocyte Ratio	9.00 (3.00)*

Platelet-to-Lymphocyte Ratio	300.71 $\pm$ 188.14
Elevated NLR	74 (84.1%)
Elevated PLR	69 (78.4%)
28-Day Mortality	26 (29.5%)

*Continuous variables expressed as median (IQR) or mean $\pm$ SD; categorical variables as n(%).

The diagnostic performance of elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) to predict 28-day mortality was assessed using 2x2 contingency tables. Elevated NLR had a high sensitivity (80.77%) but low specificity (14.52%) with a positive predictive value (PPV) of 28.38% and a negative predictive value (NPV) of 64.29%. NLR was less sensitive (65.38%) and also lacked specificity (16.13%). Both ratios had low diagnostic accuracy (Table 2).

Table 2: Prognostic Performance of Elevated NLR and PLR for Prediction of 28-Day Mortality (n=88)

Biomarkers	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Elevated NLR	80.77	14.52	28.38	64.29	34.09
Elevated PLR	65.38	16.13	24.64	52.63	30.68

This study used Receiver Operating Characteristic (ROC) curve analysis to evaluate the predictive ability of NLR and PLR for 28-day mortality. The NLR had moderate predictive performance with a larger area under the curve (AUC) than PLR (Table 3).

Table 3: ROC Curve Analysis of NLR and PLR for Prediction of 28-Day Mortality

Biomarkers	AUC (95% CI)	Optimal Cutoff	Sensitivity (%)	Specificity (%)
NLR	0.58 (0.45-0.70)	>6.74	80.77	14.52
PLR	0.52 (0.39-0.65)	>203.6	65.38	16.13

Post-stratification analysis of elevated NLR was done to examine its diagnostic capabilities in various subgroups. The sensitivity was higher in males (82.61%) than in females (66.67%), and the specificity was low in each group. The diagnostic accuracy of patients with age ≥ 65 years was higher (44.74%) than in younger patients. In all stratified variables, high NLR sensitivity and low specificity were observed (Table 4).

Table 4: Post-Stratification Diagnostic Performance of Elevated NLR for 28-Day Mortality (n=88)

Stratification Variables	Category	Sensitivity (%)	Specificity (%)	Diagnostic Accuracy (%)
Gender	Male	82.61	17.65	37.84
	Female	66.67	0.00	14.29
Age (years)	<65	76.92	8.11	26.00
	≥ 65	84.62	24.00	44.74
Duration of Exacerbation	<10 Days	75.00	9.09	32.35
	≥ 10 Days	85.71	17.50	35.19

Monthly Income	≤75,000	78.26	15.52	33.33
	>75,000	100.00	0.00	42.86
Occupational Status	Employed	100.00	14.29	40.00
	Unemployed	78.26	14.55	33.33

DISCUSSION

The paper compared NLR and PLR as predictors of 28-day mortality in patients with AECOPD. The ratios of inflammation were frequently elevated, and their diagnostic ability varied across subgroups of patients. According to Fu *et al.* systemic inflammatory indices, including NLR, PLR, and others, tend to be elevated in AECOPD, which implies the heightened degree of inflammatory processes [11]. It aligns with the current research, where a high percentage of patients were identified with high NLR (84.1%) and PLR (78.4%). Yu *et al.* developed a risk prediction model of in-hospital mortality in AECOPD and discovered that inflammatory markers were potential [12], but not independent, predictors of mortality, which is consistent with the low overall diagnostic quality of NLR and PLR in this study. The GOLD 2023 report also indicates that the change of systemic inflammatory response during exacerbations depends upon the severity of the disease and the peculiarities of the patient [13], which is consistent with the heterogeneous diagnostic performance, which is present in stratified patient groups in the current study. Liu *et al.* found that use of NLR along with other clinical measures enhanced the prognostic capacity in critically ill COPD patients, suggesting that the use of NLR individually has poor predictive capacity [14]. Similarly, Fayiad and Amer demonstrated that values of NLR and PLR predictors yield varying results [15], which are in line with the sensitivity, specificity, and the variation in the predictive value in the present study. The same authors noted that the predictor of higher mortality in this study is higher NLR, not just in the short term as reported by Liu *et al.* [16], but also in this study, higher NLR is a relatively high sensitivity but low specificity predictor of 28-day mortality. In COPD, El-Gazzar *et al.* have concluded that the discriminatory ability of poor outcome of NLR and PLR is weak, which is parallel to the low values of diagnostic accuracy in this analysis [17]. Paliogiannis *et al.* concluded that even though NLR in COPD is always higher, it varies in prognostic value, and the heterogeneity of the results among stratified subgroups has the same consistency [18]. Ye *et al.* found that in their study, the NLR prognostic value is dependent on the severity of disease and clinical outcomes, and in line with the fluctuation in age and length of exacerbation [19]. The baseline considerations and comorbidities mentioned by Sørensen *et al.* influence the relationship between NLR and mortality, which is in line with the differences in the stratified outcomes of the diagnostic findings in the study

[20]. Overall, these findings indicate that high values of NLR and PLR can be expected in AECOPD, but they do not have a high degree of diagnostic utility in terms of the 28-day mortality, and they require patient-specific factors and heterogeneity of the disease.

The present study has several limitations due to its single-center design and relatively small sample size ($n = 88$), which can influence the extent of generalizability. It is also observational, and its causal inference is not possible; the possible confounders (comorbidities and severity of infection) had not been completely controlled. Baseline NLR and PLR have also been evaluated only and not serially, and other inflammatory (e.g., CRP, procalcitonin) and long-term outcomes beyond 28 days were not evaluated, which limited a more comprehensive assessment of prognostic value. To enhance the external validity, future studies must use larger and multicenter cohorts. Serial biomarker measurements and other inflammatory and clinical parameters would be valuable to increase the prognostic models. Integration of NLR and PLR with the existing clinical scoring systems can enhance risk stratification, and follow-up studies should be conducted over a long period to enhance risk evaluation, including readmission and prolonged mortality.

CONCLUSIONS

The present study showed that the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are both common in patients with acute exacerbation of COPD and indicate an increase in the systemic inflammatory response. Nonetheless, both biomarkers exhibited poor prognostic performance as they were associated with 28-day mortality, but are less specific and have a moderate overall predictive ability, with NLR being marginally better than PLR. In general, NLR and PLR can be used as simple and inexpensive indicators of inflammation in AECOPD, but not as independent prognostic factors. They are probably more useful in combination with other clinical parameters and known risk assessment models.

Authors' Contribution

Conceptualization: AA

Methodology: AA, FA, NS, RN

Formal analysis: AA, RN, MA

Writing and Drafting: AA, NS, KS, MA

Review and Editing: AA, FA, NS, RN, KS, MA

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

Conflicts of Interest

All the authors declare no conflict of interest.

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Original Article



Diagnostic Accuracy of the Oxygen Desaturation Index for Screening Severe Obstructive Sleep Apnea

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ABSTRACT

Obstructive sleep apnea (OSA) is a common disorder with significant cardiovascular and metabolic effects. Although polysomnography-derived Apnea-Hypopnea Index (AHI) is the diagnostic gold standard, limited access has increased interest in simpler alternatives like Oxygen Desaturation Index (ODI). **Objective:** To determine the diagnostic accuracy of the ODI in identifying severe OSA compared with the AHI. **Methods:** This cross-sectional study was conducted at the Pulmonology department, Pak Emirates Military Hospital, from 01-03-2025 to 30-11-2025, including 126 patients with a STOP-BANG score >5. Overnight monitoring was performed for 4-8 hours using polysomnography with integrated pulse oximetry. ODI was calculated as a $\geq 3\%$ drop in oxygen saturation lasting at least 10 seconds. All participants underwent polysomnography for AHI assessment. SPSS version 27.0 was used for analysis. Pearson correlation, linear weighted kappa measure, and ROC curve analysis were performed. **Results:** The patients' mean age was 54.6 ± 11.9 years, and BMI was 34.1 ± 5.5 kg/m², predominantly male. Many patients had severe OSA. AHI and ODI showed a strong positive correlation with significant predictive value, and substantial agreement was observed between their severity classifications ($\kappa=0.676$, $p<0.001$). ROC analysis showed good diagnostic performance of ODI for identifying severe OSA (AUC=0.961, 95% CI: 0.932-0.990, $p<0.001$), with a sensitivity (94.3%) and specificity (79.5%) at an ODI cutoff ≥ 35 . **Conclusion:** ODI shows a strong association with AHI and good accuracy for detecting severe OSA. It may be used as a non-invasive screening tool in resource-limited settings, but it cannot replace polysomnography.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder where periodic hypoxemia, arousal, and disjointed sleep are prevalent. OSA is a severe worldwide health problem, and the level of prevalence varies among adults, including all the severities of the disease [1]. OSA has been linked with the high risk of cardiovascular diseases, including hypertension, heart failure, stroke, cardiac arrhythmias, myocardial infarction, and pulmonary arterial hypertension. It is also associated with metabolic dysregulation, such as insulin resistance and lipid abnormalities, which are risk factors for cardiovascular

disease. Neuro-cognitive and psychiatric ailments are also associated with it [2]. According to a recent meta-analysis, the prevalence of OSA in Pakistan was estimated at 35; yet, this figure represents mainly those who have been screened or suspected to have OSA, rather than the definitive diagnosis of polysomnography, which is why there is a pressing need to perform targeted screening and early intervention, to perform early diagnosis, and to effectively manage OSA [3]. Some predisposing factors for the development of OSA include structural (Anatomical variations, Micrognathia, retrognathia, adenotonsillar



hypertrophy, palatal deformities, etc.) and non-structural risk factors (Male gender, Obesity, advanced age, smoking/ alcoholism, and medical conditions such as hypothyroidism, acromegaly, PCOS, and chronic cardiopulmonary disorders). OSA causes fragmented sleep, which causes daytime sleepiness, lack of concentration, mood swings, and cognitive impairments. This eventually impacts the quality of life, such as family life and work performance. Diagnosis of OSA can be made by calculating the Apnea-Hypopnea Index (AHI), which is done using overnight in-laboratory Polysomnography (PSG), by recording airflow, respiratory effort, oxygen saturation, heart rate, and brain activity [4]. Although the gold standard of diagnosis of OSA should be AHI calculation by PSG, it is an arduous procedure, which requires proper sleep labs and trained staff. It is not readily available, expensive, and technically sophisticated, which is a barrier to its extensive use in developing countries such as Pakistan [5]. Over the years, pulmonologists and sleep study experts have proposed different, simpler, and more cost-effective methods of diagnosing OSA. Among them is the measurement of Oxygen Desaturation Index (ODI), a relatively practical and readily available method as an alternative to PSG for OSA diagnosis [6, 7]. It is done by applying a finger pulse oximeter to sleeping patients and observing them overnight for pre-defined oxygen desaturation episodes without the need for a sleep lab. This data is then compared to the standard values available for diagnosing OSA and interpreted for the presence of OSA or otherwise [8, 9]. In addition to desaturation episodes, lowest oxygen saturation (LSpO₂) and cumulative time below 92% oxygen saturation (TBSpO₂) can also be calculated using ODI protocols and used to increase diagnostic accuracy [10]. Despite being an attractive option for OSA diagnosis, there have been question marks on the sensitivity, specificity, positive and negative predictive values of ODI as compared to AHI [11].

Limited availability and cost of polysomnography necessitate simpler screening tools for OSA. However, the diagnostic accuracy of ODI for detecting severe OSA remains insufficiently validated in the local population of Pakistan. Therefore, this study aimed to evaluate the diagnostic accuracy of the ODI in detecting severe OSA, using AHI as the reference standard.

METHODS

This cross-sectional study was conducted from 1st March 2025 to 30th November 2025 at the Department of Pulmonology, Pak Emirates Military Hospital (PEMH), Rawalpindi. Sample size for this study was 126, calculated through 'diagnostic study sample size calculator (web)', keeping the sensitivity of ODI as 96.6% and the specificity of 69.6% in diagnosing severe OSA, [8] the prevalence of

OSA in the Pakistani population as 35% [3], confidence level of 95%, and 80% power of test. After approval from the Ethical Committee (Ref# A28/ERC/156/2025; dated 1st March 2025), 126 patients were selected from the Pulmonology Outpatient department using a non-probability consecutive sampling technique during the study period. The inclusion criteria were patients of either gender, aged 18-75 years, with suspected OSA with a STOP-BANG Score > 5. The exclusion criteria include individuals diagnosed with central sleep apnea, patients with chronic lung diseases such as COPD or interstitial lung disease, and patients who use supplemental oxygen or sedative drugs that can modify sleep architecture or patterns of oxygen saturation, or are unwilling to participate. A standardized questionnaire was used to collect demographic and clinical data, including age, sex, body mass index (BMI), neck circumference, and related comorbidities, such as hypertension and diabetes. All patients were then observed overnight, 4-8 hours after the onset of sleep, in the polysomnography suite, where sleep assessment was done using the Philips Alice Night One device. In the study, various parameters were measured simultaneously, such as the ODI, which is defined as the number of oxygen desaturation events per hour of sleep, and each event was characterized by a decrease in oxygen saturation of over 3 per cent of the baseline, which lasts longer than 10 seconds. The Lowest Oxygen Saturation (LSpO₂) or the lowest oxygen saturation level recorded during the whole night was also recorded. In addition, AHI was measured and analyzed.

IBM SPSS version 27 was used to analyze the data. Mean with standard deviation was used to express quantitative variables like age, BMI, AHI, and ODI, whereas frequencies and percentages were used to express qualitative variables. Pearson correlation analysis and simple linear regression analysis were used to determine the relationship between ODI and AHI. The agreement between the OSA severity classification based on AHI and that based on ODI was assessed using linear weighted kappa statistics. This was done by receiver operating characteristic (ROC) curve analysis to determine the diagnostic performance of ODI in identifying severe OSA (AHI ≥ 30 events/hour). The sensitivity, specificity, and area under the curve (AUC) were calculated. Several ODI cutoff points (≥15, ≥20, ≥25, ≥30, ≥35, and ≥40) were considered to identify the diagnostic performance over a clinically relevant range. The best cutoff value was determined using the Youden index (sensitivity + specificity - 1). A p-value ≤ 0.05 was considered statistically significant.

RESULTS

This study included 126 patients, predominantly middle-aged males (70.6%). The mean age of the patients was 54.6 ± 11.9 , and the mean BMI was 34.1 ± 5.5 kg/m². About 38.1% of patients had no comorbidities; the rest commonly had ischemic heart disease, hypertension, diabetes, or multiple comorbidities. Sleep study results showed a mean AHI of 46.2 ± 24.2 and ODI of 56.3 ± 31.9 , with average and lowest SpO₂ of $90.8 \pm 3.5\%$ and $73.2 \pm 10.8\%$, respectively. Most participants had moderate-to-severe OSA, with 81.7% classified as severe by ODI and 69.0% by AHI (Table 1).

Table 1: Baseline Information (n=126)

Variables	Mean $\pm$ SD / n (%)
Age (Years)	54.56 $\pm$ 11.913
BMI (kg/m ²)	34.096 $\pm$ 5.5224
Gender	
Male	89 (70.6%)
Female	37 (29.4%)
Comorbidities	
No Comorbidities	48 (38.1%)
IHD	27 (21.4%)
HTN	25 (19.8%)
DM	18 (14.3%)
Multiple Comorbidities	8 (6.3%)
AHI	46.177 $\pm$ 24.1906
ODI	56.319 $\pm$ 31.9027
Average SpO ₂ during sleep (%)	90.79 $\pm$ 3.516
Lowest SpO ₂ during sleep (%)	73.20 $\pm$ 10.804
Monitoring Time (minutes)	274.89 $\pm$ 31.472
Severity of OSA (ODI-based)	
Mild	3 (2.4%)
Moderate	20 (15.9%)
Severe	103 (81.7%)
Severity of OSA (AHI-based)	
Mild	5 (4.0%)
Moderate	34 (27.0%)
Severe	87 (69.0%)

The severity of OSA as classified by AHI fell parallel to ODI with all participants having severe OSA as categorized by AHI which also corresponded to severe as categorized by ODI. Overall agreement was measured using linear weighted kappa ($\kappa=0.676$, 95% CI: 0.533-0.818, $p<0.001$), which shows that there is a great deal of agreement between the two classification methods beyond chance. This helps to support the reliability of ODI as a surrogate tool to classify the severity of OSA. The positive correlation between ODI and AHI was very strong ($r=0.921$), which shows that ODI closely follows changes in AHI and is a good indicator of the severity of the disease. Also, ODI was moderately positively correlated with BMI ($r=0.359$), indicating that higher BMI is positively correlated with more oxygen desaturation events during sleep (Table 2).

Table 2: Agreement between AHI- and ODI-based OSA severity classification using linear weighted kappa (n=126)

AHI-based OSA	ODI-based OSA			Linear Weighted Kappa	CI	p-value
	Mild	Moderate	Severe			
Mild	3 (60.0%)	1 (20.0%)	1 (20.0%)	0.676	0.533-0.818	<0.001
Moderate	0 (0.0%)	19 (55.9%)	15 (44.1%)			
Severe	0 (0.0%)	0 (0.0%)	87 (100.0%)			

Linear regression analysis revealed a strong positive relationship between ODI and the Apnea-Hypopnea Index (AHI). The ODI strongly predicted AHI ($\beta=0.698$, $p<0.001$). The model explained 84.8% of the variance in AHI ($R^2=0.848$), demonstrating that ODI is responsible for a significant fraction of the variability. The regression model showed significant results ($F(1,124)=691.866$, $p<0.001$). For every one-unit rise in ODI, AHI increased by about 0.7 occurrences per hour (Table 3).

Table 3: Correlation analysis of study variables

Variables	Pearson Correlation (r)	p-value
ODI vs AHI	0.921	<0.001
ODI vs BMI	0.359	0.057

The scatterplot demonstrates a strong, positive linear correlation between the Apnea-Hypopnea Index (AHI) and the ODI. This tight clustering validates the use of ODI cutoffs as reliable predictive surrogates for AHI-defined OSA severity in clinical diagnostics (Figure 1).

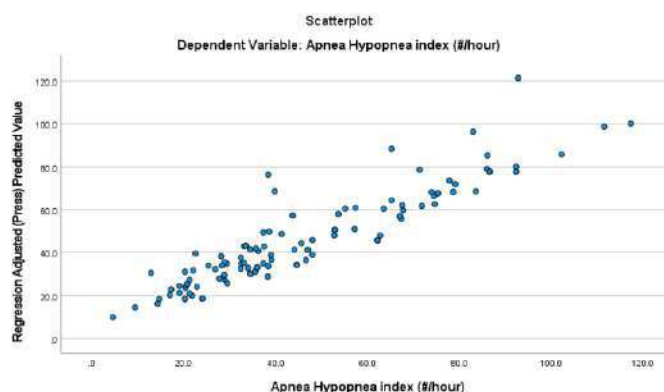


Figure 1: Scatterplot illustrating the relation of AHI and ODI values. The blue line in the ROC graph represents the diagnostic performance of the ODI. The curve rises sharply toward the upper left corner of the graph, indicating high diagnostic accuracy in identifying severe OSA. Furthermore, since the blue line lies well above the diagonal reference line, it demonstrates that ODI performs significantly better than chance in predicting severe OSA (Figure 2).

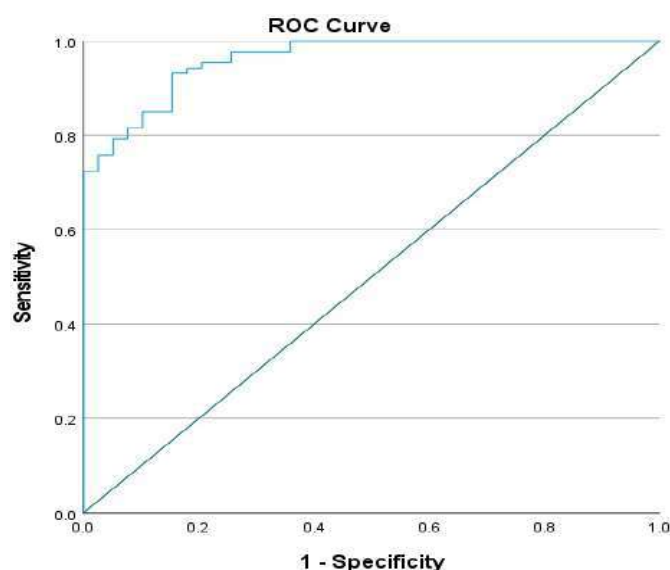


Figure 2: ROC Analysis Demonstrated that ODI Sensitivity

The ROC analysis shows that the ODI has very good diagnostic accuracy for detecting severe OSA (AHI ≥ 30 /hour), with an area under the curve (AUC) of 0.961 (95% CI: 0.932–0.990, $p < 0.001$) (Table 4).

Table 4: Area under the curve for ODI based on ROC

Area Under Curve	95% C. I	p-value
0.961	0.932-0.990	<0.001*

Lower ODI cutoffs (≥ 15 to ≥ 30) demonstrate 100% sensitivity but low specificity (7.7%–59%), indicating a high false-positive rate. As the cutoff increases to ≥ 35 , sensitivity slightly decreases to 94.3% while specificity improves to 79.5%, suggesting a more balanced diagnostic performance. At ≥ 40 , specificity further increases to 89.7%, although sensitivity declines to 81.6% (Table 5).

Table 5: Sensitivity and Specificity of ODI Cutoffs for Severe OSA

AHI ≥ 30 /hr	Sensitivity	Specificity
ODI ≥ 15	100%	7.7%
ODI ≥ 20	100%	30.8%
ODI ≥ 25	100%	43.6%
ODI ≥ 30	100%	59%
ODI ≥ 35	94.3%	79.5%
ODI ≥ 40	81.6%	89.7%

DISCUSSION

The findings of this study indicate that there is a strong positive relationship between the ODI and AHI, i.e., higher values of the ODI are associated with increased severity of OSA. These results agree with the use of ODI as a practical screening and triage instrument for severe OSA. ODI in resource-limited settings: ODI can be used as a primary screening modality; nevertheless, it cannot be utilized to definitively diagnose the issue. The American Academy of Sleep Medicine (AASM) supports the use of limited-channel

and home-based testing strategies, such as oximetry, when access is limited, and the clinical pretest probability is high. Substantial prospective studies have also demonstrated that ODI is strongly correlated with AHI and can be successfully used to stratify patients to refer to definitive sleep testing. This assists in specific early detection and early therapeutic response. The variability in hypopnea scoring criteria (3 vs. 4 desaturation thresholds), oximeter technology, altitude, baseline lung function, and population case mix are likely to explain the variability in reported diagnostic efficacy across studies. Based on the clinical applicability perspective, ODI has a number of advantages. Pulse oximetry is cheap, non-invasive and commonplace (pocket pulse oximeters, smart watches, etc.). This facilitates easy screening within outpatient and resource-limited facilities. In high-risk populations, an elevated ODI may support prioritization for Polysomnography and facilitate earlier initiation of treatment, such as continuous positive airway pressure. Chen et al also tested the validity of ODI as compared to AHI / REI and concluded that ODI was strongly correlated with apnea-hypopnea index (AHI) ($r = 0.941$) [12]. These results were not only consistent with our study's findings, but their study's findings were further supported by a bigger sample size ($n = 440$). Additionally, Undrajavarapu et al. found a strong association ($r = 0.734$, $p = 0.001$) between ODI and AHI. When it came to identifying OSA (ODI > 5), home oximetry had sensitivity, specificity, and diagnostic accuracy of 69%, 100%, and 71%, respectively [13]. However, instead of inpatient overnight monitoring, they opted for home monitoring by a trained staff member, as opposed to our study. However, the higher proportion of severe OSA identified by ODI compared to AHI in our study suggests a tendency of ODI to overestimate disease severity. This may be attributed to the fact that ODI captures all oxygen desaturation events, including those not meeting strict hypopnea criteria in AHI scoring. Additionally, ODI is influenced by baseline oxygen saturation and may reflect non-obstructive desaturation events, thereby increasing the likelihood of misclassification. Despite this, its high sensitivity makes it a useful screening and triage tool, particularly in high-risk populations. Sinthia et al. also tested ODI to predict OSA and concluded that it indeed was able to diagnose OSA as accurately as AHI [14]. Sinthia et al used an automated monitor, whereas our study used observer-based monitoring. Karhu et al. compared different desaturation event quantification parameters and concluded that ODI was superior in determining the OSA presence and severity as compared to the lowest saturation or total time below cut-off saturation [15]. This contrasts with the findings of our study, in which LSpO₂ did correlate with a higher number of desaturation events, but we did not compare the two indices head-to-head.

Additionally, Fabius *et al.* confirmed the association between ODI and AHI and found that, when assessed concurrently with the same oximeter during PSG, an ODI <5 predicted an AHI <5 with excellent sensitivity (97%) and specificity (97%) [16]. They, however, documented that at higher AHI and ODI scores, this correlation wasn't as strong. Levendowski *et al.* also compared ODI and AHI for OSA diagnosis, as well as studying the effect of posture on the two. They found that the overall correlation between AHI and ODI was 0.97, with supine recording times being 0.94 and non-supine recording times being 0.96 (all $p < 0.001$). The AHI and ODI differences for the majority of patients were negligible; 14% of the records had an AHI-ODI difference greater than 5 events per hour, and 6% had a difference greater than 10 events per hour [17]. The ROC analysis in the present study demonstrated excellent diagnostic accuracy of ODI for detecting severe OSA (AHI ≥ 30 /hour), with an AUC of 0.961 (95% CI: 0.932–0.990). This is comparable to previously reported AUC values ranging from 0.98 to 0.997 in similar populations, indicating consistently high discriminative ability of ODI. In our study, an ODI cutoff ≥ 35 yielded a sensitivity of 94.3% and specificity of 79.5%, which aligns with prior studies reporting sensitivity ranging from 32% to 98.5% and specificity from 47.7% to 98%. These findings reinforce that ODI demonstrates high sensitivity with moderate-to-high specificity, making it a reliable screening tool, although variability across studies may be influenced by differences in study design, population characteristics, and desaturation thresholds [18, 19]. In the present study, BMI showed a weak positive correlation with ODI; however, this association was not statistically significant ($p > 0.05$), limiting its clinical interpretability. The same association was studied by Leppänen *et al.* According to their research, all OSA categories showed statistically significant increases in AHI, ODI, and hypopnea index values with increasing BMI ($\beta = 0.10$, $P = 0.002$), except the moderate OSA category, where increases in AHI and ODI did not reach the threshold of statistical significance ($\beta = 0.047$, $P = 0.20$) [20]. Similarly, Novkovic *et al.* were also not able to conclusively correlate higher BMI with a higher ODI score in patients with OSA but did validate ODI for the diagnosis of OSA independent of obesity [21]. Finally, Azakli *et al.* also documented the predictive value of ODI in OSA with respect to long-term mortality and demonstrated that it could be used as a prognostic tool in addition to being a diagnostic tool. ODI was the only polysomnography metric found to be an independent predictor of OSA patients' mortality in a research sample of 3541 individuals [22]. However, such a prospective analysis was not done in our study, so similar conclusions or otherwise cannot be drawn. There are several limitations to be taken into account. ODI can be influenced by baseline oxygen saturation and

comorbid cardiopulmonary conditions, which may lead to overestimation of OSA severity, and these confounders were not adjusted. Technical measurement bias (e.g., motion artifacts, probe problems) can also affect the results. Moreover, the relatively low monitoring period (mean 4.6 hours) as compared to full-night polysomnography may have an impact on event detection; nevertheless, it is still similar to the studies conducted in resource-limited environments. Validation should be done by more multi-center full-night monitoring.

CONCLUSIONS

This study indicates that there is a strong positive correlation between the ODI and AHI, and that it has a good diagnostic sensitivity to detect severe OSA. ODI could be regarded as a practical, non-invasive screening and triage instrument, especially in the context of resource-limited settings, but it should not be considered as a substitute of polysomnography, which is still considered the gold standard in diagnosis. These findings need to be viewed in the light of some limitations, such as the single-center design, the application of non-probability consecutive sampling, the relatively short period of monitoring, and the absence of correction of such potential confounding factors. Also, the fact that the relationship between ODI and demographic variables (age, gender, and BMI) was not statistically significant should be viewed with reservations. Substantial, multi-center, large-scale research is required to confirm these results.

Authors' Contribution

Conceptualization: MUIM

Methodology: MUIM

Formal analysis: MI, KA, MR, SA

Writing and Drafting: MUIM, KA, MUIM

Review and Editing: MUIM, MI, KA, MR, SA, MUIM

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



Intermittent Bolus via Surgeon-Placed Adductor Canal Catheter for Postoperative Analgesia in Total Knee Arthroplasty: An Observational Longitudinal Study

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ABSTRACT

Effective postoperative pain control after total knee arthroplasty (TKA) is essential for early mobilization and better outcomes. The adductor canal block (ACB) provides effective, motor-sparing analgesia. **Objectives:** To evaluate the efficacy of surgeon-placed ACB in reducing postoperative pain and analgesic requirements in patients undergoing TKA. **Methods:** This observational longitudinal study was conducted in the hospital's Orthopedic Department from 14th February 2026 to 13th May 2026. A total of 38 patients were enrolled through consecutive sampling and underwent standard TKA under spinal anesthesia, with ACB placement by an experienced surgeon. Pain was assessed using the visual analogue scale preoperatively and at 24 and 48 hours postoperatively. Data on time to first analgesia and analgesia consumption during 0-48 hours were collected. Statistical analysis included the Friedman test with Bonferroni-corrected post-hoc comparisons for longitudinal data, and the Wilcoxon Signed-Rank test for postoperative analgesia consumption. **Results:** Overall mean age was 63.7 ± 7.4 years, and 31 (81.6%) were females. Median pain VAS score decreased from baseline 7.0 (1.0) to 4.0 (2.0) at 24 hours, and 1.0 (2.0) at 48 hours. Similarly, 29 (76.3%) patients required no rescue medication in the first 24 hours, and 32 (84.2%) during the 24-48 hours period. Median analgesia consumption dropped from 0.0 (25.0) mg to 0.0 (0.0) mg across these intervals ($p=0.007$). **Conclusions:** The surgeon-placed ACB was associated with low postoperative pain scores and minimal need for rescue analgesia among patients undergoing TKA in this setting.

INTRODUCTION

Total Knee Arthroplasty (TKA) is a procedure that is frequently associated with intense post-operative pain despite comprehensive multimodal analgesia [1]. Various modes of analgesia have been used in the past for effective control of pain post-operatively after TKA [2]. Relieving pain without compromising motor function is a challenge for the operating surgeon in the early post-operative period [3]. Early mobilization is now standard in most orthopedic surgeries, especially following total joint replacement, to promote early ambulation and rapid recovery [4]. Epidural analgesia is frequently associated with a high failure rate

and side effects such as urinary retention, blocking motor power, and hence delaying early mobilization are limitations of this technique. Femoral nerve block provides excellent analgesia, but there is usually a motor blockade, and hence the risk of in-hospital falls is increased [5]. The saphenous nerve is a distal sensory branch that supplies sensation to the skin of the medial, anteromedial, and posteromedial surfaces of the lower leg. Saphenous nerve block has been tested in a few case studies and found to be effective in reducing pain during knee flexion during the first 24 hours after TKA. Further improvement in the safe and effective



perioperative pain control measures has shifted the TKAs to an outpatient setting [6]. The Adductor Canal Block (ACB) is a relatively new block with encouraging results, as quadriceps muscle strength is minimally affected, as only the motor nerve to the vastus medialis of the quadriceps muscle is compromised. In this technique, the surgeon performs an intraoperative trans articular ACB guided by anatomical landmarks [6, 7]. Samuel *et al.* conducted a study and observed that the mean pain score after 24 hours was 5.05 ± 1.84 , and the mean morphine consumption was 44.67 ± 26.45 mg [6]. Jenstrup *et al.* also observed that Morphine consumption from 0 to 24 h was less with ACB as compared to placebo (40 ± 21 vs. 56 ± 26 mg, $p=0.006$). Pain was significantly reduced with ACB during 45° flexion of the knee ($p=0.001$), but not at rest ($p=0.006$) [8].

The rationale of this study was to evaluate the outcomes of the surgeon-placed ACB for the management of postoperative pain in patients undergoing TKA. Postoperative pain relief and early ambulation after primary TKA are the primary objectives of surgeons to achieve a successful primary TKA. Multiple modalities have been used in the past. Surgeon-placed ACB is a relatively newer technique that can help to reduce pain and the need for postoperative analgesia. But, limited work has been done before, and no local evidence exists in the literature in this regard. Therefore, this study was aimed to evaluate the efficacy of surgeon-placed ACB in reducing postoperative pain and analgesic requirements in patients undergoing TKA.

METHODS

This observational longitudinal study was carried out at the Department of Orthopedics, Doctors Hospital, Lahore, from 14th February 2026 to 13th May 2026. The study received approval from the Institutional Review Board of Doctors Hospital & Medical Centre Lahore (Letter No. IRB/01/2025/01, dated February 3, 2025) and from the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan (Letter No. CPSP/REU/OSG-2023-090-3007, dated February 13, 2026). Written informed consent was obtained from all patients. A total of 38 patients undergoing primary TKA under spinal anesthesia were included using a non-probability consecutive sampling technique. Other inclusion criteria were patients of either gender, aged 30 to 80 years, irrespective of body mass index (BMI). The exclusion criteria were patients with bilateral TKA, contraindications, or allergic to analgesic drugs, neurological disorders, or severe bleeding disorders [prothrombin time (PT) >20 seconds and/ or international normalized ratio (INR) >2]. A minimum sample size of 30 cases was calculated by using the following formula: $n = Z^2 \cdot \frac{2}{d^2}$; where parameters were set at a 95% confidence level ($Z=1.96$), precision ($d=0.7$), and pain visual analogue

scale (VAS) score 5.05 ± 1.84 after 24 hours post-surgery [6]. An addition of 25% attrition rate due to expected loss to follow-up or missing data led to a final sample of 38 cases. An experienced surgeon performed all procedures under spinal anesthesia. In accordance with the approved protocol, surgeon-placed ACB was defined as a regional anesthetic block involving the injection of a local anesthetic around the adductor canal, targeting the saphenous nerve, to provide analgesia for the knee joint and surrounding structures. During standard TKA, the adductor canal was exposed. To facilitate intermittent dosing, a 5 French feeding tube was placed into the adductor canal under direct vision using a trocar and pituitary rongeur. The skin and tube were placed deep into the adductor canal under vision. The tube was anchored to the skin with the help of steri-strips. Sixty mL of solution was prepared, including one vial of Tramadol (1ml/50mg), Decadron (1ml/4mg), and two vials of Bupivacaine (10ml/50mg each) in normal saline. Tramadol was added to the solution as an off-label perineural adjuvant to prolong the analgesic effect of bupivacaine and reduce postoperative opioid needs, representing an approach that requires further clinical validation for this specific site. The feeding tube was attached to a drip set, allowing 20 ml of the solution to be administered every 8 hours in the form of an intermittent bolus. The first dose of this solution was administered after shifting the patient to the post-surgical ward. In case of a spike of pain, an additional 10 ml of solution was injected. The patient was followed up there until recovery. Those patients who were non-responsive to ACB were given a 100mg injection of Liometacen in one liter of normal saline drip over 24 hours. Demographic data, including age (years), gender (male/ female), and BMI (Kg/m^2), were recorded using a structured proforma. Operative time (minutes) was measured from the initial skin incision to the completion of skin closure [9]. Intraoperative blood loss (ml) was estimated by summing the volume of fluid collected in the suction container and the gravimetric measurement of surgical sponges, calculated as the difference between their wet and dry weights [10]. Time to first analgesia (hours) was measured from the administration of spinal anesthesia until the patient requested rescue analgesia due to a VAS score ≥ 4 . Analgesia consumption (mg) was the cumulative amount of rescue medication administered during the first 24 hours (0–24 h) and the second 24 hours (24–48 h) postoperatively, when the pain VAS score was ≥ 4 . Pain was assessed using a 0–10 VAS preoperatively and at 24 and 48 hours postoperatively [11]. Preoperative variables included age and BMI, which were collected as continuous variables and subsequently categorized into ordinal groups: age (≤ 63 years and >63 years) and BMI ($<25 \text{ kg}/\text{m}^2$ and $\geq 25 \text{ kg}/\text{m}^2$). Gender was recorded as a nominal variable. Intraoperative

variables, including operative time and intraoperative blood loss, were measured as continuous data and then dichotomized into ordinal categories (≤ 120 min vs. >120 min and ≤ 300 ml vs. >300 ml, respectively). Postoperative variables consisted of time to first analgesia and analgesia consumption, both treated as continuous variables. Pain VAS score was recorded as a discrete variable.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Normality was assessed via the Shapiro-Wilk test. Normally distributed data (age, BMI, and time to first analgesia) were expressed as mean $\pm$ SD; non-normally distributed data (operative time, blood loss, VAS scores, and analgesia consumption) were presented as median (IQR). Due to the non-normal distribution of pain scores, the non-parametric Friedman test was utilized for longitudinal hypothesis testing, followed by post-hoc pairwise comparisons with Bonferroni correction. The Wilcoxon Signed-Rank test was used to compare analgesia consumption between the two postoperative time blocks. Subgroup comparisons (stratification). The Mann-Whitney U test was used to test for VAS scores. A p-value ≤ 0.005 was considered statistically significant.

RESULTS

A total of 38 patients underwent TKA with a mean age of 63.7 ± 7.4 years (range: 50.0–76.0). The majority were female, 31 (81.6%). Median operative time was 120.0 (30.0%) minutes, while median blood loss was 300.0 (100.0%) ml. The mean time to first analgesia was 6.3 ± 3.2 hours (Table 1).

Table 1: Baseline and Intraoperative Characteristics of The Study Population

Parameters		n	Mean $\pm$ SD / (%)	Median, IQR
Gender	Male	7	18.4%	—
	Female	31	81.6%	—

blood loss >300 mL reported significantly higher pain at both 24 hours ($p=0.003$) and 48 hours ($p=0.009$). Similarly, operative times exceeding 120 minutes were associated with significantly higher VAS scores at the 24-hour ($p=0.003$) and 48-hour ($p=0.024$) intervals (Table 3).

Table 3: Post-Stratification Comparisons of Pain VAS Scores

Parameters	Category	n	At 0 Hours, n (%)	p-value	At 24 Hours, n (%)	p-value	At 48 Hours, n (%)	p-value
Age (Years)	≤ 63	21	8.0 (1.0%)	0.561	3.0 (1.5%)	0.399	1.0 (1.5%)	0.467
	>63	17	7.0 (1.0%)		4.0 (3.0%)		2.0 (2.0%)	
Gender	Female	31	8.0 (1.0%)	0.234	3.0 (2.0%)	0.506	1.0 (1.0%)	0.317
	Male	07	7.0 (2.0%)		4.0 (4.0%)		2.0 (3.0%)	
Body Mass Index (Kg/M ²)	<25.0	11	7.0 (1.0%)	0.899	4.0 (3.0%)	0.225	2.0 (2.0%)	0.045
	≥ 25.0	27	7.0 (1.0%)		3.0 (2.0%)		1.0 (1.0%)	
Operative Time (Min)	≤ 120	35	8.0 (1.0%)	0.168	3.0 (2.0%)	0.003	1.0 (1.0%)	0.024
	>120	03	7.0 (0.0%)		6.0 (0.0%)		3.0 (0.0%)	
Intraoperative Blood Loss (mL)	≤ 300	33	7.0 (1.0%)	0.009	3.0 (2.0%)	0.003	1.0 (1.0%)	0.009
	>300	05	8.0 (1.0%)		5.0 (3.0%)		3.0 (4.0%)	

* Comparisons between strata for pain VAS score via the Mann-Whitney U Test

Age (years)	38	63.7 ± 7.4	—
Body Mass Index (kg/m ²)	38	26.2 ± 2.7	—
Operative Time (min)	38	—	120.0 (30%)
Intraoperative Blood Loss (mL)	38	—	300.0 (100%)
Time to First Analgesia (hours)	9	6.3 ± 3.2	—

Following the surgeon-placed ACB, a highly significant reduction in pain was observed over the 48-hour study period. The median VAS score decreased from a baseline of 7.0 (1.0%) to 4.0 (2.0%) at 24 hours, and further declined to 1.0 (2.0%) at 48 hours. The reduction in pain at each specific time interval was confirmed by post-hoc analysis ($p<0.001$). Regarding analgesia consumption, 29 (76.3%) patients required no rescue medication in the first 24 hours, which increased to 32 (84.2%) during the 24–48-hour interval. Correspondingly, analgesia consumption dropped significantly from a median of 0.0 (25.0) mg in the first 24 hours to 0.0 (0.0) mg in the second 24-hour period ($p=0.007$) (Table 2).

Table 2: Longitudinal Pain Scores and Analgesia Requirements

Parameters	Baseline, n (%)	At 24 Hours, n (%)	At 48 Hours, n (%)	p-value
Pain VAS Score	7.0 (1.0%)	4.0 (2.0%)	1.0 (2.0%)	$<0.001^a$
Liometacin Dose (Mg)	—	0.0 (25.0%)	0.0 (0.0%)	0.007 ^b

^aDue to non-normal distribution, overall significance across time points was determined by the Friedman Test. Post-hoc pairwise comparisons with Bonferroni correction confirmed significant differences for all pairs (pre-op vs. 24h, 24h vs. 48h, Pre-op vs. 48h).

^bComparison between 24 h and 48 h analgesia consumption via the Wilcoxon Signed-Rank Test

Stratification analysis revealed that patients' age and gender did not significantly influence postoperative pain scores ($p>0.05$). However, a BMI ≥ 25.0 was associated with significantly lower pain scores at 48 hours compared to the lower BMI group ($p=0.045$). Patients with intraoperative

DISCUSSION

Postoperative pain management following TKA remains a critical determinant of early mobilization, functional recovery, and overall patient satisfaction. In the present study, the use of ACB showed a statistically and clinically significant association with low VAS pain score, along with a distinct reduction in analgesic requirements. The median preoperative VAS score of 7.0 (1.0%) decreased significantly to 4.0 (2.0%) on postoperative day 1 and further to 1.0 (2.0%) on postoperative day 2. This progressive decline in pain scores was found to be statistically significant ($p < 0.001$), suggesting the effectiveness of ACB in providing sustained postoperative analgesia. These findings are consistent with previous studies that have demonstrated significant reductions in postoperative pain with ACB in TKA patients [12]. The median time to first analgesia (6.3 ± 3.2 hours) observed in this study indicates a prolonged duration of analgesic action. As all cases were under spinal anesthesia, this interval includes both the spinal block and ACB effect. Since spinal anesthesia usually lasts 2 to 3 hours, this extended duration shows that ACB effectively increased the initial period of analgesia. This delay is both statistically and clinically meaningful, particularly in the immediate postoperative period when pain intensity is highest. Similar findings have been reported in contemporary literature, where ACB significantly prolonged analgesia compared to conventional systemic approaches [13]. The prolonged analgesia and low rescue drug needs in this study are likely due to using Tramadol as a perineural adjuvant, which is known to enhance block duration via local anaesthetic-like effects [14]. Furthermore, analgesia consumption in this study was minimal, with a median requirement of zero on postoperative days 1 and 2 ($p=0.007$), reflecting a significant opioid-sparing effect. This finding is particularly important as part of improved postoperative recovery pathways (ERAS) protocols, which focus on minimising opioid use to decrease adverse effects, including nausea, vomiting, sedation, and respiratory depression. [15, 16]. The demographic characteristics of the population studied, which had an average age of 63.7 ± 7.4 years and a mean BMI of 26.2 ± 2.7 Kg/m², are consistent with the typical population undergoing TKA. This similarity enhances the external validity and generalizability of the study findings [17]. Although a direct comparison group was not included, the analgesic outcomes observed in this study are comparable to those reported for femoral nerve block (FNB). ACB has been shown to provide equivalent analgesia while preserving quadriceps muscle strength, thereby facilitating early ambulation and reducing the risk of postoperative falls [18, 19]. The continued reduction in VAS scores from postoperative day 1 to 2 further supports

the sustained analgesic efficacy of ACB, as reported in randomized controlled trials [20, 21].

Despite these encouraging results, it is important to recognise that there are several limitations. Its observational longitudinal design and the absence of a control group restrict the ability to establish definitive causality. Because of the limited sample size and non-inclusion of pediatric population in this study and the single-center design, the conclusions may not apply to other populations. Furthermore, the stratification of the sample into subgroups, for instance ($n=3$ for operative time >120 and $n=5$ for blood loss >300), resulted in even smaller cohorts, potentially reducing the statistical power of those specific comparisons. Finally, functional outcomes such as quadriceps strength, time to resume walking, and duration of hospitalization were not assessed, which prevents a more comprehensive evaluation of the overall postoperative recovery. Additionally, using tramadol as an ACB adjuvant is an off-label technique. While a lack of formal electrophysiological assessments leaves the precise neurotoxicity risk profile undetermined, routine clinical monitoring revealed no neurological deficits, prolonged motor blocks, or nerve injuries during the hospital stay. Larger-scale, randomized controlled studies comparing the efficacy of the ACB with other regional anaesthesia methods should be done in the future. These investigations should incorporate a broader range of metrics, evaluating both analgesic effectiveness and long-term functional outcomes.

CONCLUSIONS

The surgeon-placed ACB was linked with low postoperative pain scores and minimal rescue analgesia requirements among patients undergoing TKA in this setting. The low frequency of the need for rescue analgesia suggests the potential effectiveness of this technique in the acute recovery phase.

Authors' Contribution

Conceptualization: AM, JAS

Methodology: HUR

Formal analysis: AK, ABS

Writing and Drafting: UAB

Review and Editing: AM, HUR, AK, JAS, UAB, ABS

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

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Case Series

Pulley-Augmented EIP to EPL Transfer: A Novel Solution to Prevent Ulnar Subluxation at MCPJ

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ABSTRACT

In zone 3 injuries, the Extensor indicis Pollicis to Extensor Pollicis Longus tendon transfer comes with the problem of ulnar subluxation at the metacarpophalangeal joint (MCPJ), which results in ineffective extension of the thumb, which, in the long term, results in boutonniere deformity. **Objectives:** To observe the effects of stabilizing this transferred tendon at the MCPJ by adding a tendinous pulley and achieving significant improvement in extension of the thumb. **Methods:** This descriptive case series study was approved by the Institutional Review Board of Postgraduate Medical Institute, Ameer-ud-Din Medical College, Lahore General Hospital, Lahore (Approval No: 114; dated 3rd January 2022). A Total of 12 patients were in this study with delayed presentation (i.e., 6 to 12 weeks after trauma) of zone 3 EPL injuries, over a period of 2 years. Among these patients, 8 were males, and 4 were females. Surgery was performed under local anesthesia in 10 patients and general anesthesia in 2 patients. The EIP tendon was transferred to the transected EPL with a tendinous pulley reconstructed at the MCPJ. Postoperatively, a splint was applied for 4 weeks. Physiotherapy started on the first post-op day. Mean follow-up time was 5 months. **Results:** As per the Geldmacher score, an excellent score was achieved in 7(58.3%) patients, a good score in 3(25%), and a satisfactory score in 1(8.3%) patient, a poor score in 1(8.3%) patient. No extension lag was observed in the index finger in any case. **Conclusions:** This traditional transfer done in zone 3 gives excellent results when done with the addition of a pulley at MCPJ, improving the vector of excursion of the transferred tendon by stabilization at MCPJ and inhibiting its ulnar subluxation.

INTRODUCTION

Extensor tendon injuries of the thumb are frequent, and most of the most debilitating injury is the extensor pollicis longus tendon. The extensor pollicis longus(EPL)muscle is the major extensor of the Indicis Pollicis (IP) and the MCP joints of the thumb. Its origin is on the posterior side of the end of the third of the ulna and the interosseous membrane. The tendon traverses the 3rd compartment of the extensor retinaculum, bends radially at the lister tubercle, and eventually inserts on the back of the distal phalanx base. This tendon lies centrally at the metacarpophalangeal joint (MCPJ) through the extensor

expansion with ulnar and radial attachments. It is the muscle that enables a retropulsion hyperextension of the thumb [1]. Injury leads to loss of MCPJ and IPJ extension, which is not compensable by other muscles [2]. Trauma zone 3, i.e., in MCPJ, can lead to injury of EPL, EPL extensor expansion with its ulnar or radial attachments, and EPB. The sharp trauma is the most frequent cause of EPL tendon transaction or rupture in zone 3. It may also be caused by tenosynovitis with subcutaneous rupture, ischemia caused by impaired blood supply, and/or repetitive mechanical friction/stress. It is mostly a clinical diagnosis



or, at times, diagnosed on surgical exploration [3, 4]. The response varies according to the cause of injury and the time of presentation or the period of proper diagnosis following rupture. Sharp injuries can be presented immediately, and primary tendon repair is made possible [5]. In cases of delayed presentation/diagnosis, the tendon stumps are not suitable for primary repair due to a significant defect usually present because of tendon retraction [6]. In these delayed cases, secondary reconstructive procedures are the options, such as tendon graft or tendon transfer. In comparison to tendon graft, tendon transfer comes with the advantages of minimal donor site morbidity, shorter operating time with single-pulverized weave, relatively easier technique, early healing, easy cortical reeducation as EIP is synergistic to EPL, and fewer chances of complications such as avascular necrosis and tendon adhesions [7]. The most commonly described tendon transfer is of the extensor indicis proprius (EIP) tendon to the extensor pollicis longus EPL. A lot of research work has been done on this transfer for proximal EPL injuries at the wrist, but there is less literature available on this transfer in distal injuries in Zones 3 and 2. But the donor tendon (EIP) is of adequate length and is a good transfer for these distal injuries as well [8]. In our clinical experience, this study has observed that this transfer done for zone 3 injuries come with the problem of ulnar subluxation, which results in ineffective extension of the thumb, which in the long-term results in boutonniere deformity [9] (Figure 1).

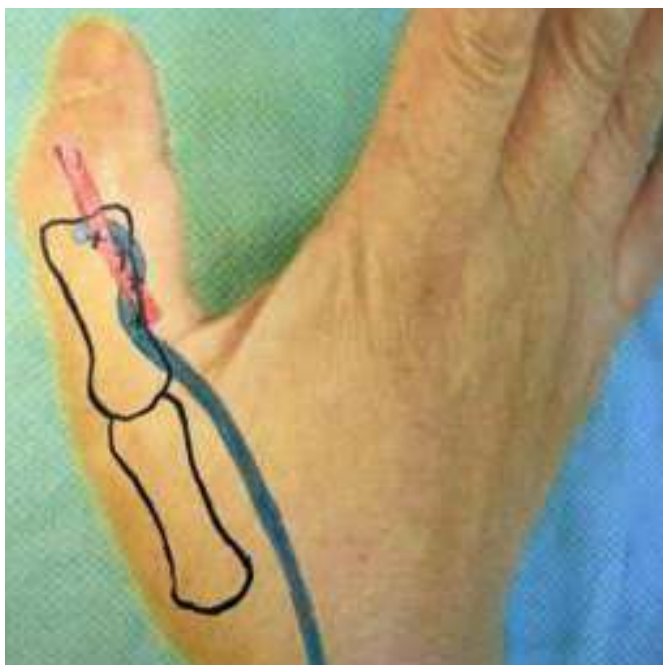


Figure 1: Ulnar Subluxation of the Transferred EIP to the EPL Tendon at the MCPJ

As Zone 3 injuries of the thumb may cause direct injury to the EPL extensor expansion or the EPL extensor expansion

may need to be sacrificed surgically to achieve sufficient length of the distal stump of the tendon for pulverate weave, which results in instability of the EPL tendon at the metacarpophalangeal joint and causes ulnar subluxation, which in turn causes extension lag.

There is a dearth of literature on EIP-to-EPL tendon transfer in zone 3 extensor injuries; most studies have been done on proximal injuries at the wrist. The issue of ulnar subluxation at MCPJ after this transfer in distal injuries has not been previously studied or measured. The small size (n=12) restricts the statistical power and generalizability, but it is explained by the infrequency of delayed zone 3 EPL injuries. Lahore General Hospital is limited to a single-center design, which limits its applicability to other populations and surgical environments. This study aims to overcome this instability of EPL at the metacarpophalangeal joint or ulnar subluxation and resultant extension lag by adding a pulley at the metacarpophalangeal joint, which stabilizes the EPL tendon and improves its vector of excursion, which in turn corrects extension lag at the MCPJ and IPJ of the thumb (Figure 2).

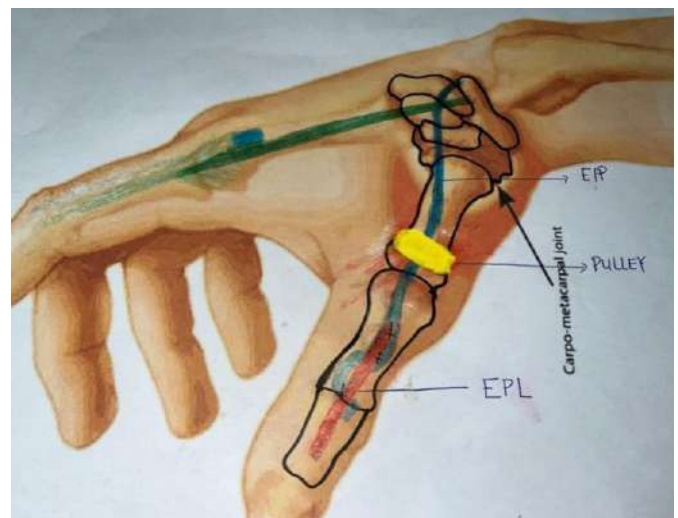


Figure 2: Stabilization of Transferred EIP to EPL Tendon at MCPJ by Reconstruction of the Pulley at the Head of the Metacarpal

METHODS

This descriptive case series study was approved by the Institutional Review Board of Postgraduate Medical Institute, Ameer-ud-Din Medical College, Lahore General Hospital, Lahore (Approval No: 114; dated 3rd January 2022). Written informed consent was obtained from all participants before enrollment. Data were obtained from 12 patients who underwent tendon transfers for EPL tendon rupture from January 2022 to December 2023. The patients in this study had delayed rupture presentation or transaction of the EPL tendon 6 to 12 weeks after trauma. Twelve patients (8 males and 4 females), with 32 years

mean age of (20 to 45 years), presented with loss of extension of the thumb after trauma (Table 2). These patients presented with missed diagnosis, inadequate repair, loss of tendon tissue, or unnoticed injury of the EPL tendon. Among these, mostly were sharp cuts and a few blunt traumata, due to RTA or domestic accidents. One patient had infective arthritis of the metacarpophalangeal joint, which resulted in EPL rupture. The average time interval between the transaction and the procedure was 8.4 weeks, with a range of 6 to 12 weeks. Diagnoses of all patients were made clinically. The presence of EIP and its function were evaluated before surgery. These patients underwent tendon transfer under local anesthesia, except for a few cases, which were done under general anesthesia due to accompanying other injuries. Five months was the average follow-up duration. Postoperative assessments were conducted at 3 to 5 months postoperatively by more than one observer using a standardized protocol. However, a formal inter-observer reliability analysis was not performed. The functional outcome of the thumb was assessed using the Geldmacher evaluation scheme, which evaluates four key components of thumb function. Each parameter is graded on a point-based scale, with higher scores indicating better function (Table 1).

Table 1: Geldmacher Evaluation Scheme

Function		Score (Points)
Radial abduction angle (angle between thumb and index finger)(°)	>70	6
	51-70	4
	31-50	2
	9-30	0
Elevation deficit (cm)	1.0-1.0	6
	1.1-2.0	4
	2.1-3.0	2
	>3	0
Opposition distance (distance of thumb tip to MP of the little finger)(cm)	1.0-2.5	6
	2.5-4.0	4
	4.1-6.0	2
	>6	0
Flexion extension deficit (difference from non-operated hand)(°)	0-5	6
	6-30	4
	31-60	2
	>60	0

Radial abduction was measured as the angle between the thumb and index finger. Angles >70° scored 6 points, 51-70° scored 4, 31-50° scored 2, and 9-30° scored 0. Elevation deficit was assessed as the loss of thumb elevation from the plane of the palm and measured in centimeters. Deficits of 0-1.0 cm scored 6 points, 1.1-2.0 cm scored 4, 2.1-3.0 cm scored 2, and >3 cm scored 0. Opposition was measured as the distance between the thumb tip and the metacarpophalangeal joint of the little finger. Distances of 0-2.5 cm scored 6 points, 2.5-4.0 cm scored 4, 4.1-6.0 cm

scored 2, and >6 cm scored 0. Flexion-extension deficit was calculated as the difference in total range of motion between the operated and contralateral thumb. Differences of 0-5° scored 6 points, 6-30° scored 4, 31-60° scored 2, and >60° scored 0. Based on the cumulative Geldmacher score (maximum 24 points), functional outcomes were categorized as follows: excellent (19-24 points), good (13-18 points), satisfactory (7-12 points), and poor (≤6 points). EIP function was assessed and marked preoperatively by asking the patient to extend the index finger while the other 3 fingers were held in a flexed position (Figure 3).



Figure 3: Incision Marked for EIP to EPL Transfer

Most of the patients were operated on with wide awake local anesthesia, except for a few who had other injuries as well, along with EPL tendon injury. Local anesthetics with adrenaline were given, and 3 incisions were marked. Through a first small transverse incision given at the metacarpophalangeal joint, EIP is identified ulnar to EDC. The anatomical variation of the EIP tendon should be kept in mind. A tiny transverse incision was made on the wrist's radial side, and EIP was identified as it glides when pulled distally through the first incision. EIP is cut at the metacarpophalangeal joint and retrieved through the second incision. The third incision was given at the base of the thumb or previous scar and extended accordingly to get enough length of the distal stump of EPL (in doing so, ulnar and radial attachments of EPL at the metacarpophalangeal joint may be sacrificed). The EIP tendon is then retrieved through the third incision by the subcutaneous route. A pulley is reconstructed and sutured with 5/0 Prolene to the periosteum just proximal to the MCPJ (the tendon graft pulley was reconstructed with a redundant portion of the EIP tendon, the EPL tendon, or with the transacted EPB tendon). The EIP tendon was passed through the pulley and sutured to the EPL by using the Pulvertaft weaving technique with 4/0 Prolene. Tension of repair is adjusted

such that "the thumb is in full flexion when the wrist is in full extension, and the thumb is in full extension when the wrist is in full flexion". Skin closed and dressing applied. Splint given in a position of thumb in full extension, wrist in 30-degree extension, MCPJ of other fingers in 60-degree flexion, and IPs straight (Figure 4).



Figure 4: Final Position of the Thumb in the Splint

Splint was continued for 4 weeks. Within the splint, passive extension of the thumb started from the first post op day. Active motion started after 1 week, with an increase in the flexion angle of the splint at the MCPJ every week. Splint discontinued after 4 weeks. The results were scored using the Geldmacher scheme.

RESULTS

The study included 12 patients with a male predominance (8 males, 4 females). The age range was 20–45 years, with most patients in their third decade of life, indicating that young, working-age individuals were primarily affected. The most common etiologies were road traffic accidents (RTA) and blunt trauma, followed by sharp injuries such as knife and glass cuts. One case was secondary to infective osteoarthritis. The time lag before presentation ranged from 6 to 12 weeks, with the majority presenting between 6 and 8 weeks, suggesting delayed referral or late reconstruction in most cases (Table 2).

Table 2: Patient Characteristics

Sr. No.	Gender	Age (Years)	Etiology	Time Lag
1	Female	38	Knife Cut	8 Weeks
2	Male	27	Rta	6 Weeks
3	Male	25	Glass Cut	7 Weeks
4	Male	20	Rta	8 Weeks
5	Female	45	Knife Cut	6 Weeks
6	Male	30	Blunt Trauma	12 Weeks
7	Female	30	Grinder Injury	8 Weeks
8	Male	40	Blunt Trauma	10 Weeks

9	Male	24	Blunt Trauma	11 Weeks
10	Female	40	Infective Osteoarthritis	12 Weeks
11	Male	26	Rta	7 Weeks
12	Male	21	Glass Injury	6 Weeks

The functional outcome was measured by the Geldmacher scheme. Individual scoring of each patient for each variable. The functional outcomes demonstrated overall favorable recovery. The mean total score was 20.0 ± 5.26 , with an interquartile range (IQR) of 6, indicating clustering toward higher functional performance. Mean scores for radial abduction and elevation deficit were 5.17 ± 1.34 each (IQR = 2), reflecting near-normal thumb positioning in most patients. Flexion-extension deficit and opposition distance showed mean scores of 4.83 ± 1.59 (IQR = 2), indicating mild residual limitations (Table 3).

Table 3: Functional Outcome Results

Patients	Radial Abduction in Angle	Elevation Deficit	Flexion Deficit	Opposition Distance	Total Score	Outcomes
1	6	6	4	4	20	Good
2	6	6	6	6	24	Excellent
3	6	4	6	6	22	Excellent
4	4	6	4	4	18	Good
5	6	6	6	6	24	Excellent
6	4	4	2	2	12	Satisfactory
7	4	6	6	6	22	Excellent
8	2	2	2	2	8	Poor
9	6	6	6	6	24	Excellent
10	6	6	6	6	24	Excellent
11	6	4	4	4	18	Good
12	6	6	6	6	24	Excellent
Mean $\pm$ SD	5.17 ± 1.34	5.17 ± 1.34	4.83 ± 1.59	4.83 ± 1.59	20 ± 5.26	—
IQR	2.00	2.00	2.00	2.00	6.00	—
Min	2.00	2.00	2.00	2.00	8.00	—
Max	6.00	6.00	6.00	6.00	24.00	—

Results of this study based on the Geldmacher score were excellent in 7 (58.3%) patients, good in 3 (25%), satisfactory in 1 (8.3%), and poor in 1 (8.3%) patient (Figure 5).

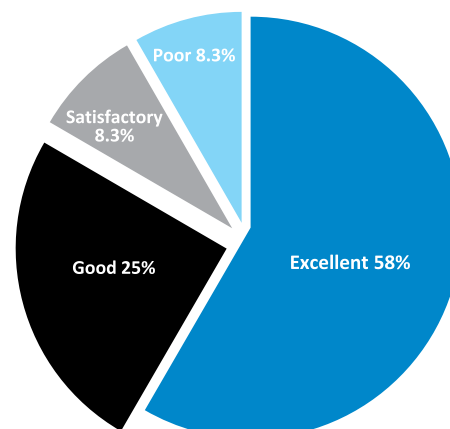


Figure 5: Results of This Study Based on the Geldmacher Score

DISCUSSION

EPL is the prime extensor of the MCPJ and IP of the thumb. The injury results in dropped thumb deformity with loss of elevation of the thumb to the plane of the palm. Injuries in the extensor Zone 3 of the thumb may involve the EPL tendon, the extensor expansion (extensor hood), or the Extensor pollicis brevis [10]. In zone 3, due to the broad width of the extensor apparatus at the metacarpophalangeal joint, incomplete lacerations are common [11]. On the other hand, partial lacerations can be easily missed because the remaining tendon may be able to extend the thumb. Still, with continuous use (repetitive trauma), the tendon may rupture completely [12]. Also, injury to the extensor expansion itself results in instability of the EPL tendon over the MCPJ. Infective osteoarthritis may also result in tendon rupture. Delayed presentation of transacted EPL results in significant retraction of the proximal stump of the transacted tendon [13]. So, tendon ruptures and delayed presentations result in a significant gap between the two cut ends of the tendon, making primary repair difficult. For chronic or longstanding EPL rupture, the only available treatments are tendon graft and tendon transfer [14]. Both treatment options come with their own advantages and disadvantages. EIP is generally not offered to high-demanding patients, e.g., musicians, and these patients usually are offered an intercalated palmaris tendon graft. According to Atilgan et al. the comparison showed no significant difference in the outcome of thumb function between the Extensor indicis proprius transfer and the Palmaris longus tendon graft [15]. But in most of the undemanding cases, EIP is the first choice, as it comes with the advantages of a simple and easy procedure, a single suture site, quick healing, easy cortical reeducation, and a lower chance of avascular necrosis [16, 17]. Trauma in the extensor Zone 3 of the thumb may cause direct injury to the extensor expansion (extensor hood) or during operative procedure EPL attachments at MCPJ may also be sacrificed to achieve adequate length of distal tendon stump for pulvertaft weave, which results in initialization of repaired tendon at MCPJ during active extension and causes ulnar subluxation because it comes to lie palmar to the center of rotation of the metacarpophalangeal joint to act as a flexor instead of an extensor [18]. To stabilize the tendon at MCPJ, a tendon graft pulley is reconstructed at the head of the metacarpal, which gives effective extension of the thumb by improving the vector of excursion. As in Extensor zone 5 injuries of other fingers, chronic degenerative sagittal band rupture may require a tendon graft pulley for stabilization of the extensor tendon at the MCPJ [19, 20]. The functional outcome of the thumb was used in this study; it was measured using the Geldmacher scheme. Four functions

are to be scored under this scheme, which include: radial abduction angle, deficit of elevation, distance of opposition, flexion, and deficit of extension of the MP and IP joints. Postoperative thumb extension was achieved in all patients, with functional scores detailed. The 12 patients showed no extension lag in the index finger (i.e., no donor site morbidity in any case). The thumbs of both hands were comparable in terms of function and full range of motion (except in one patient with a poor outcome). There were no notable complications after surgery. Results of this study based on the Geldmacher score were excellent in 7 (58.3%) patients, good in 3 (25%), satisfactory in 1 (8.3%), and poor in 1 (8.3%) patient.

This study has several limitations. The small sample size, inherent to the rarity of delayed zone 3 EPL injuries, may limit the generalizability of the results. Its single-center design and lack of a control group prevent direct comparison with standard EIP-to-EPL transfer or tendon graft techniques. Functional assessment using the Geldmacher score, although validated, includes subjective elements and may be prone to observer bias. In addition, the relatively short follow-up may not fully reflect long-term outcomes or late complications. Larger, prospective, comparative studies are needed to further establish the role of MCPJ pulley reconstruction in chronic zone 3 EPL injuries. A novel technical report presenting promising preliminary results by presenting evidence for its effectiveness in enhancing functional results for patients with delayed presentation of zone 3 EPL injuries, this study provides a useful clinical perspective into tendon transfers. The addition of a tendinous pulley at MCPJ has produced encouraging results, with 83.3% patients having excellent or good results using the Geldmacher score. Also, there was no lag in extension in the index finger in all the patients, indicating the success of this method.

CONCLUSIONS

This procedure of EIP to EPL transfer is an excellent, simple, and easy technique for delayed presentation of distal EPL tendon ruptures. This technique is a very good option when used particularly for zone 3 EPL injury, as the donor tendon is of adequate length for these distal injuries, but it comes with a problem of extension lag at MCPJ and IP due to instability and ulnar subluxation of the transferred EIP to EPL tendon at MCPJ. But just adding a simple pulley at MCPJ improves the vector, allowing linear excursion of the EPL tendon in the right direction, which helps to achieve full extension at MCPJ and IPJ of the thumb.

Authors' Contribution

Conceptualization: SI

Methodology: SF, HRA, AL

Formal analysis: RA, MN, MAA

Writing and Drafting: SI

Review and Editing: SI, RA, MM, MAA, SF, HRA, AL

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


Biochemical Markers and Physiological Dysregulation Associated with Sleep Deprivation: A Systematic Review

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ABSTRACT

Sleep deprivation has become increasingly common in modern society and is associated with various adverse health outcomes. Evidence suggests that inadequate sleep may disrupt biochemical regulation and contribute to systemic physiological disturbances. **Objectives:** To synthesize current evidence on biochemical markers and physiological dysregulation associated with sleep deprivation in adult populations. **Methods:** This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A literature search was conducted in PubMed, Scopus, and the Cochrane Library for studies published between January 2017 and March 2024. Original human studies reporting biochemical or physiological outcomes related to sleep deprivation or sleep restriction were included. Titles and abstracts were screened, followed by full-text evaluation. Data on study characteristics, sleep assessment methods, and outcomes were extracted. Study quality was assessed using the National Institutes of Health Quality Assessment Tool. Due to heterogeneity across studies, findings were synthesized narratively. **Results:** Fourteen studies met the inclusion criteria. The evidence consistently showed that sleep deprivation is associated with neuroendocrine stress activation, metabolic disturbances, inflammatory responses, and oxidative stress. Increased cortisol levels, impaired glucose metabolism, elevated inflammatory markers such as C-reactive protein and interleukin-6, and increased oxidative stress markers were commonly reported. Physiological consequences included cardiovascular strain, autonomic imbalance, cognitive impairment, mood disturbances, and reduced immune function. **Conclusions:** Sleep deprivation is associated with significant biochemical alterations and multi-system physiological dysregulation. Adequate sleep duration and quality appear to be important modifiable determinants of cardiometabolic and neuroimmune health.

INTRODUCTION

Sleep is an essential biological process that plays a critical role in neuroendocrine regulation, immune function, metabolic stability, and cardiovascular health [1]. Modern lifestyles, including demanding work schedules, academic pressures, shift work, and excessive screen exposure, have contributed to reduced sleep duration and disrupted sleep patterns among adults [2]. Although temporary sleep deprivation may appear tolerable, growing evidence

suggests that recurrent or chronic sleep deprivation can lead to measurable biochemical alterations that reflect systemic physiological stress [3, 4]. Mechanistically, sleep deprivation is closely associated with dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and disruption of circadian rhythms, resulting in altered cortisol secretion and impaired nocturnal hormonal signaling [5]. These endocrine disturbances may interact with appetite

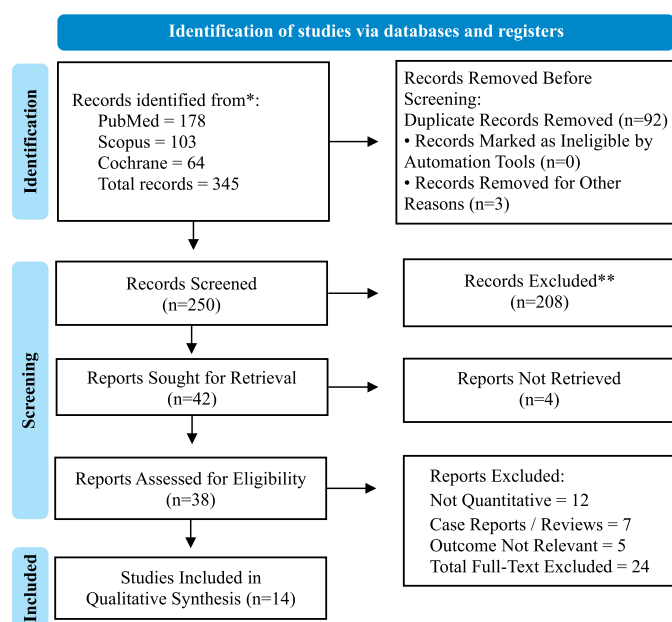
regulation and glucose metabolism, potentially leading to insulin resistance and adverse lipid profiles [6]. In addition, sleep deprivation has been linked to increased inflammatory activity and oxidative stress, which together contribute to endothelial dysfunction and impaired physiological adaptation [7, 8]. These biochemical disturbances may translate into broader physiological consequences, including autonomic imbalance, elevated blood pressure, reduced heart rate variability, impaired cognitive performance, mood disturbances, and weakened immune function [9-11]. However, existing human studies [12] differ substantially in terms of exposure definitions (acute total deprivation versus partial sleep restriction), measurement methods (subjective questionnaires versus objective monitoring), and reported outcome variables, making it difficult to draw consistent conclusions [13].

This systematic review establishes a number of critical gaps in the literature of sleep deprivation that are critical. Sleep deprivation (acute total vs partial vs chronic) does not have a universally accepted definition and standardized classification, which results in heterogeneity between studies. The major issue is that there is a significant methodological heterogeneity among the studies, with the most common sleep deprivation techniques (24-72 hours total deprivation vs 4-6 hours partial restriction over varying periods), different methods of measurement (polysomnography vs actigraphy vs PSQI), and biomarker measurement timing and method, which undermined the possibility of meta-analysis. Therefore, this systematic review aimed to synthesize and critically evaluate human evidence on biochemical markers and physiological dysregulation associated with sleep deprivation, providing an integrated framework for understanding its mechanistic pathways and potential clinical implications.

METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to synthesize evidence on biochemical markers and physiological dysregulation associated with sleep deprivation in adult populations. A comprehensive literature search was performed using electronic databases, including PubMed, Scopus, and the Cochrane Library, to identify relevant studies published between January 2017 and March 2024. The search strategy was developed using a combination of controlled vocabulary (Medical Subject Headings) and free-text keywords related to sleep deprivation and biochemical outcomes. Boolean operators (AND, OR) were used to combine search terms appropriately. For PubMed, the following search strategy was used: ("Sleep Deprivation" (MeSH Terms) OR "sleep deprivation" OR "sleep restriction" OR "short sleep duration") AND ("Hormones" (MeSH Terms)

OR "cortisol" OR "growth hormone" OR "melatonin") AND ("Metabolism" [MeSH Terms] OR "glucose" OR "insulin" OR "lipid profile") AND ("Inflammation" (MeSH Terms) OR "CRP" OR "interleukin-6") AND ("Oxidative Stress" (MeSH Terms) OR "MDA" OR "SOD"). Filters were applied to include human studies published in English within the specified time frame. For Scopus, the search was conducted using the following syntax: TITLE-ABS-KEY ("sleep deprivation" OR "sleep restriction" OR "short sleep") AND TITLE-ABS-KEY ("cortisol" OR "growth hormone" OR "melatonin") AND TITLE-ABS-KEY ("glucose" OR "insulin" OR "lipid profile") AND TITLE-ABS-KEY ("CRP" OR "interleukin-6" OR "inflammation") AND TITLE-ABS-KEY ("oxidative stress" OR "MDA" OR "SOD") AND PUBYEAR > 2016 AND PUBYEAR < 2025 AND (LIMIT-TO (LANGUAGE, "English")). For the Cochrane Library, the following search strategy was applied: ("sleep deprivation" OR "sleep restriction" OR "short sleep") AND ("cortisol" OR "growth hormone" OR "melatonin") AND ("glucose" OR "insulin" OR "lipid profile") AND ("CRP" OR "interleukin-6" OR "inflammation") AND ("oxidative stress" OR "MDA" OR "SOD"). The search strategy was adapted for each database to ensure optimal retrieval of relevant studies. All identified records were exported into reference management software, and duplicate records were removed prior to screening. Studies were included if they were original human research articles involving adult participants and reported biochemical or physiological outcomes associated with sleep deprivation or restriction. Both experimental and observational study designs were eligible. Studies involving animals, pediatric populations, reviews, meta-analyses, case reports, pilot studies, or non-English publications were excluded. The screening process was conducted in two stages. In the first stage, titles and abstracts were independently screened by two reviewers based on predefined inclusion and exclusion criteria. In the second stage, full-text articles of potentially relevant studies were independently assessed by the same reviewers for final inclusion. Any disagreements were resolved through discussion, and a third reviewer was consulted if consensus could not be reached. The diagram illustrates the process of study identification, screening, eligibility assessment, and inclusion following PRISMA 2020 guidelines (Page et al. 2021). A total of 345 records were identified through database searches. After removing duplicates and screening titles and abstracts, 38 full-text articles were assessed for eligibility, and 14 studies were included in the qualitative synthesis. The study selection process followed PRISMA 2020 guidelines, and a flow diagram is presented (Figure 1).

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

Data were extracted using a standardized form that included study characteristics, participant demographics, sleep measurement methods, and reported biochemical and physiological outcomes. Only studies using validated sleep assessment tools such as polysomnography, actigraphy, or the Pittsburgh Sleep Quality Index (PSQI)

were included. The methodological quality of the included studies was evaluated using the National Institutes of Health (NIH) Quality Assessment Tool for Observational and Interventional Studies. This assessment considered factors such as clarity of research objectives, population definition, exposure and outcome measurement, and control of confounding variables. Due to methodological heterogeneity across studies, a quantitative meta-analysis was not performed. Instead, findings were summarized using qualitative narrative synthesis, and biochemical and physiological outcomes were grouped into thematic categories for interpretation.

RESULTS

A total of 14 studies met the eligibility criteria and were included in the qualitative synthesis. The studies were conducted across multiple geographic regions and included both experimental crossover trials and observational cross-sectional designs. Sample sizes ranged from 9 to 486 participants, and most studies were conducted among healthy adult populations. Sleep deprivation protocols mainly involved acute total sleep deprivation or partial sleep restriction, with sleep exposure commonly assessed using polysomnography, actigraphy, or validated questionnaires such as the Pittsburgh Sleep Quality Index (Table 1).

Table 1: Summary of Included Studies and Key Characteristics

References	Country	Study Design	Sample Size	Population	Sleep Deprivation Type	Sleep Measurement
[15]	Taiwan	Cross-sectional	281	Menopausal women	Chronic short sleep	PSQI
[16]	Japan	Randomized crossover	9	Healthy adults	Partial restriction	Laboratory protocol
[17]	Japan	Randomized crossover	16	Young adults	Partial restriction	Actigraphy
[18]	Sweden	Experimental	218	Healthy adults	Acute total deprivation	Laboratory protocol
[19]	Netherlands	Experimental	101	Healthy adults	Acute total deprivation	Laboratory protocol
[20]	Japan	Randomized crossover	24	Healthy adults	Partial restriction	Sleep protocol
[21]	Sweden	Crossover	44	Adults (healthy/obese)	Acute deprivation	Laboratory protocol
[22]	USA	Randomized crossover	14	Postmenopausal women	Partial restriction	Laboratory protocol
[23]	Poland	Observational	77	Adults	Acute deprivation	PSG + actigraphy
[24]	USA	Randomized crossover	15	Healthy adults	Partial restriction	PSG
[25]	UK	Cross-sectional	312	Community adults	Chronic short sleep	PSQI
[26]	USA	Randomized trial	17	Healthy adults	Partial restriction	PSG
[27]	Netherlands	Crossover	16	Healthy adults	Partial restriction	Actigraphy
[28]	China	Cross-sectional	486	Community adults	Chronic short sleep	PSQI

Results demonstrate that sleep deprivation is associated with significant hormonal and metabolic disturbances. Cortisol levels were consistently elevated (15–30%), indicating activation of the hypothalamic pituitary adrenal axis, while growth hormone and melatonin levels were reduced, reflecting impaired tissue repair and circadian disruption. Metabolic alterations included increased fasting glucose (5–15 mg/dL) and insulin levels, suggesting insulin resistance. Additionally, appetite-regulating hormones were affected, with decreased leptin (15–20%) and increased ghrelin (10–25%), promoting increased appetite and potential weight gain. Sleep deprivation also resulted in adverse changes in lipid profile, inflammatory markers, and oxidative stress. Total cholesterol and LDL levels increased, while HDL levels decreased, indicating a shift toward an atherogenic profile. Inflammatory markers such as CRP and IL-6 were elevated, reflecting low-grade systemic inflammation. Furthermore, increased malondialdehyde and reduced superoxide dismutase activity indicated enhanced oxidative stress and compromised antioxidant defense. Overall, these findings highlight the widespread

physiological impact of inadequate sleep, contributing to increased risk of metabolic and cardiovascular disorders (Table 2).

Table 2: Biochemical Markers Associated with Sleep Deprivation with Effect Estimates

Variables	Marker Category	Direction of Change	Effect Size / Estimate	Physiological Interpretation
Stress Hormones	Cortisol	↑ Increased	Increase of approximately 15–30% across experimental studies	Activation of the HPA axis
	Growth Hormone	↓ Decreased	Reduction of approximately 20–40% during sleep restriction	Reduced tissue repair and recovery
	Melatonin	↓ Decreased	Significant suppression of nocturnal peak levels (up to 50%)	Circadian rhythm disruption
Metabolic Markers	Fasting Glucose	↑ Increased	Mean increase of 5–15 mg/dL reported in sleep-deprived individuals	Insulin resistance
	Insulin	↑ Increased	Elevated levels indicate compensatory hyperinsulinemia	Impaired glucose metabolism
	Leptin	↓ Decreased	Reduction of approximately 15–20%	Reduced satiety signaling
	Ghrelin	↑ Increased	Increase of approximately 10–25%	Increased appetite and caloric intake
Lipid Profile	Total Cholesterol	↑ Increased	Mild elevation (~5–10%) observed in short sleep duration	Increased cardiovascular risk
	LDL	↑ Increased	Increase of approximately 10–20%	Atherogenic lipid profile
	HDL	↓ Decreased	Reduction of approximately 5–10%	Reduced cardioprotective effect
Inflammatory Markers	C-reactive Protein (CRP)	↑ Increased	Elevated levels up to 20–50% in several studies	Low-grade systemic inflammation
	Interleukin-6 (IL-6)	↑ Increased	Significant increase in circulating levels reported	Immune system activation
Oxidative Stress Markers	Malondialdehyde (MDA)	↑ Increased	Increased lipid peroxidation levels observed	Oxidative cellular damage
	Superoxide Dismutase (SOD)	↓ Decreased	Reduction in antioxidant enzyme activity	Impaired antioxidant defense

Effect estimates are summarized from included studies and presented as approximate ranges due to heterogeneity in study designs, populations, and measurement techniques

The findings illustrate the distribution of physiological alterations associated with sleep deprivation across major body systems reported in the included studies. Cardiovascular and psychological systems demonstrated the highest number of increased physiological responses, while neurocognitive and metabolic systems showed a combination of increased and decreased functional outcomes. Autonomic, endocrine, and immune systems also exhibited measurable dysregulation, reflecting the broad systemic impact of insufficient sleep on cardiovascular regulation, metabolic balance, cognitive performance, mood status, and immune surveillance.

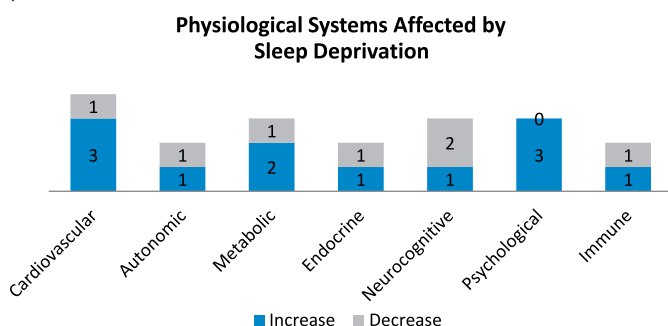


Figure 2: Physiological Systems Affected by Sleep Deprivation

The methodological quality of the included studies was assessed using the National Institutes of Health (NIH) Quality Assessment Tool. Most studies demonstrated moderate methodological quality, while several randomized crossover trials showed a lower risk of bias due

to controlled experimental designs and objective sleep measurements (Table 3).

Table 3: Risk of Bias Assessment of Included Studies

References	Clear Question	Defined Population	Valid Sleep Measure	Confounders Controlled	Overall, Bias
[15]	Yes	Yes	Yes	Partial	Moderate
[16]	Yes	Yes	Yes	Yes	Moderate
[17]	Yes	Yes	Yes	Partial	Moderate
[18]	Yes	Yes	Yes	Partial	Moderate
[19]	Yes	Yes	Yes	Yes	Moderate
[20]	Yes	Yes	Yes	Yes	Low-Moderate
[21]	Yes	Yes	Yes	Yes	Low-Moderate
[22]	Yes	Yes	Yes	Yes	Low-Moderate
[23]	Yes	Yes	Yes	Partial	Moderate
[24]	Yes	Yes	Yes	Partial	Low-Moderate
[25]	Yes	Yes	Yes	Partial	Moderate
[26]	Yes	Yes	Yes	Yes	Low
[27]	Yes	Yes	Yes	Yes	Low
[28]	Yes	Yes	Yes	Partial	Moderate

DISCUSSION

This systematic review synthesizes evidence from human studies investigating the biochemical and physiological consequences of sleep deprivation. The findings indicate that insufficient sleep is consistently associated with neuroendocrine stress activation, metabolic

dysregulation, inflammatory responses, and oxidative stress, which collectively contribute to broader physiological disturbances across multiple body systems. One of the most consistent findings across the included studies was the activation of stress-endocrine pathways, particularly the hypothalamic pituitary adrenal (HPA) axis. Experimental sleep restriction has been shown to increase cortisol levels and disrupt circadian hormonal regulation. These endocrine alterations may promote a catabolic hormonal environment and contribute to downstream metabolic disturbances such as insulin resistance and impaired glucose regulation. Previous controlled studies have also demonstrated that experimental sleep restriction increases ambulatory blood pressure and sympathetic activity, supporting the link between neuroendocrine stress responses and cardiovascular regulation [29]. Metabolic disturbances were also consistently reported across the included studies. Sleep deprivation was associated with impaired glucose metabolism, altered appetite-regulating hormones, and increased energy intake. Experimental studies have demonstrated that restricted sleep reduces insulin sensitivity and may contribute to unfavorable fat distribution and metabolic imbalance [30]. These findings suggest that sleep deprivation may contribute to cardiometabolic risk through both hormonal mechanisms and behavioral pathways, including increased appetite and caloric intake [31]. Inflammatory activation represents another important pathway linking sleep deprivation to systemic physiological dysfunction. Several human studies reported increased circulating inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) following sleep restriction. These findings support the concept that inadequate sleep may trigger low-grade systemic inflammation, which is known to play a role in the development of cardiovascular and metabolic diseases [32]. Population-based studies have also shown that irregular sleep patterns and insufficient sleep are associated with elevated inflammatory biomarkers in real-world settings [33]. Evidence from laboratory studies further indicates that sleep deprivation contributes to oxidative stress and endothelial dysfunction. Increased lipid peroxidation markers and reduced antioxidant defenses have been observed following sleep loss, suggesting a shift toward a pro-oxidative physiological environment. These oxidative changes may impair vascular function and contribute to cardiovascular risk [34]. In addition, experimental studies have demonstrated that acute sleep deprivation can weaken cardiorespiratory and autonomic regulation, further supporting the physiological disturbances summarized in figure 2 and table 3 [35]. Beyond metabolic and inflammatory

pathways, sleep deprivation also influences broader physiological systems, including cognitive performance, mood regulation, and immune function. Several studies reported reduced attention, impaired memory performance, increased daytime sleepiness, and psychological symptoms following sleep loss. These findings highlight the widespread impact of insufficient sleep on neurological and psychological functioning. Similarly, immune alterations such as increased white blood cell counts and reduced natural killer cell activity have been reported, suggesting that chronic sleep deprivation may impair immune surveillance and host defense mechanisms. Overall, the findings of this systematic review demonstrate that sleep deprivation is associated with multi-system physiological dysregulation, including cardiovascular, metabolic, neurocognitive, psychological, and immune alterations. These interconnected biological responses highlight the importance of adequate sleep duration and quality for maintaining physiological homeostasis.

Being a systematic review, the results are constrained by the quality and design of primary studies included, which are inherently limited. Quantitative synthesis of effect sizes cannot be done because of the heterogeneity in the effects of different studies, which does not allow conducting a meta-analysis. It is not possible to exclude the possibility of publication bias, whereby less research with null results should be underrepresented. The search involved English-language publications and three databases (PubMed, Scopus, Cochrane), which may have missed any other relevant studies that are published in other languages or in regional journals. Studies are needed on the best sleep duration in various groups in the context of age, sex, and comorbidity conditions. Findings could be translated into practice through implementation studies of the programs of sleep health in the workplace to investigate the shift worker population.

CONCLUSIONS

The evidence synthesized in this systematic review indicates that sleep deprivation is consistently associated with significant biochemical and physiological disturbances. Insufficient sleep activates stress-related endocrine pathways, disrupts metabolic regulation, increases inflammatory signaling, and promotes oxidative stress. These biochemical changes contribute to broader physiological consequences, including cardiovascular strain, autonomic imbalance, impaired cognitive performance, and reduced immune function. Collectively, these findings support the concept that sleep duration and sleep quality represent important modifiable determinants of cardiometabolic and neuroimmune health. Future research should focus on standardized definitions of sleep

deprivation, consistent biomarker measurement protocols, and well-controlled experimental designs to better understand the dose-response relationships and long-term health implications of sleep loss.

Authors' Contribution

Conceptualization: SYK

Methodology: AA, GM

Formal analysis: SYK

Writing and Drafting: SYK, BI, KI, AA, NF, GM

Review and Editing: SYK, BI, KI, AA, NF, GM

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



Placental Implantation Sites, Uterine Anatomy, and Uterine Physiology in Relation to Postpartum Hemorrhage: A Systematic Review

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ABSTRACT

Postpartum hemorrhage (PPH) remains a major cause of maternal morbidity and mortality worldwide. Increasing evidence suggests that the placental implantation site and uterine structural characteristics influence the effectiveness of hemostasis after placental separation, particularly in placenta previa and placenta accreta spectrum (PAS). **Objectives:** To systematically review human studies examining the relationship between placental implantation site, uterine anatomy, uterine physiology, and the risk of postpartum hemorrhage.

Methods: This systematic review followed PRISMA 2020 guidelines. PubMed, Web of Science, and Scopus were searched for studies published between January 2018 and December 2025. Eligible studies included observational human studies and imaging-based diagnostic studies evaluating placental implantation or uterine structural or physiological factors in relation to PPH. Animal studies, case reports, and review articles were excluded. Data were extracted using a standardized form, and methodological quality was assessed using the Newcastle-Ottawa Scale. Due to heterogeneity in study design and outcome definitions, a narrative synthesis was performed. **Results:** Eighteen studies met the inclusion criteria. Abnormal placental implantation, particularly lower uterine segment placentation, placenta previa, pernicious placenta previa, and PAS, was consistently associated with increased PPH risk. Structural factors, including reduced myometrial thickness and disruption of the uteroplacental interface, were frequently reported contributors to excessive bleeding.

Conclusions: Abnormal placental implantation and associated uterine structural changes are important contributors to postpartum hemorrhage. Antenatal imaging may assist in identifying high-risk pregnancies and guiding delivery planning.

INTRODUCTION

Postpartum hemorrhage (PPH) remains one of the leading causes of preventable maternal morbidity and mortality worldwide. Although uterine atony accounts for a large proportion of cases, anatomical and placental factors also play a critical role in determining the risk and severity of hemorrhage following placental separation [1]. Identifying these factors is essential for improving antenatal risk stratification and guiding delivery planning in high-risk

pregnancies [2]. Physiological hemostasis after delivery relies on myometrial contraction and compression of uterine vessels at the placental bed. Normally, myometrial contraction and spiral artery constriction limit postpartum bleeding [3]. This mechanism may be impaired when placental implantation occurs in the lower uterine segment or near cesarean scars, where reduced myometrial thickness and distortion of the uteroplacental interface



can increase bleeding risk [4]. Placenta previa and placenta accreta spectrum (PAS) are the most recognized forms of abnormal placentation associated with severe obstetric hemorrhage. In PAS, abnormal trophoblastic invasion disrupts the decidual layer, preventing normal placental separation and often leading to significant blood loss, transfusion, and occasionally peripartum hysterectomy [5]. Advances in obstetric imaging, particularly ultrasound and magnetic resonance imaging, have improved antenatal detection of abnormal placental location and invasion, allowing earlier identification of pregnancies at high risk of hemorrhage [6, 7].

Despite increasing research in this area, existing studies vary considerably in design, imaging criteria, and outcome definitions. Moreover, most previous reviews have focused primarily on specific conditions such as placenta previa or placenta accreta spectrum. Less attention has been given to the broader mechanistic relationship between placental implantation site, uterine structural characteristics, and physiological factors that influence hemostatic function after placental separation. As a result, the integrated role of placental location, uterine anatomy, and uterine physiology in the development of postpartum hemorrhage remains insufficiently synthesized. Therefore, this systematic review aims to synthesize human evidence published between 2018 and December 2025, examining how the placental implantation site, uterine anatomical features, and uterine physiological characteristics contribute to postpartum hemorrhage. By integrating findings across these domains, the review seeks to clarify mechanistic pathways linking abnormal placentation to hemorrhage risk and to support improved clinical risk assessment and management strategies.

METHODS

This systematic review was conducted to evaluate the relationship between placental implantation sites, uterine anatomy, uterine physiology, and the risk of postpartum hemorrhage (PPH). The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Due to substantial heterogeneity in study design, imaging modalities, populations, and outcome definitions, a qualitative narrative synthesis was performed, and meta-analysis was not undertaken. A comprehensive literature search was conducted in three electronic databases: PubMed, Web of Science, and Scopus. Studies published between January 2018 and December 2025 were considered eligible. The search strategy incorporated combinations of Medical Subject Headings (MeSH) and free-text terms related to placental implantation and postpartum hemorrhage. The primary Boolean search strategy used in PubMed was: ("postpartum hemorrhage"

OR "postpartum hemorrhage" OR PPH) AND ("placenta previa" OR "placenta accreta spectrum" OR PAS OR "placental implantation" OR "placental location") AND ("uterine anatomy" OR "uterine physiology" OR "myometrial thickness" OR "uteroplacental interface" OR "lower uterine segment" OR "uterine vascularity"). Similar search combinations were adapted for Web of Science and Scopus using database-specific syntax. Reference lists of all eligible studies were also manually screened to identify additional relevant publications. Original human studies using observational designs, including prospective cohort, retrospective cohort, case-control, cross-sectional, and imaging-based diagnostic studies, were eligible for inclusion. Studies were included if they evaluated the placental implantation site, uterine anatomical features, or uterine physiological parameters in relation to postpartum hemorrhage or objectively measured obstetric blood loss. Studies involving animal experiments, case reports, case series, narrative reviews, systematic reviews, meta-analyses, editorials, conference abstracts, or studies not reporting postpartum hemorrhage outcomes were excluded. Only studies published in the English language were included due to feasibility and resource limitations. This restriction may introduce language bias and has been acknowledged as a limitation of the review. All identified records were imported into a reference management software, and duplicate records were removed before screening. Title and abstract screening as well as full-text eligibility assessment were performed independently by two reviewers to minimize selection bias. Disagreements between reviewers were resolved through discussion and consensus. The database search initially identified 835 records. After the removal of 112 duplicates, 723 articles underwent title and abstract screening. A total of 642 records were excluded during the initial screening stage due to a lack of relevance. Eighty-one full-text articles were assessed for eligibility, of which 63 were excluded for reasons including absence of postpartum hemorrhage outcomes, non-human studies, or review articles. Finally, 18 studies met the inclusion criteria and were included in the qualitative synthesis. The study selection process is illustrated using the PRISMA 2020 flow diagram. Data were extracted using a standardized data extraction form to ensure consistency and accuracy. Extracted information included author name, year of publication, country, study design, study population, sample size, placental or uterine characteristics assessed, assessment methods, delivery mode where reported, and outcomes related to postpartum hemorrhage. Extracted data were cross-checked to minimize extraction errors. The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies. The scale evaluates three domains: selection of

study groups (maximum 4 stars), comparability of groups (maximum 2 stars), and outcome assessment (maximum 3 stars), giving a maximum score of 9 stars. Studies scoring 7–9 stars were classified as low risk of bias, 5–6 stars as moderate risk of bias, and ≤ 4 stars as high risk of bias. Quality assessment results were used to interpret study reliability, but no studies were excluded solely based on quality score. Because of substantial heterogeneity in study design, imaging criteria, measurement of placental invasion, and definitions of postpartum hemorrhage, statistical pooling of results was not feasible. Therefore, heterogeneity indices such as I^2 could not be calculated, and findings were synthesized using a structured narrative approach.

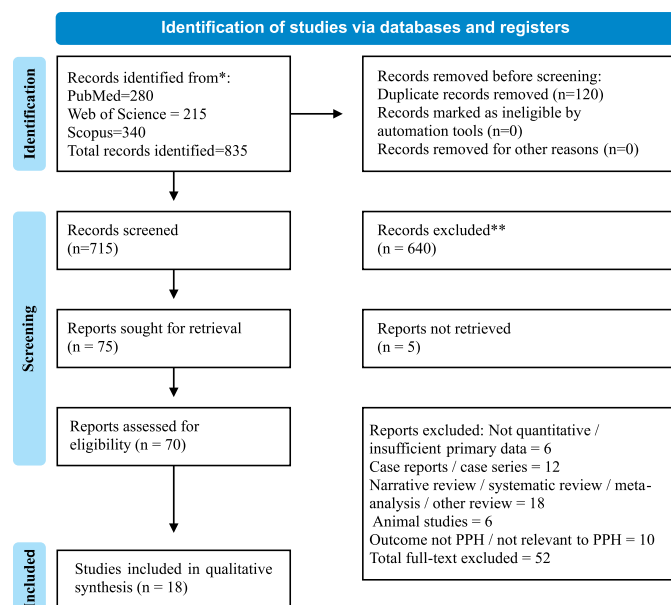


Figure 1: PRISMA 2020 flow diagram illustrating the study selection process for the systematic review on placental

implantation sites, uterine anatomy, and uterine physiology in relation to postpartum hemorrhage. A total of 835 records were identified through database searches, and after screening and eligibility assessment, 18 studies met the inclusion criteria and were included in the qualitative synthesis

RESULTS

The characteristics of the 18 observational studies included in the qualitative synthesis were published between 2018 and 2025 across multiple geographic regions. Most studies employed retrospective cohort or imaging-based observational designs and predominantly investigated pregnancies complicated by placenta previa or placenta accreta spectrum disorders. The majority of studies evaluated structural placental or uterine factors using ultrasound or magnetic resonance imaging, while several studies also incorporated intraoperative findings or clinical outcomes. Overall, the included studies consistently explored the relationship between placental implantation characteristics and the occurrence of postpartum hemorrhage (Table 1).

Table 1: Characteristics of Included Studies (2018–2025)

S. No.	References	Country	Study Design	Study Population	Sample Size	Placental/Uterine Factor Studied	Outcome Related to PPH
1	[8]	China	Observational diagnostic	Placenta previa/accreta undergoing cesarean	122	Ultrasound predictors of placental invasion	Severe hemorrhage >1500 mL
2	[9]	China	Retrospective cohort	Placenta previa	246	Placental implantation depth	Severe PPH
3	[10]	China	Retrospective cohort	Suspected PAS	40	MRI placental features	Massive intraoperative hemorrhage
4	[11]	Japan	Imaging observational	Placenta previa	94	Anterior vs posterior placental location	Surgical blood loss
5	[12]	USA	Retrospective observational	Placenta accreta spectrum	88	MRI placental invasion parameters	Intraoperative blood loss
6	[13]	USA	Retrospective cohort	Placental adhesion disorder	131	MRI placental bed abnormalities	Massive PPH
7	[14]	Italy	Observational cohort	Placenta previa	156	Combined ultrasound/MRI markers	Hemorrhagic morbidity
8	[15]	Japan	Retrospective cohort	Total vs partial placenta previa	183	Placental type and implantation site	PPH and transfusion
9	[16]	USA	Cohort study	Resolved low-lying placenta	628	Prior LUS placentation	Postpartum hemorrhage
10	[17]	China	Retrospective modelling	Pernicious placenta previa	212	Placental implantation pattern	PPH prediction
11	[18]	China	Imaging cohort	Placenta accreta spectrum	101	Myometrial thickness	Severe blood loss
12	[19]	Slovakia	Prospective observational	Vaginal and cesarean deliveries	92	LUS vascularity	Postpartum uterine perfusion
13	[20]	China	Retrospective validation	Pernicious placenta previa	268	Imaging-clinical model	PPH risk

14	[21]	China	Observational cohort	Placenta accreta spectrum	146	PAS subtype and placental invasion	Hemorrhage severity
15	[22]	South Korea	Multicenter cohort	Placenta previa	1248	Anterior vs non-anterior placentation	Transfusion and PPH
16	[23]	USA	Retrospective cohort	Resolved low-lying placenta	512	Previous LUS implantation	PPH
17	[24]	Japan	Imaging predictive study	Placenta previa	85	MRI radiomics placental bed	Massive hemorrhage >2000 mL
18	[25]	Australia	Observational cohort	Singleton pregnancies	3214	Placental implantation mapping	Postpartum hemorrhage

The association between placental implantation site and postpartum hemorrhage. Abnormal placental implantation, particularly involving the lower uterine segment, placenta accreta spectrum, and anterior placenta previa, was frequently associated with increased bleeding risk. Where reported, effect estimates such as odds ratios or relative risks indicated higher odds of postpartum hemorrhage in pregnancies with abnormal placental implantation. Among the seventeen studies that directly evaluated this association, fifteen reported an increased risk of postpartum hemorrhage, while two studies reported comparable bleeding risks between specific placental subtypes. These findings support the consistent role of placental location as an important determinant of postpartum bleeding. Most studies reporting severe hemorrhage outcomes involved cesarean delivery or cesarean hysterectomy, particularly in cases of placenta accreta spectrum, whereas a smaller number of studies included mixed delivery modes (vaginal and cesarean deliveries) (Table 2).

Table 2: Association Between Placental Implantation Site and Postpartum Hemorrhage

S. No.	References	Implantation / Placental Location	Comparator	Mode of Delivery	Effect Estimate (OR/RR, 95% CI)	Association With PPH	Key Findings
1	[8]	Placenta previa with invasive implantation	Non-invasive previa	Cesarean section	NR	Increased risk	Deep placental invasion associated with severe hemorrhage (>1500 mL)
2	[9]	Lower uterine segment implantation	Upper uterine segment	Cesarean section	OR 2.84 (1.45–5.23)	Increased risk	Lower implantation depth predicted severe PPH
3	[10]	Placenta accreta spectrum	Non-PAS placenta	Cesarean section	NR	Markedly increased risk	Massive intraoperative bleeding
4	[11]	Anterior placenta previa	Posterior placenta previa	Cesarean section	NR	Increased risk	Higher surgical blood loss
5	[12]	Deep placental invasion	Superficial invasion	Cesarean hysterectomy	NR	Increased risk	Greater invasion depth correlated with bleeding
6	[13]	Placental adhesion disorder	Normal placentation	Cesarean section	NR	Increased risk	MRI markers predicted massive PPH
7	[14]	Placenta previa with PAS	Placenta previa without PAS	Cesarean section	OR 3.10 (1.70–5.60)	Increased risk	Combined imaging markers predicted hemorrhage
8	[15]	Total placenta previa	Partial/marginal previa	Cesarean section	RR 1.05 (0.78–1.42)	Comparable risk	No significant bleeding difference
9	[16]	Resolved low-lying placenta	Normal placenta	Mixed delivery	OR 2.30 (1.25–4.10)	Increased risk	Persistent PPH risk despite migration
10	[17]	Pernicious placenta previa	Non-pernicious previa	Cesarean section	OR 3.45 (1.90–6.30)	Increased risk	Implantation over cesarean scar increased bleeding
11	[18]	Placenta accreta	Non-accreta placenta	Cesarean section	NR	Increased risk	Myometrial thinning predicted severe blood loss
12	[20]	Abnormal lower-segment placentation	Normal implantation	Cesarean section	OR 2.90 (1.60–5.10)	Increased risk	Imaging model predicted hemorrhage
13	[21]	PAS involving LUS	Upper-segment PAS	Cesarean hysterectomy	NR	Increased risk	Greater hemorrhage severity
14	[22]	Anterior placenta previa	Non-anterior placenta previa	Cesarean section	OR 1.88 (1.32–2.68)	Increased risk	Higher transfusion requirement
15	[23]	Resolved low-lying placenta	Normal placental location	Mixed delivery	OR 2.10 (1.20–3.70)	Increased risk	History of LUS implantation increased PPH
16	[24]	Placental bed involvement	Limited involvement	Cesarean section	NR	Increased risk	Radiomics predicted massive hemorrhage
17	[25]	Lower uterine segment placentation	Fundal/lateral placentation	Mixed delivery	RR 1.92 (1.30–2.84)	Increased risk	LUS implantation is independently associated with PPH

Summary: 15 increased risks; 2 comparable risks. The majority of studies demonstrated elevated PPH risk with abnormal placental implantation

Uterine anatomical and physiological factors associated with postpartum hemorrhage. The most frequently reported structural contributors included reduced myometrial thickness at the placental implantation site, abnormalities of the uteroplacental interface, and impaired contractility of the lower uterine segment. Imaging findings obtained from ultrasound and magnetic resonance imaging demonstrated that disruption of the placental bed or thinning of the myometrium may compromise effective physiological hemostasis following placental separation. In addition, altered vascular indices in the lower uterine segment were suggested as potential physiological contributors to excessive postpartum bleeding (Table 3).

Table 3: Uterine Anatomical and Physiological Factors Associated with PPH

S. No.	References	Factor	Method	Timing	Association	Mechanistic Insight
1	[8]	Placental invasion depth	Ultrasound + surgery	Antepartum/Intrapartum	Increased	Disrupts myometrial contraction
2	[9]	Reduced myometrial thickness	Ultrasound	Antepartum	Increased	Reduced contractile capacity
3	[10]	Placental bed disruption	MRI	Antepartum	Increased	Loss of muscle architecture
4	[11]	Anterior LUS implantation	MRI	Antepartum	Increased	Reduced contractility
5	[12]	Uteroplacental interface distortion	MRI	Antepartum	Increased	Impaired vessel occlusion
6	[13]	Placental bed abnormalities	MRI	Antepartum	Increased	Failed placental separation
7	[14]	Decidual disruption	Ultrasound/MRI	Antepartum	Increased	Spiral artery closure impaired
8	[15]	Placental extension across LUS	Surgical findings	Intrapartum	Variable	Larger bleeding surface
9	[16]	Persistent LUS remodeling	Ultrasound	Antepartum/Postpartum	Increased	Structural changes persist
10	[17]	Placenta over cesarean scar	Ultrasound	Antepartum	Increased	Scar reduces contractility
11	[18]	Myometrial thickness <2 mm	MRI	Antepartum	Increased	Severe contractile deficit
12	[19]	Altered vascular indices	3D Doppler	Early puerperium	Physiological	Higher vascular flow
13	[20]	Combined impairment	MRI + ultrasound	Antepartum	Increased	Amplified bleeding risk
14	[21]	PAS subtype involving LUS	MRI	Antepartum	Increased	Higher hemorrhage severity
15	[22]	Anterior placenta previa	Clinical/imaging	Intrapartum	Increased	Reduced uterine compression
16	[23]	Residual LUS remodeling	Ultrasound	Postpartum	Increased	Predisposes to atony
17	[24]	Placental bed radiomics	MRI	Antepartum	Increased	Large dysfunctional bed
18	[25]	LUS vs fundal implantation	Clinical mapping	Antepartum	Increased	Fundal uterus provides better hemostasis

The methodological quality assessment of the included studies using the Newcastle–Ottawa Scale. Most studies demonstrated adequate selection of study populations and objective assessment of outcomes. Based on the predefined scoring criteria, fourteen studies were classified as having low risk of bias, while four studies were categorized as having moderate risk of bias. The most common limitation identified across studies was incomplete adjustment for potential confounding factors such as maternal characteristics or previous obstetric history (Table 4).

Table 4: Risk of Bias Assessment (Newcastle–Ottawa Scale)

References	Selection	Comparability	Outcome	Total	Risk
[8]	★★★★	★★	★★★★	9	Low
[9]	★★★★	★★	★★★★	8	Low
[10]	★★★★	★★	★★	7	Low
[11]	★★★★	★★	★★	7	Low
[12]	★★★★	★★	★★	7	Low
[13]	★★★★	★★	★★	7	Low
[14]	★★★★	★★	★★	7	Low
[15]	★★★★	★	★★	6	Moderate
[16]	★★★★	★★	★★★★	9	Low
[17]	★★★★	★	★★	6	Moderate

[18]	★★★★	★★	★★	7	Low
[19]	★★★★	★	★★	6	Moderate
[20]	★★★★	★★	★★	7	Low
[21]	★★★★	★★	★★	7	Low
[22]	★★★★	★★	★★★★	9	Low
[23]	★★★★	★★	★★	7	Low
[24]	★★★★	★	★★	6	Moderate
[25]	★★★★	★★	★★★★	9	Low

Low risk = 7–9 stars

Moderate risk = 5–6 stars

DISCUSSION

This systematic review synthesizes available evidence on the relationship between placental implantation sites, uterine anatomy, uterine physiology, and the risk of postpartum hemorrhage (PPH). The findings indicate that abnormal placental implantation, particularly placenta previa, low-lying placenta, and placenta accreta spectrum (PAS), is consistently associated with an increased risk of postpartum bleeding due to structural and physiological alterations in the uteroplacental interface and impaired uterine hemostasis. A number of systematic reviews conducted in recent years confirm that abnormal placental implantation is a major determinant of PPH. Bonanni *et al.* 2025 reported in the systematic review and meta-analysis

reported that low-lying placenta or placenta previa diagnosed during pregnancy increases the risk of postpartum hemorrhage approximately twofold compared with normal placental location [26]. Our findings are consistent with these reports and further suggest that even a resolved low-lying placenta may still carry a persistent risk of hemorrhage, possibly due to structural remodeling and altered lower uterine segment physiology. Placenta previa is widely recognized as one of the most important obstetric risk factors for PPH because implantation within the lower uterine segment limits effective myometrial contraction after placental separation. Epidemiological studies indicate that placenta previa complicates approximately 1–2% of pregnancies and is strongly associated with maternal morbidity due to severe bleeding [27]. In addition, placenta previa frequently coexists with placenta accreta spectrum disorders, in which abnormal trophoblastic invasion penetrates the myometrium and disrupts the normal decidual interface. Such pathological implantation prevents controlled placental separation and substantially increases the likelihood of massive hemorrhage, transfusion requirement, and cesarean hysterectomy [28]. The importance of PAS in severe obstetric hemorrhage is further supported by recent systematic evidence demonstrating that increasing depth of trophoblastic invasion is associated with higher surgical complexity and greater blood loss [29]. International consensus classifications such as the FIGO grading system also recognize that the extent of placental invasion correlates with hemorrhage severity and surgical management complexity. Imaging studies increasingly support the use of magnetic resonance imaging as a complementary modality to ultrasound for identifying myometrial invasion and placental bed abnormalities that may predispose to PPH [30, 31]. Placental location within the lower uterine segment and anterior uterine wall may further influence hemorrhage risk. Emerging cohort evidence suggests that anatomical differences in placental position may affect imaging characteristics and bleeding severity, highlighting the potential role of placental mapping in antenatal risk stratification [32, 33]. Another key observation of this review relates to the contribution of uterine structural and physiological characteristics to postpartum bleeding. Implantation in the lower uterine segment may lead to reduced myometrial thickness and impaired contractile capacity, limiting the ability of the uterus to achieve physiological hemostasis following placental separation. Disruption of the uteroplacental interface caused by abnormal placentation or underlying uterine structural abnormalities has also been associated with retained placenta and failed uterine contraction [34]. Altered vascularity within the lower uterine segment may represent another important contributor to PPH

pathophysiology. Doppler imaging studies have demonstrated abnormal vascular indices and altered uterine perfusion patterns in pregnancies complicated by abnormal placentation. However, it should be noted that several studies included in this review inferred hemorrhage risk primarily from imaging findings rather than direct quantitative measurement of postpartum blood loss. Therefore, mechanistic interpretations derived from imaging observations should be interpreted cautiously. The findings of this review have important clinical implications for antenatal risk assessment and delivery planning. Routine ultrasound evaluation of placental location, particularly in women with previous cesarean delivery or uterine surgery, allows early identification of pregnancies at risk of severe hemorrhage. Early recognition of PAS or abnormal placental implantation enables referral to tertiary care centers where multidisciplinary teams, interventional radiology, and adequate blood product availability can improve maternal outcomes. Conservative surgical approaches and placenta-preserving strategies have also shown promising results in selected PAS cases, although standardized clinical protocols are still evolving [35].

Risk stratification models such as the Placenta Accreta Index and FIGO classification have been proposed to guide clinical decision-making; however, their predictive performance varies across populations and healthcare settings. In addition, this review did not quantitatively evaluate diagnostic accuracy measures such as sensitivity, specificity, or predictive values of antenatal imaging modalities, and therefore imaging findings should be interpreted primarily as indicators of hemorrhage risk rather than definitive predictors. Several limitations should be acknowledged. Most included studies were observational and heterogeneous in design, imaging criteria, and outcome definitions. Definitions of PPH varied between studies (≥ 500 mL vs ≥ 1000 mL blood loss or transfusion-based outcomes), limiting comparability. Some studies relied on imaging-based inference rather than direct hemorrhage measurement, and only English-language publications were included. Future research should focus on large prospective multicenter studies using standardized hemorrhage definitions and integrated imaging-clinical prediction models.

CONCLUSIONS

This systematic review synthesizes available evidence on the relationship between placental implantation sites, uterine anatomy, uterine physiology, and the risk of postpartum hemorrhage (PPH). The findings indicate that abnormal placental implantation, particularly placenta previa, low-lying placenta, and placenta accreta spectrum (PAS), is consistently associated with an increased risk of postpartum bleeding due to structural and physiological

alterations in the uteroplacental interface and impaired uterine hemostasis.

Authors' Contribution

Conceptualization: DESA, SA

Methodology: AM, MA, SF, RUJ

Formal analysis: AM, SF

Writing and Drafting: DESA, SA, MA, RUJ

Review and Editing: DESA, AM, SA, MA, SF, RUJ, NNC

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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