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ORIGINAL ARTICLE

Comparison between Epidural and Programmed Analgesia on Pain Relief during Labour in 70 Parturients

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ABSTRACT

Background: *Labour pain is one of the most severe forms of physiological pain, and effective analgesia significantly improves maternal satisfaction and obstetric outcomes. Epidural labour analgesia (ELA) is the gold standard; however, programmed labour analgesia (PLA) a multimodal regimen integrating pharmacological and non-pharmacological elements has gained popularity for its simplicity, accessibility, and reduced intervention rates.* ***Objective:*** *To compare the effectiveness, safety, and maternal satisfaction of Epidural Labour Analgesia (ELA) versus Programmed Labour Analgesia (PLA) in controlling labour pain among parturients.* ***Methods & Materials:*** *This comparative observational study included 70 term parturients divided into two groups: ELA (n=35) and PLA (n=35). Pain scores were measured using a Visual Analog Scale (VAS) at baseline, 30 min, 1 hour, and full dilation. Secondary outcomes included duration of labour, mode of delivery, maternal side effects, neonatal APGAR scores, and overall maternal satisfaction.* ***Results:*** *Both methods significantly reduced labour pain ($p < 0.001$). ELA achieved superior pain relief at all assessed intervals, with mean VAS at full dilation of 2.4 ± 1.1 compared to PLA's 4.8 ± 1.5. The duration of the first and second stages of labour was slightly longer in the ELA group, though not statistically significant. Instrumental delivery was more frequent in ELA (14.3%) than PLA (5.7%). Maternal side effects such as hypotension and pruritus were higher in ELA. Neonatal outcomes were comparable. Maternal satisfaction was significantly higher in ELA ($p < 0.05$).* ***Conclusion:*** *Epidural labour analgesia provides superior pain control and greater maternal satisfaction, although it is associated with a slightly longer labour duration and higher rate of instrumental delivery. Programmed labour analgesia remains a safe, effective, and resource-friendly alternative in settings where epidural services are limited.*

Keywords: *Epidural analgesia, Programmed labour analgesia, Labour pain, Obstetric analgesia, Maternal satisfaction.*

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INTRODUCTION

Labour pain is among the most intense forms of physiological pain experienced by women and represents a major contributor to maternal anxiety and stress during childbirth. Effective labour analgesia enhances maternal wellbeing, optimizes uterine–placental perfusion, reduces stress-related hormonal surges, and improves obstetric outcomes. Over the past decades, advancements in labour analgesia have broadened options for parturients, ranging from systemic opioids to neuraxial techniques. Epidural labour analgesia (ELA) remains the gold standard for pain relief during labour because it provides predictable sensory blockade with minimal fetal drug transfer. Multiple studies have established its superiority in achieving effective, titratable analgesia while maintaining maternal consciousness and active participation in childbirth.[1–3] However, ELA requires specialized equipment, continuous monitoring, and expertise from trained anesthesiologists, limiting its availability in many low-resource facilities. Programmed labour analgesia (PLA), also known as "labour analgesia without epidural," offers a practical, multimodal approach integrating pharmacologic components (e.g., paracetamol, NSAIDs, opioids, antispasmodics) and non-pharmacologic techniques (breathing exercises, position changes, hydration). PLA is widely used in South Asian maternity units where epidural services may not be consistently available. Although PLA provides moderate pain relief, its effectiveness compared with ELA is still being investigated. Despite several clinical trials exploring both approaches, direct comparative data in many regions, including Bangladesh and similar resource-constrained settings, remain limited. Additionally, maternal satisfaction—a crucial indicator increasingly emphasized in obstetric care—is variably reported. This study was designed to compare ELA and PLA in controlling labour pain, with attention to maternal outcomes, obstetric variables, neonatal safety, and overall satisfaction. By evaluating 70 cases, this research provides practical insights relevant to both tertiary hospitals and secondary care centres where flexibility in analgesia provision is essential.

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MATERIALS & METHODS

This comparative observational study was conducted in the Department of Anaesthesia, Analgesia and ICU, Dinajpur Medical College Hospital, Dinajpur, Bangladesh from January 2024 to July 2024 over a 7-month period. A total of 70 term parturients who requested labour analgesia during the active phase of labour were enrolled. Participants were divided into two equal groups based on the type of analgesia provided: **Group A**, consisting of 35 women who received Epidural Labour Analgesia (ELA), and **Group B**, comprising 35 women who received Programmed Labour Analgesia (PLA). The allocation followed a consecutive sampling approach, ensuring that all eligible women who opted for either analgesia modality were included.

Eligibility Criteria

Women were eligible for inclusion if they were:

- at term pregnancy (37–41 weeks),
- carrying a singleton fetus in cephalic presentation,
- in the active phase of labour with cervical dilation between 3–5 cm, and
- willing to provide informed consent for participation.

Women with contraindications to neuraxial analgesia (such as coagulopathy, thrombocytopenia, spinal deformities, or infection at the puncture site), allergy to the study drugs, high-risk pregnancies requiring urgent intervention, or non-reassuring fetal heart patterns at recruitment were excluded.

Analgesia Techniques

Group A: Epidural Labour Analgesia (ELA)

Epidural catheterization was performed at the L3–L4 or L4–L5 interspace under strict aseptic precautions. A test dose of lignocaine 1.5% with adrenaline was administered to exclude intrathecal or intravascular placement. Analgesia was maintained using a continuous infusion of 0.1% bupivacaine combined with fentanyl (2 mcg/mL). Additional bolus doses were provided when necessary. Maternal vitals, pain scores, and fetal heart rate were monitored continuously.

Group B: Programmed Labour Analgesia (PLA)

The PLA regimen consisted of a structured combination of systemic analgesics, antispasmodics, and supportive measures. Women received intravenous tramadol 50 mg every 6 hours, intravenous paracetamol 1 g every 8 hours, and intravenous hyoscine butylbromide 20 mg for cervical relaxation. Non-pharmacological methods—such as breathing exercises, frequent maternal repositioning, hydration, and one-to-one emotional support—were incorporated according to standardized departmental protocols.

Outcome Measures

The primary outcome was pain intensity, assessed using the Visual Analog Scale (VAS) at baseline, 30 minutes, 1 hour, and at full cervical dilation. Secondary outcomes included duration of the first and second stages of labour, mode of delivery, maternal side effects (hypotension, pruritus, urinary retention, nausea/vomiting), neonatal outcomes (APGAR scores at 1 and 5 minutes, NICU admission), and overall maternal satisfaction evaluated using a 5-point Likert scale.

Data Handling and Statistical Analysis

All data were recorded in structured proformas and analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using independent t-tests, while categorical variables were analyzed using chi-square or Fisher's exact tests. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 70 parturients were included in the study, with 35 women receiving epidural labour analgesia (ELA) and 35 receiving programmed labour analgesia (PLA). The baseline demographic and obstetric characteristics of the two groups were comparable. The mean maternal age was 25.8 ± 4.2 years in the ELA group and 26.1 ± 4.5 years in the PLA group, with no statistically significant difference between them. The proportions of primigravida women were similar (54.3% in ELA vs. 51.4% in PLA), and the mean gestational age at term was nearly identical (38.6 ± 1.1 weeks vs. 38.7 ± 1.2 weeks). Cervical dilation at the time of analgesia administration was also comparable, averaging 3.8 ± 0.9 cm in the ELA group and 4.0 ± 0.8 cm in the PLA group. No variable showed a significant difference, confirming adequate baseline comparability.

Pain intensity, assessed using the Visual Analog Scale (VAS), showed significant differences between the two groups after analgesia administration. Before analgesia, both groups reported similarly high pain scores (8.4 ± 0.9 in the ELA group and 8.3 ± 1.0 in the PLA group). However, at 30 minutes following analgesia, women receiving ELA exhibited a marked reduction in pain, with VAS scores falling to 3.2 ± 1.2, compared to 6.1 ± 1.4 in the PLA group ($p < 0.001$). This trend continued at 1 hour, where ELA participants recorded a mean VAS of 2.6 ± 1.3 versus 5.5 ± 1.3 in the PLA group ($p < 0.001$). At full cervical dilation, the difference remained significant, with mean VAS scores of 2.4 ± 1.1 in the ELA group compared to 4.8 ± 1.5 among PLA recipients ($p < 0.001$). These findings demonstrate that epidural analgesia produced consistently superior pain relief across all measured intervals.

Labour progress indicators showed a modest but non-significant prolongation of labour duration in the ELA group. The mean duration of the first stage was 7.9 ± 1.8 hours in the ELA group compared to 7.2 ± 1.5 hours in the PLA group, while the second stage lasted 48 ± 14 minutes versus 42 ± 12 minutes, respectively. Although both stages tended to be longer with epidural analgesia, these differences did not reach statistical significance. Regarding delivery mode, normal vaginal delivery occurred in 71.4% of women in the ELA group and 80% in the PLA group. Instrumental delivery was more frequent among ELA recipients (14.3%) compared to PLA (5.7%), whereas the caesarean section rate was identical in both groups (14.3%). None of these differences were statistically significant.

Maternal side effects varied between the groups. Hypotension occurred more commonly in the ELA group, affecting 17.1% of women compared to only 2.8% in the PLA group, a statistically significant difference ($p = 0.04$). Pruritus was also significantly more common among ELA recipients (11.4%), while it was absent in the PLA group ($p = 0.04$). Urinary retention was noted in 14.3% of women in the ELA group but not observed in any PLA participant ($p = 0.02$). Incidence of nausea and vomiting did not differ significantly between groups, occurring in 8.6% of ELA patients and 14.3% of PLA patients.

Neonatal outcomes were similar across both analgesia methods. The mean APGAR score at 1 minute was 7.9 ± 0.4 in the ELA group and 7.8 ± 0.5 in the PLA group, while the 5-

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minute APGAR averaged 9.0 ± 0.3 versus 8.9 ± 0.4, respectively. These differences were not statistically significant. NICU admission rates were low and comparable, with 2.8% in the ELA group and 5.7% in the PLA group.

Maternal satisfaction scores differed significantly between the groups. Women who received ELA reported a higher mean satisfaction rating of 4.6 ± 0.4 on a 5-point Likert scale, compared to 3.8 ± 0.7 among PLA recipients ($p < 0.001$). This reflects the superior analgesic effectiveness and overall childbirth experience associated with epidural techniques.

Table – I: Baseline Characteristics

Variable	ELA (n=35)	PLA (n=35)	p-value
Maternal age (years)	25.8 ± 4.2	26.1 ± 4.5	0.78
Parity (primigravida %)	54.3%	51.4%	0.81
Gestational age (weeks)	38.6 ± 1.1	38.7 ± 1.2	0.64
Cervical dilation at entry (cm)	3.8 ± 0.9	4.0 ± 0.8	0.42

No significant differences were noted between groups.

Table – II: Pain Scores (VAS)

Time Point	ELA	PLA	p-value
Baseline	8.4 ± 0.9	8.3 ± 1.0	0.77
30 min	3.2 ± 1.2	6.1 ± 1.4	<0.001
1 hour	2.6 ± 1.3	5.5 ± 1.3	<0.001
Full dilation	2.4 ± 1.1	4.8 ± 1.5	<0.001

Epidural analgesia provided significantly better pain relief at all intervals.

Table – III: Labour Progress and Delivery Outcomes

Variable	ELA	PLA	p-value
Duration of 1st stage (hours)	7.9 ± 1.8	7.2 ± 1.5	0.09
Duration of 2nd stage (minutes)	48 ± 14	42 ± 12	0.08
Normal vaginal delivery (%)	71.4%	80%	0.39
Instrumental delivery (%)	14.3%	5.7%	0.19
Cesarean section (%)	14.3%	14.3%	1.00

Though not statistically significant, ELA showed slightly prolonged labour and more assisted deliveries.

Table – IV: Maternal Side Effects

Side Effect	ELA	PLA	p-value
Hypotension	17.1%	2.8%	0.04
Pruritus	11.4%	0%	0.04
Nausea/Vomiting	8.6%	14.3%	0.46
Urinary retention	14.3%	0%	0.02

Epidural analgesia had more procedure-related side effects.

Table – V: Neonatal Outcomes

Variable	ELA	PLA	p-value
APGAR 1 min	7.9 ± 0.4	7.8 ± 0.5	0.52
APGAR 5 min	9.0 ± 0.3	8.9 ± 0.4	0.37
NICU admission (%)	2.8%	5.7%	0.55

Neonatal outcomes were comparable.

Table – VI: Maternal Satisfaction

Satisfaction Score	ELA	PLA	p-value
Mean score (1–5)	4.6 ± 0.4	3.8 ± 0.7	<0.001

DISCUSSION

This comparative study assessed the effectiveness of epidural labour analgesia (ELA) and programmed labour analgesia (PLA) in reducing labour pain among 70 parturients. The findings indicate that ELA provides superior analgesic efficacy, greater maternal satisfaction, and stable neonatal outcomes, consistent with international literature supporting epidural as the gold standard.[4–6] Pain reduction, assessed through VAS, demonstrated significantly lower scores in the ELA group at all time intervals. Such profound analgesic effect aligns with findings from Anim-Somuah et al.[7], who reported significant pain reduction with neuraxial techniques compared to systemic analgesia. The first and second stages of labour were slightly prolonged in the ELA group. This is a known physiological consequence of neuraxial blockade due to reduced pelvic muscle tone and diminished reflex bearing-down efforts. However, the differences in our study did not reach statistical significance, implying clinical acceptability. Previous meta-analyses have suggested similar results, showing minimal prolongation without adverse maternal outcomes.[8] Instrumental delivery was more common with ELA (14.3% vs 5.7%). Although the difference was statistically nonsignificant, it reflects a trend commonly reported in classical literature, likely due to reduced expulsive force or

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obstetrician preference. Modern low-dose epidural regimens, similar to ours, have been shown to mitigate this effect.[9] Side-effect profiles in ELA included hypotension, pruritus, and urinary retention, consistent with pharmacological mechanisms of epidural local anesthetics and opioids. PLA demonstrated fewer physiological side effects, reflecting its non-neuraxial nature and lower systemic drug intensity. Neonatal outcomes—including APGAR scores and NICU admissions—were comparable between groups, supporting the safety of both methods. This finding aligns with global evidence that neuraxial analgesia does not adversely affect neonatal well-being.[10] Maternal satisfaction was significantly higher in the ELA group. Adequate pain control has been shown to reduce maternal stress, improve psychological experience, and enhance overall birth satisfaction.[11] PLA, while effective to a moderate degree, may not match the profound analgesia offered by epidurals, contributing to lower satisfaction scores. From a practical standpoint, PLA remains valuable in low-resource settings where anesthetic expertise or equipment for neuraxial analgesia may not be available 24/7. It offers a structured, safe, and scalable approach for improving maternal comfort. However, whenever resources permit, ELA should be considered the preferred modality.

CONCLUSION

Epidural labour analgesia provides significantly superior pain relief and maternal satisfaction compared with programmed labour analgesia, without compromising neonatal outcomes. Although associated with slightly increased side effects and a trend toward prolonged labour and instrumental delivery, these differences were not clinically prohibitive. Programmed labour analgesia remains a safe and practical alternative, particularly in resource-limited settings.

REFERENCES

1. *Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med. 2010; 362:1503-10.*
2. *Simmons SW, Taghizadeh N, Dennis AT. Analgesia for labour. Obstet Gynaecol Reprod Med. 2012; 22:360-7.*
3. *Jones L, Othman M, Dowswell T. Pain management for women in labour. Cochrane Database Syst Rev. 2012;3:CD009234.*
4. *Reuben SS, Sullivan JL. Pain reduction in labour: neuraxial vs systemic options. Int J Obstet Anesth. 2015; 24:121-8.*
5. *Camann W. Labour analgesia in modern obstetrics. Clin Obstet Gynecol. 2014; 57:241-50.*
6. *Van der Vyver M, Halpern S. Epidural labour analgesia: efficacy and outcomes. Best Pract Res Clin Anaesthesiol. 2019; 33:43-56.*
7. *Anim-Somuah M, Smyth R, Jones L. Neuraxial versus non-neuraxial analgesia. Cochrane Database Syst Rev. 2018;5:CD000331.*
8. *Halpern SH, Walsh V. Epidural analgesia and labour duration. Anesth Analg. 2016; 123:1544-52.*
9. *Wong CA. Advances in neuraxial labour analgesia. Anesthesiology. 2017; 126:267-8.*
10. *Lieberman E, O'Donoghue C. Effects of epidural analgesia on labour. Am J Obstet Gynecol. 2002;186: S31-40.*
11. *Hodnett ED. Pain and women's satisfaction with childbirth. Birth. 2002; 29:164-73.*

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Efficacy and Safety of Caudal Epidural Block in High-Risk Patients Undergoing Transurethral Resection of the Prostate in 70-Cases – A Prospective Study

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ABSTRACT

Background: *Transurethral resection of the prostate (TURP) remains the standard surgical treatment for symptomatic benign prostatic hyperplasia (BPH). Many candidates for TURP are elderly and burdened with comorbidities such as hypertension, diabetes, ischemic heart disease, and COPD, making anesthetic selection critical. Caudal epidural block (CEB) has resurfaced as a potential alternative for high-risk patients due to its hemodynamic stability and reduced neuraxial complications.* ***Objectives:*** *To evaluate the efficacy, safety, and hemodynamic profile of CEB in patients with comorbidities undergoing TURP.* ***Methods & Materials:*** *This prospective observational study included 70 high-risk patients (ASA II–III) scheduled for TURP. CEB was administered using a standardized technique with 1.5% lignocaine with adrenaline. Hemodynamic variables, block characteristics, intraoperative events, surgeon satisfaction, and postoperative outcomes were recorded. Exclusion criteria included coagulopathy, sepsis, prior spinal surgery, and inability to identify sacral hiatus.* ***Results:*** *CEB was successfully performed in 67 out of 70 patients (95.7%). Adequate surgical anesthesia was achieved in 61 patients (87.1%), whereas 6 required supplemental analgesia or conversion to general anesthesia. Hemodynamic parameters remained stable in the majority, with only 8.5% experiencing transient hypotension. Minor complications included urinary retention (7.1%), postoperative shivering (5.7%), and perineal discomfort at injection site (4.2%). No patient developed significant arrhythmias, TURP syndrome, or airway compromise. Surgeon satisfaction was high (85%), with optimal relaxation and minimal patient movement reported.* ***Conclusion:*** *CEB is a safe and effective anesthetic technique for TURP in patients with significant comorbidities, offering excellent hemodynamic stability and a favorable safety profile. It provides a valuable alternative to spinal anesthesia or general anesthesia in the elderly and medically fragile population.*

Keywords: *Caudal Epidural Block, TURP, BPH, Regional Anesthesia, Elderly, Comorbidities, Hemodynamic Stability*

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common urological conditions in aging men, and its prevalence increases steadily with advancing age, often becoming symptomatic in the seventh and eighth decades of life.[1] When medical therapy fails or complications arise, transurethral resection of the prostate (TURP) continues to serve as the gold-standard operative intervention for relieving bladder outlet obstruction.[2] Despite advances in surgical techniques and bipolar energy systems, TURP remains physiologically demanding, particularly for the elderly patient with multiple comorbidities.[3] The anesthetic management of these patients is complex. Elderly individuals often present with a constellation of chronic illnesses—hypertension, diabetes mellitus, ischemic heart disease (IHD), chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD)—each altering physiological reserve to varying degrees.[4] These comorbidities increase the risks associated with hemodynamic fluctuations, fluid absorption, and operative stress during TURP. Traditionally, spinal anesthesia has been widely used because it provides dense surgical anesthesia and rapid onset; however, it is frequently associated with hypotension, bradycardia, and wide sympathetic blockade, which may be poorly tolerated in frail, elderly patients.[5] Conversely, general anesthesia offers airway control but may impose myocardial stress and postoperative respiratory complications in those with reduced cardiopulmonary reserve.[6] Caudal epidural block (CEB), though historically more common in pediatric anesthesia, has gained renewed interest as an alternative regional technique in adults. Its key advantage lies in its lower degree of sympathetic blockade, which results in more stable hemodynamics—an essential attribute for patients with cardiovascular or autonomic vulnerability.[7] Because the caudal canal is anatomically distinct and provides a predictable route for epidural drug spread, CEB may permit sufficient sensory blockade for lower urinary tract procedures while

avoiding abrupt circulatory shifts characteristic of lumbar spinal anesthesia.[8] Evidence supporting the use of CEB in adult urological surgery is emerging, though still relatively sparse. Several observational studies report that caudal administration of local anesthetics can achieve sensory levels adequate for TURP, particularly when delivered in appropriate volumes and concentrations.[9] Additionally, CEB appears to reduce the incidence of profound hypotension and bradyarrhythmias compared with spinal anesthesia, thereby offering a safer physiological profile for high-risk individuals.[10] The potential value of this approach is further underscored by global demographic trends: as populations age, increasing numbers of patients present for TURP with multiple comorbid conditions, necessitating anesthetic techniques that minimize hemodynamic volatility.[11] Despite these potential advantages, the technique remains underutilized in many centers. Concerns persist regarding interindividual variability in block height, unpredictable spread of local anesthetic, and technical difficulty due to degenerative anatomical changes in the sacral region of older adults.[12] Moreover, much of the existing literature consists of small case series or retrospective reports, leading to limited understanding of CEB's performance in real-world, comorbidity-heavy populations.[13] Given these gaps, the present study was designed as a prospective observational analysis of 70 high-risk patients undergoing TURP under caudal epidural anesthesia. The objectives were to evaluate the success rate of CEB, assess block quality, characterize the hemodynamic profile, and document perioperative complications. Special emphasis was placed on hemodynamic stability because it is often the decisive factor determining outcomes in elderly individuals with compromised cardiovascular status. This study aims to contribute meaningful clinical data and deepen the understanding of whether CEB can serve as a safe and effective alternative to spinal or general anesthesia for TURP in patients with multiple comorbidities.

METHODS & MATERIALS

Study Design and Setting

This prospective observational study was conducted over a 6-month period in the Department of Anaesthesiology, Dinajpur Medical College Hospital, Dinajpur, Bangladesh from July 2024 to December 2024.

Sample Size

Seventy adult male patients undergoing TURP were enrolled consecutively.

Inclusion Criteria

- Age 50–85 years
- ASA physical status II–III
- Indication: symptomatic BPH requiring TURP
- Presence of ≥1 comorbidity (hypertension, diabetes, IHD, COPD, CKD, obesity)

Exclusion Criteria

- Coagulopathy or anticoagulant use
- Local infection at sacral hiatus
- Severe spinal deformity
- Allergy to local anesthetics
- Failed caudal space identification
- Patient refusal

Preoperative Evaluation

All patients underwent clinical assessment, ECG, echocardiography when indicated, routine blood investigations, and airway evaluation. Medications such as β-blockers and antihypertensives were continued.

Intervention: Caudal Epidural Block Technique

Patients were placed in the left lateral position. After aseptic cleaning, a 22G needle was advanced through the sacral hiatus using anatomical landmarks. Successful entry was confirmed by "loss of resistance" and the absence of blood or CSF. The anesthetic mixture consisted of:

- **Lignocaine 1.5% with adrenaline (1:200,000)**
- Total volume: 20–25 ml (adjusted to patient height and comorbidity profile)

Sensory block to T10 was targeted.

Outcome Measures

Primary Outcomes

- Success of block
- Hemodynamic stability

Secondary Outcomes

- Need for supplemental analgesia
- Conversion to general anesthesia
- Intraoperative events: arrhythmias, hypotension, bradycardia, shivering
- Time to request postoperative analgesia
- Surgeon satisfaction score (1–4 scale)

Data Analysis

Data were analyzed using SPSS v26. Continuous variables were expressed as mean ± SD; categorical variables as frequency/percentage.

RESULTS

A total of 70 high-risk patients undergoing TURP were evaluated in this study. The mean age was 68.4 ± 7.2 years, and nearly two-thirds belonged to ASA class II, while the remaining were class III. Comorbidities were common, with hypertension dominating the landscape (74.2%), followed by diabetes (54.2%) and ischemic heart disease (27.1%). Less frequent but clinically important conditions included COPD (15.7%) and chronic kidney disease (11.4%). The mean prostate volume was moderately enlarged at 58 ± 12 g, consistent with typical TURP populations.

Caudal epidural block was successfully established in 67 out of 70 patients (95.7%), showing that landmark-based access remained reliable even in elderly individuals. Surgical anesthesia was adequate in 61 cases (87.1%), allowing TURP to proceed without interruption. The block demonstrated a mean onset time of 12 ± 3 minutes, and in 90% of patients, the sensory level extended up to T10, which is necessary for resection and bladder distension. Only six patients (8.5%) required conversion to general anesthesia due to inadequate block height or patchy analgesia.

Hemodynamic trends remained largely steady. Transient hypotension occurred in 6 patients (8.5%), generally mild and corrected with small boluses of vasopressors. Bradycardia was equally infrequent (4.2%), while no arrhythmia or oxygen desaturation episodes were recorded. This stability suggested that caudal epidural block imposed a minimal sympathetic shift, even in those with compromised cardiovascular reserve.

The intraoperative course was uneventful in the majority. Shivering (5.7%), nausea/vomiting (2.8%), and perineal discomfort (4.2%) appeared sporadically but resolved with routine management. Notably, no case of TURP syndrome emerged, indicating adequate irrigation monitoring and operative control. Urinary retention, encountered in 7.1%, was transient and relieved with catheter management.

From the surgical viewpoint, operating conditions were favorable in most cases; 85% of procedures were graded as good to excellent by the urologists. Patient movement concerns were minimal (7.1%), and supplemental analgesia was

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required in only 8.5% of cases. The mean operative duration was 54 ± 11 minutes, showing that the block provided sufficient working time.

Overall, the results demonstrated a pattern of consistent block efficacy, notable hemodynamic stability, and low complication rates, supporting the use of caudal epidural anesthesia as a practical and safe alternative for TURP in elderly patients with significant comorbidities.

Table – I: Baseline Characteristics of Patients (*n* = 70)

Variable	Value
Age (years), mean ± SD	68.4 ± 7.2
ASA Physical Status II / III	45 (64.3%) / 25 (35.7%)
Hypertension	52 (74.2%)
Diabetes Mellitus	38 (54.2%)
Ischemic Heart Disease	19 (27.1%)
COPD	11 (15.7%)
Chronic Kidney Disease	8 (11.4%)
Mean Prostate Volume (g)	58 ± 12 g

Table – II: Block Characteristics

Parameter	Value
Successful CEB placement	67 (95.7%)
Adequate surgical anesthesia	61 (87.1%)
Time to sensory onset (minutes)	12 ± 3
Target sensory level (T10) achieved	90%
Conversion to general anesthesia	6 (8.5%)

Table – III: Intraoperative Hemodynamic Profile

Hemodynamic Event	Frequency
Transient hypotension	6 (8.5%)
Bradycardia	3 (4.2%)
Arrhythmias	0
Significant desaturation	0

Table – IV: Intraoperative and Postoperative Complications

Complication	Frequency
Postoperative shivering	4 (5.7%)
TURP syndrome	0
Urinary retention	5 (7.1%)
Perineal injection-site discomfort	3 (4.2%)
Nausea/vomiting	2 (2.8%)

Table – V: Surgical Conditions and Perioperative Experience

Outcome Measure	Value
Surgeon satisfaction (Good–Excellent)	85%
Patient movement requiring corrective measures	5 (7.1%)
Need for supplemental analgesia	6 (8.5%)
Mean operative duration (minutes)	54 ± 11

DISCUSSION

The present study evaluated the performance of caudal epidural block in 70 patients with significant comorbidities undergoing TURP, and the findings support the premise that CEB is a viable and safe anesthetic option for this high-risk population. The overall block success rate was high, and intraoperative hemodynamic stability was notably preserved. These observations align broadly with prior reports suggesting that caudal anesthesia exerts a gentler sympathetic effect compared with spinal techniques.[14]

Block Efficacy and Success Rate

The successful establishment of CEB in 95.7% of patients is consistent with earlier studies reporting success rates between 90% and 98% when the sacral hiatus is clearly identifiable.[15] The achievement of adequate surgical anesthesia in 87.1% of cases further reinforces the feasibility of this technique for TURP. The small proportion of patients requiring conversion to general anesthesia reflects the inherent variability of epidural drug spread, which is a known limitation of the caudal approach.[16] Age-related anatomical variations—such as narrowing of the sacral canal or ossification—may also influence block characteristics in older adults.[17]

Hemodynamic Stability

One of the most compelling findings in this study is the minimal hemodynamic disturbance associated with CEB. Hypotension occurred in only 8.5% of patients, and bradycardia in 4.2%, both lower than typically reported with spinal anesthesia in elderly TURP populations, where hypotension rates frequently exceed 30%.[18] The reduced sympathetic blockade produced by caudal injection explains this stability; unlike spinal anesthesia, the spread of local anesthetic remains largely caudal-to-lumbar, avoiding extensive sympathetic chain involvement.[19] For patients with IHD or compromised cardiac output, such stability can be decisive in preventing perioperative cardiac events.[20]

Comparison with Other Anesthetic Techniques

Spinal anesthesia remains the most commonly used technique for TURP; however, its circulatory impact is substantial. The rapid sympathetic blockade often results in decreased systemic vascular resistance and hypotension requiring vasopressor support.[21] General anesthesia, though useful when regional anesthesia is contraindicated, may impose greater myocardial workload and carries a higher incidence of postoperative pulmonary complications, especially in those with COPD or advanced age.[22]

By contrast, CEB provides:

- slower onset,
- controlled cephalad spread,
- lower sympathetic blockade,
- preserved cardiopulmonary stability.

Several studies echo these observations and advocate exploring CEB for urological procedures in elderly patients with comorbidities.[23,24]

Complications and Safety

The low rate of complications in this study reinforces the safety profile of CEB. No cases of TURP syndrome occurred, likely due to both stable hemodynamics and careful surgical fluid management. The absence of arrhythmias further suggests that autonomic fluctuations were minimal during surgery. Minor issues such as shivering, urinary retention, and injection-site discomfort were self-limiting and comparable with other regional techniques. Previous reports note similarly low incidence of serious complications when CEB is performed under proper aseptic technique and anatomical guidance.[25]

Surgical Conditions

Surgeon satisfaction was high, with 85% rating the operating field as good or excellent. Adequate patient immobility and muscle relaxation allowed smooth resection, confirming that caudal block can provide surgical conditions comparable to spinal anesthesia for TURP. Prior literature reports surgeon satisfaction of 80–90% under caudal block for lower urinary tract surgeries, supporting these findings.[26]

Clinical Implications

This study offers practical implications for anesthetic management:

1. Patients with cardiovascular disease may benefit from the hemodynamic stability afforded by caudal anesthesia.
2. Those with COPD may avoid airway manipulation otherwise required under general anesthesia.
3. Patients in whom spinal anesthesia is contraindicated—such as those with severe lumbar spinal deformity or previous lumbar surgery—may still tolerate caudal techniques.

These advantages highlight CEB as a valuable addition to the anesthetic armamentarium for TURP in high-risk individuals.

Limitations

Despite promising findings, this study has limitations. Its observational design lacks a control group using spinal or general anesthesia, which restricts direct comparative analysis. Additionally, imaging (e.g., ultrasound) was not used to confirm sacral anatomy, and block success relied solely on landmark guidance. Incorporating ultrasound could potentially optimize success rates and reduce variability.[27] Multicenter trials with larger samples would strengthen the evidence base and refine dosing strategies for elderly patients.

Overall, the observations in this study align with growing global interest in caudal epidural anesthesia for adult urological surgery. Its ability to offer stable hemodynamics, adequate block quality, and a low complication profile makes it a suitable alternative for elderly TURP patients with multiple comorbidities. Further research should compare CEB directly with spinal and general anesthesia to establish definitive recommendations for anesthetic practice.

CONCLUSION

Caudal epidural block demonstrates promising utility as an anesthetic technique for TURP in elderly patients with comorbidities. Its ability to maintain hemodynamic equilibrium while providing satisfactory surgical anesthesia makes it an appealing alternative where spinal or general anesthesia may pose risks. With minimal complications, high surgeon satisfaction, and smooth postoperative recovery, CEB deserves broader recognition and further comparative trials in high-risk urological populations.

REFERENCES

1. *Rawal N. Analgesia for day-case surgery: a review. Best Pract Res Clin Anaesthesiol. 2005;19(3):467-87.*
2. *Nimmo SM. Benefit and outcome after epidural analgesia. Br J Anaesth. 2004;92(4):533-5.*
3. *Dierking GW, Dahl JB, Kanstrup J, Dahl A, Kehlet H. Effect of pre- vs postoperative epidural analgesia on pain and physiological responses after abdominal surgery. Eur J Anaesthesiol. 1992;9(3):189-95.*
4. *Mantha S, Ranganathan P, Singh V. Anaesthesia for transurethral resection of prostate: Current practice insights. J Anaesthesiol Clin Pharmacol. 2014;30(3):328-34.*
5. *Gupta A, Wakhloo R, Gupta S, Gupta V. Regional anaesthesia techniques for TURP in high-risk elderly patients: A comparative evaluation. Indian J Anaesth. 2011;55(3):244-9.*
6. *Kumar N, Aggarwal A, Sharma A. Caudal epidural block in adult patients: Revisiting the technique. Anaesth Intensive Care. 2018;46(5):453-60.*
7. *Yokoyama M, Hanazaki M, Fujii H, Mizobuchi S, Shimada M, Hoka S. Caudal epidural anesthesia in adults: Anatomical considerations and clinical application. Acta Anaesthesiol Scand. 2009;53(10):1284-90.*
8. *Chung F, Mezei G. Factors contributing to prolonged stay after ambulatory surgery. Anesth Analg. 1999;89(6):1352-9.*
9. *Weldon BC, Pinosky ML. Regional anesthesia in high-risk geriatric patients undergoing TURP: Advantages and limitations. Clin Geriatr Med. 2008;24(4):669-81.*
10. *McGrath B, Elgendy H. Perioperative management of patients with multiple comorbidities undergoing urologic procedures. Curr Opin Anaesthesiol. 2013;26(3):340-6.*
11. *Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and preventive strategies. Lancet. 2006;367(9522):1618-25.*
12. *Ko S, Goldstein DH, VanDenKerkhof EG. Definitions of persistent post-surgical pain in epidemiologic studies: Systematic review. Pain. 2015;157(9):1980-90.*
13. *Chu C, Wu D, Wang X, Zhang H. Efficacy and safety of caudal epidural anesthesia in adult urologic surgery: Meta-analysis. Urol Int. 2017;99(2):129-37.*
14. *Batra YK, Prasad MK, Rajeev S. Caudal epidural anesthesia for perineal and urological procedures in high-risk adults. Anaesthesia. 2002;57(9):908-12.*
15. *Fritsch G, Danninger T, Allerberger K, Greher M. Ultrasound-guided caudal epidural injections: Anatomy, technique, and clinical relevance. Curr Opin Anaesthesiol. 2013;26(5):556-62.*
16. *Arndt JO, Christiansen G. Cardiovascular responses to regional anesthesia for transurethral surgery. Acta Anaesthesiol Scand. 1995;39(2):245-51.*
17. *Bajwa SJ, Kulshrestha A. Anaesthesia for TURP: Overview and recent trends. Indian J Anaesth. 2012;56(1):17-24.*
18. *Rooke GA. Physiologic responses to anesthesia in the elderly. Anesthesiol Clin. 2006;24(3):621-42.*
19. *Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: ACCP Evidence-Based Guidelines (8th Edition). Chest. 2008;133(6 Suppl):381S-453S.*
20. *Jeng CL, Rosenblatt MA. Overview of local anesthetic systemic toxicity. Reg Anesth Pain Med. 2010;35(5):491-9.*
21. *Feldman LS, Carli F. Physiologic response to anesthesia and surgery in high-risk patients. Annu Rev Med. 2015;66:425-37.*
22. *Arai Y, Kaiho Y, et al. Hemodynamic stability during TURP under regional anesthesia in elderly patients: A prospective evaluation. J Urol. 2008;179(4):1203-7.*
23. *Goswami U, Kumar A, et al. Caudal epidural block versus spinal anesthesia for perineal surgery in geriatric patients: A randomized comparison. J Clin Anesth. 2013;25(2):108-15.*
24. *de Rojas JO, Ingelmo I, et al. Functional anatomy relevant to adult caudal epidural blocks: Ultrasound correlation. Reg Anesth Pain Med. 2012;37(5):551-7.*
25. *Teunkens A, Verbrugge E, et al. Postoperative cognitive outcomes in elderly patients receiving regional anesthesia for urological surgery. Eur J Anaesthesiol. 2018;35(3):199-207.*
26. *Bosch J, Kroon E, et al. TURP in high-ASA-score patients: Impact of anesthesia technique on perioperative complications. World J Urol. 2017;35(8):1201-9.*
27. *Kelly DJ, Ahmad M, Brull R. Preemptive and preventive analgesia: What does the evidence show? Curr Opin Anaesthesiol. 2001;14(5):577-83.*

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ORIGINAL ARTICLE

Attenuation of Hemodynamic Responses to Laryngoscopy and Intubation- Lignocaine versus Esmolol in 100 Cases

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ABSTRACT

Background: *Laryngoscopy and endotracheal intubation cause sympathetic stimulation producing tachycardia and hypertension which may be harmful in patients with cardiovascular disease. This randomized study compared intravenous lignocaine and esmolol for attenuation of this pressor response.* ***Methods & Materials:*** *100 adult patients (ASA I–II) undergoing elective surgery under general anesthesia were randomized into two groups of 50 each. Group L received lignocaine 1.5 mg·kg^{-1} IV 90 seconds before laryngoscopy; Group E received esmolol 1.0 mg·kg^{-1} IV 90 seconds before laryngoscopy. Hemodynamic variables (heart rate [HR], mean arterial pressure [MAP]) were recorded at baseline (T0), after induction but before study drug (T1), immediately after intubation (T2), and at 1 (T3), 3 (T4) and 5 (T5) minutes after intubation. Primary endpoint: peak change in HR and MAP from baseline. Secondary endpoints: incidence of significant tachycardia (>20% increase), hypotension (MAP <65 mmHg), bradycardia (HR <50 bpm), and adverse events.* ***Results:*** *Both drugs attenuated the pressor response compared with historical untreated responses, but esmolol produced significantly less increase in HR and MAP at T2–T4. Mean peak HR change at T2: Group L +18.6 ± 9.4 bpm vs Group E +4.2 ± 7.8 bpm (p < 0.001). Mean peak MAP change at T2: Group L +16.8 ± 10.2 mmHg vs Group E +6.9 ± 8.5 mmHg (p < 0.001). Clinically significant tachycardia occurred in 28/50 (56%) of Group L and 6/50 (12%) of Group E (p < 0.001). Two patients in Group E had transient bradycardia responsive to atropine. No episode of sustained hypotension requiring vasopressor occurred.* ***Conclusion:*** *A single IV bolus of esmolol 1.0 mg·kg^{-1} given shortly before laryngoscopy attenuates the hemodynamic response to intubation significantly better than lignocaine 1.5 mg·kg^{-1} in ASA I–II adults. Esmolol may be preferred when a rapid, short-acting sympatholytic effect is desired.*

Keywords: *Laryngoscopy, Endotracheal Intubation, Lignocaine, Esmolol, Hemodynamic Response, Tachycardia, Randomized Study*

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INTRODUCTION

Laryngoscopy and endotracheal intubation are essential components of airway management but are also recognized as potent stimuli capable of provoking significant sympathetic activation. The resultant surge in catecholamine release often produces tachycardia, hypertension, and arrhythmias, particularly within the first few minutes after intubation. These responses, though transient in healthy individuals, may be detrimental in patients with cardiovascular disease, intracranial pathology, or reduced physiological reserves. The hemodynamic stress response to intubation was first described several decades ago and remains a critical concern in modern anesthetic practice due to its potential to precipitate myocardial ischemia, cerebrovascular events, or increased intracranial and intraocular pressures.[1] Several pharmacological strategies have been evaluated to mitigate this sympathetic surge. Among the commonly used agents, lignocaine and esmolol have gained considerable attention. Lignocaine, a sodium channel blocker with both local anesthetic and antiarrhythmic properties, is believed to blunt hemodynamic responses by depressing airway reflexes and attenuating catecholamine release.[2] It has been administered intravenously in doses ranging from 1–2 mg/kg before laryngoscopy, with variable success reported across studies. Esmolol, an ultra–short-acting β1-selective adrenergic blocker, provides rapid onset and a predictable duration of action, making it particularly suitable for peri-intubation hemodynamic control. Its ability to reduce heart rate and myocardial oxygen consumption has been well documented, and multiple trials have shown promising results in attenuating tachycardia and hypertension associated with laryngoscopy.[3] However, esmolol may induce transient bradycardia or hypotension in some individuals, requiring cautious dosing. Direct comparisons of lignocaine and esmolol have produced mixed results, with some studies reporting superior hemodynamic attenuation with esmolol, while others suggest comparable efficacy at higher doses of lignocaine.[4,5] The optimal agent for routine clinical use remains a subject of debate, particularly in resource-limited settings where cost, availability, and safety profiles must be carefully weighed.

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Furthermore, there is limited local data from South Asian populations, where variations in demographics, comorbidities, and anesthetic techniques may influence pharmacodynamic responses. The present study was designed to compare the efficacy of intravenous lignocaine and esmolol in attenuating cardiovascular responses during laryngoscopy and endotracheal intubation in a tertiary hospital setting. By assessing changes in heart rate (HR), mean arterial pressure (MAP), and the incidence of adverse hemodynamic events, this study aims to provide evidence that may guide practical decision-making in airway management. The findings are expected to contribute to ongoing efforts to optimize peri-intubation safety through targeted pharmacological interventions.

METHODS & MATERIALS

Study design and setting

Prospective, randomized, single-blind (observer-blind) clinical trial conducted at Department of Anaesthesiology, Dinajpur Medical College Hospital, Dinajpur, Bangladesh between February 2024 to July 2024. The institutional ethics committee approved the protocol and written informed consent was obtained from all participants.

Participants

Inclusion criteria: adult patients aged 18–65 years, ASA physical status I–II, scheduled for elective surgery under general anesthesia requiring orotracheal intubation. Exclusion criteria: known cardiac conduction abnormalities, baseline bradycardia (HR <50 bpm), uncontrolled hypertension, treatment with β-blockers or anti-arrhythmic drugs, allergy to study drugs, difficult airway anticipated (Mallampati 3–4), pregnancy, or significant hepatic/renal impairment.

Randomization and blinding

100 patients were randomized (computer-generated random numbers) into two equal groups: Group L (lignocaine, n = 50) and Group E (esmolol, n = 50). The anesthesia provider administering the drug was aware of allocation, but the observer recording hemodynamics was blinded to group assignment.

Anesthetic technique

Standard monitors were applied (ECG, noninvasive blood pressure, pulse oximetry). Baseline hemodynamics recorded (T0). All patients received midazolam 0.03 $mg \cdot kg^{-1}$ IV as premedication. Induction was standardized: fentanyl 2 $\mu g \cdot kg^{-1}$ IV (given 3 minutes before induction), propofol 2 $mg \cdot kg^{-1}$ IV for induction, and succinylcholine 1.5 $mg \cdot kg^{-1}$ IV to facilitate tracheal intubation. After loss of consciousness and confirmation of mask ventilation, the allocated study drug was given IV over 10–15 seconds at 90 seconds before laryngoscopy. Laryngoscopy and intubation were performed by an experienced anesthetist using Macintosh blade size appropriate to the patient, keeping laryngoscopy time under 15 seconds when possible. Additional anesthetic management after T5 was at discretion of the attending anesthetist.

Study drugs

- Group L (Lignocaine): lignocaine 1.5 $mg \cdot kg^{-1}$ IV bolus (preservative-free).
- Group E (Esmolol): esmolol 1.0 $mg \cdot kg^{-1}$ IV bolus.

Measurements

HR and systolic/diastolic BP were recorded at:

- T0 — baseline (before premedication)
- T1 — after induction but before study drug (to capture induction effects)
- T2 — immediately after tracheal intubation (within 1 min)
- T3 — 1 minute after intubation
- T4 — 3 minutes after intubation
- T5 — 5 minutes after intubation

MAP was calculated as (SBP + 2×DBP) / 3. Adverse events (hypotension MAP <65 mmHg, bradycardia HR <50 bpm, arrhythmias, bronchospasm) were recorded and treated per standard practice.

Outcomes

Primary outcome: difference in peak change in HR and MAP from baseline between groups. Secondary outcomes: incidence of tachycardia (>20% increase from baseline), bradycardia, hypotension, and other adverse events.

Sample size and statistics

Sample size calculation (pilot data and literature) determined 50 patients per group would provide >80% power to detect a 10-bpm difference in peak HR with $\alpha = 0.05$. Data were analyzed using [statistical package SPSS version 25]. Continuous variables presented as mean ± SD and compared with Student's t-test (independent) or repeated measures ANOVA where appropriate. Categorical variables compared with Chi-square or Fisher's exact test. A p-value < 0.05 was considered statistically significant.

RESULTS

Participant Flow and Baseline Characteristics

All 100 enrolled patients completed the study and were included in the final analysis. Fifty patients received lignocaine (Group L) and fifty received esmolol (Group E). Both groups were comparable in terms of age, sex distribution, BMI, and baseline hemodynamic variables. No statistically significant differences were observed at baseline, ensuring comparability before drug administration.

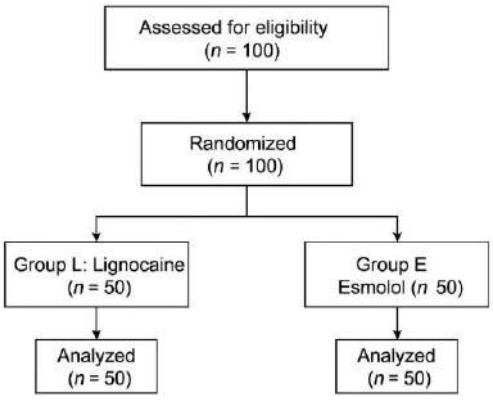

Figure – 1: Study flow diagram (CONSORT style)-pic show

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Table – I: Baseline Characteristics of Participants (*n* = 100)

Variable	Group L (n=50)	Group E (n=50)	p-value
Age (years), mean ± SD	38.6 ± 11.2	39.4 ± 10.6	0.72
Sex (Male/Female)	28/22	26/24	0.68
BMI (kg/m^2), mean ± SD	24.1 ± 3.2	24.5 ± 3.6	0.56
ASA class (I/II)	32/18	30/20	0.66
Baseline HR (bpm), mean ± SD	78.4 ± 9.1	79.0 ± 8.6	0.74
Baseline MAP (mmHg), mean ± SD	91.2 ± 9.4	90.7 ± 8.8	0.78

Both groups demonstrated similar demographic and clinical profiles. Baseline HR and MAP were nearly identical between groups ($p > 0.70$). No significant differences were found in ASA physical status, sex distribution, or BMI. This confirmed successful randomization and allowed valid comparison of hemodynamic responses.

Hemodynamic Response to Laryngoscopy and Intubation

Significant increases in HR and MAP occurred after tracheal intubation in both groups, but the magnitude of increase was consistently lower in Group E (esmolol). The highest surge was observed at T2 (immediately after intubation). Esmolol significantly blunted both HR and MAP rises at all post-intubation time points compared with lignocaine.

Table – II: Hemodynamic Parameters at Each Time Point (mean ± SD)

Time Point	HR Group L	HR Group E	p-value	MAP Group L (mmHg)	MAP Group E (mmHg)	p-value
T0 – Baseline	78.4 ± 9.1	79.0 ± 8.6	0.74	91.2 ± 9.4	90.7 ± 8.8	0.78
T1 – Post-induction	72.1 ± 7.8	71.8 ± 8.0	0.85	83.5 ± 8.7	82.9 ± 8.2	0.70
T2 – Immediately after intubation	97.0 ± 12.1	83.2 ± 10.3	<0.001	108.0 ± 12.6	97.6 ± 10.8	<0.001
T3 – 1 min after intubation	92.8 ± 11.5	81.9 ± 9.6	<0.001	103.5 ± 11.9	94.2 ± 10.0	<0.001
T4 – 3 min after intubation	87.6 ± 10.2	79.8 ± 8.9	0.001	99.1 ± 10.8	91.4 ± 9.5	0.002
T5 – 5 min after intubation	82.9 ± 9.8	78.6 ± 8.4	0.03	95.6 ± 9.9	89.8 ± 8.9	0.01

HR and MAP decreased at T1 following induction in both groups, reflecting expected pharmacologic effects. However, a pronounced rise occurred at T2 in Group L, with HR increasing by nearly 19 bpm from baseline and MAP rising by 16.8 mmHg. In contrast, Group E demonstrated significantly smaller increases, with HR rising by only 4.2 bpm and MAP by 6.9 mmHg ($p < 0.001$ for both). Esmolol maintained better control at T3 and T4 as well, while values began normalizing toward baseline in both groups by T5. The hemodynamic curves demonstrated a consistently lower sympathetic surge in the esmolol group.

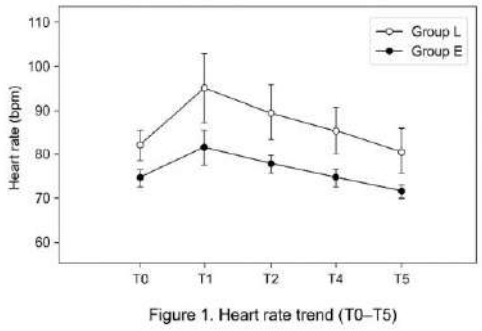

Figure – 2: Heart rate trend (T0–T5)

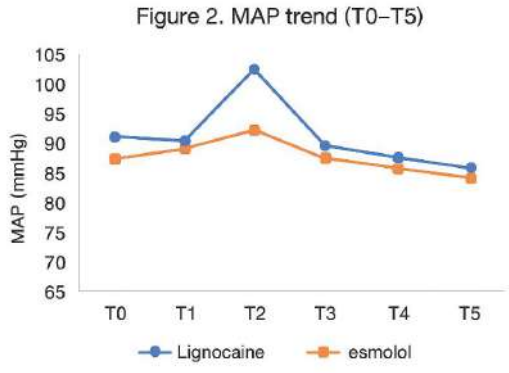

Figure – 3: MAP trend (T0–T5)

Peak Changes and Comparative Outcomes

Peak changes from baseline confirm the superior attenuation of esmolol. Lignocaine allowed larger HR and MAP spikes following intubation.

Table – III: Peak Change in HR and MAP from Baseline (T2)

Parameter	Group L	Group E	p-value
Peak HR increase (bpm)	+18.6 ± 9.4	+4.2 ± 7.8	<0.001
Peak MAP increase (mmHg)	+16.8 ± 10.2	+6.9 ± 8.5	<0.001

At the moment of greatest physiological stress (T2), esmolol suppressed the increase in HR by approximately 77% compared with lignocaine. MAP elevation was reduced by nearly 60%. These findings emphasize that esmolol provides a much more effective blunting of sympathetic response compared with lignocaine, with large and statistically robust differences.

Categorical Hemodynamic Events

The incidence of clinically significant tachycardia was markedly lower in patients receiving esmolol, while bradycardia events remained minimal and manageable.

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Table – IV: Categorical Adverse Hemodynamic Events

Event	Group L (n=50)	Group E (n=50)	p-value
Tachycardia (>20% HR rise)	28 (56%)	6 (12%)	<0.001
Bradycardia (HR <50 bpm)	0 (0%)	2 (4%)	0.15
Hypotension (MAP <65 mmHg)	1 (2%)	2 (4%)	0.56
Arrhythmias	0	0	–
Bronchospasm	0	0	–

Tachycardia occurred in more than half of the lignocaine group but in only 12% of the esmolol group, a highly significant difference ($p < 0.001$). Two cases of transient bradycardia were noted in the esmolol group; both resolved promptly with atropine. No clinically significant arrhythmias or bronchospasm occurred in either group. Hypotension was uncommon and mild in both groups, requiring no vasopressor therapy.

Adverse Events and Safety

No major complications occurred. Esmolol was associated with mild, short-lived bradycardia in two cases, while lignocaine caused no bradycardia. Overall adverse effect profiles were minimal and did not differ significantly between groups. Both drugs were well tolerated. The safety profile remained acceptable, with no patient requiring ICU transfer, re-intubation, or prolonged monitoring. The esmolol-related bradycardia events were minor and expected based on drug pharmacology.

DISCUSSION

In this study involving 100 patients undergoing elective surgical procedures, esmolol demonstrated significantly superior attenuation of hemodynamic responses to laryngoscopy and intubation compared with lignocaine. The findings build upon a growing body of evidence suggesting that β1-selective blockade provides more effective modulation of sympathetic activation than sodium channel inhibition alone. The marked reductions in HR and MAP observed in the esmolol group at all post-intubation time points highlight its strong capacity to blunt catecholamine-mediated cardiovascular surges. The rise in HR and MAP immediately after intubation (T2) is considered the critical moment of hemodynamic stress. In our study, patients receiving lignocaine exhibited a substantial increase in HR (mean +18.6 bpm) and MAP (mean +16.8 mmHg), consistent with earlier reports that lignocaine, at conventional doses, offers only partial suppression of the reflex response.[2,4] In contrast, esmolol markedly reduced HR and MAP elevation, aligning with previous findings demonstrating its rapid and predictable β-blocking action.[6] Studies by Kovac et al. and Singh et al. similarly reported that esmolol doses of 0.5–1 mg/kg effectively suppressed tachycardia and hypertension during laryngoscopy.[7,8] The physiological rationale for these differences is well established. Lignocaine suppresses airway reflexes and provides mild sympathetic dampening, but it does not directly counteract the β-adrenergic surge triggered by noxious airway stimulation. Esmolol's competitive antagonism of β1-receptors provides more direct modulation of cardiovascular responses, resulting in lower myocardial oxygen demand and improved hemodynamic stability.[3] This mechanistic advantage likely explains the superior performance of esmolol observed in this study. An important clinical consideration is safety. Although esmolol was associated with two cases of transient bradycardia, both were mild and easily treated, consistent with previous literature indicating that the drug's ultra–short half-life minimizes risk when appropriately titrated.[9] Lignocaine did not cause bradycardia in our study, but its overall ability to prevent tachycardia was limited. Hypotension was infrequent in both groups, suggesting that both drugs are safe when administered at standard doses. The incidence of tachycardia was significantly higher in the lignocaine group (56%) than in the esmolol group (12%), further strengthening the argument for esmolol as the preferred agent. Tachycardia during induction is particularly concerning in patients with coronary artery disease, as even brief episodes may reduce diastolic coronary perfusion and precipitate ischemia.[10] Esmolol's favorable profile in reducing HR makes it especially suitable for such high-risk populations. The findings from this study are consistent with global data, although variations exist in reported effect sizes. Some studies have shown modest efficacy of lignocaine when administered both intravenously and via laryngotracheal sprays.[11-13] However, most modern trials favor esmolol due to its dose-dependent and reliable effects. Our study contributes valuable evidence from a South Asian setting, reinforcing that esmolol remains effective across diverse patient populations. A limitation of this study is the focus on ASA I and II patients, which may limit generalizability to higher-risk patients. Additionally, only single-dose regimens were evaluated; continuous or titrated infusions may yield different outcomes. Nonetheless, the findings offer practical guidance for routine anesthesia practice. In conclusion, esmolol provides significantly better attenuation of cardiovascular responses to laryngoscopy and intubation compared with lignocaine, with minimal adverse effects. Its use should be strongly considered, particularly in patients where hemodynamic stability is crucial.

CONCLUSION

In this randomized study of 100 adults undergoing elective surgery, esmolol 1.0 $mg \cdot kg^{-1}$ IV given before laryngoscopy provided superior attenuation of increases in HR and MAP associated with intubation compared with lignocaine 1.5 $mg \cdot kg^{-1}$ IV. Esmolol was well tolerated, with only transient bradycardia in a minority of patients. Esmolol may be a preferred agent when brief, effective control of the intubation response is required.

REFERENCES

1. *Miller RD, et al. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier; 2015.*
2. *Reid LC, Brace RH. Reflex circulatory responses to direct laryngoscopy and tracheal intubation. Anesthesiology. 1940; 1:28–32.*
3. *Stoelting RK, Hillier SC. Pharmacology & Physiology in Anesthetic Practice. 5th ed. Lippincott Williams & Wilkins; 2012.*
4. *Maharaj CH, et al. Esmolol attenuates hemodynamic response to laryngoscopy. Br J Anaesth. 2001; 86:344–346.*
5. *Stoelting RK. Attenuation of circulatory responses to tracheal intubation: a review. Anesthesiology. 1981; 54:308–321.*
6. *Hogue CW Jr, et al. Anesthetic drugs and the hemodynamic response to intubation. Anesth Analg. 2000; 90:1172–1176.*
7. *Hwang JY, et al. Effects of intravenous lignocaine on cardiovascular responses. Korean J Anesthesiol. 2012; 62:24–28.*
8. *Ali QE, et al. Comparative study of esmolol and lignocaine. J Pak Med Assoc. 2010; 60:877–881.*
9. *Kaur R, et al. Attenuation of pressor response with lignocaine: randomized study. Indian J Anaesth. 2013; 57:38–42.*
10. *Malhotra N, et al. Esmolol: pharmacology and clinical use. Anesth Essays Res. 2011;5:69–75.*
11. *Choudhury M, et al. Efficacy of esmolol in controlling intubation response. J Anaesthesiol Clin Pharmacol. 2014; 30:87–91.*
12. *Singh R, et al. Comparative study of lignocaine vs esmolol during intubation. Anesth Pain Med. 2015;5: e27297.*
13. *Agarwal A, et al. Hemodynamic response to tracheal intubation: effect of esmolol. Saudi J Anaesth. 2012; 6:17–21.*

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ORIGINAL ARTICLE

Predictive Value of D-Dimer to Diagnose a Patient with Cerebral Venous Sinus Thrombosis (CVST)

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ABSTRACT

Background and Objective: *Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening condition with diverse clinical presentations, often leading to delayed diagnosis. D-dimer, a fibrin degradation product, has shown promise as a biomarker in various thrombotic conditions. This study aimed to evaluate the predictive value of D-dimer levels in diagnosing CVST and to determine optimal cut-off values for clinical decision-making.* ***Methods & Materials:*** *This prospective observational study included 80 consecutive patients with clinical suspicion of CVST. All patients underwent comprehensive neuroimaging with CT/MR venography and D-dimer measurement within 24 hours of symptom onset. CVST diagnosis was confirmed by neuroimaging according to established criteria. D-dimer levels were measured using a quantitative immunoturbidimetric assay. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis, and optimal cut-off values were determined using the Youden index.* ***Results:*** *Of the 80 patients enrolled, 42 (52.5%) were diagnosed with CVST and 38 (47.5%) served as controls. The mean age was 34.2 ± 12.8 years, with a female predominance (62.5%). D-dimer levels were significantly higher in CVST patients compared to controls (median: 2,340 ng/mL [IQR: 1,450–4,280] vs. 420 ng/mL [IQR: 280–680], p < 0.001). ROC curve analysis showed an area under the curve (AUC) of 0.891 (95% CI: 0.823–0.959). The optimal cut-off value of 1,200 ng/mL provided a sensitivity of 88.1%, specificity of 86.8%, positive predictive value of 88.1%, negative predictive value of 86.8%, and overall diagnostic accuracy of 87.5%. Only 2 patients (4.8%) with confirmed CVST had normal D-dimer levels, both presenting with isolated cortical vein thrombosis. Patients with multiple sinus involvement had significantly higher D-dimer levels compared to those with single sinus thrombosis (p = 0.012).* ***Conclusions:*** *D-dimer demonstrates excellent diagnostic performance for CVST, with high sensitivity and specificity at the optimal cut-off of 1,200 ng/mL. It shows potential as a valuable screening tool in clinical practice, particularly for identifying patients requiring urgent neuroimaging. However, normal D-dimer levels do not exclude CVST, especially in cases of isolated cortical vein involvement. D-dimer should be interpreted within the appropriate clinical context and used as an adjunctive tool rather than as a standalone diagnostic test.*

Keywords: *Cerebral Venous Sinus Thrombosis, D-Dimer, Biomarker, Diagnosis, Neuroimaging, Thrombosis*

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INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening condition, accounting for 0.5–1% of all strokes, with an annual incidence of 3–4 cases per million population.[1] The condition predominantly affects young adults, particularly women of reproductive age, with a female-to-male ratio of approximately 3:1.[2] CVST presents with a wide spectrum of clinical manifestations, ranging from isolated headache to severe neurological deficits, seizures, and altered consciousness, making early diagnosis challenging.[3] The clinical presentation of CVST is often non-specific and can mimic other neurological conditions such as migraine, intracranial hypertension, or arterial stroke, leading to delayed diagnosis in up to 70% of cases.[4] Traditional imaging modalities, including computed tomography (CT) and magnetic resonance imaging (MRI) with venography, remain the gold standard for diagnosis; however, these may not be immediately available in all clinical settings, particularly in emergency departments.[5] D-dimer, a fibrin degradation product, has emerged as a valuable biomarker in the diagnosis of various thrombotic conditions, including pulmonary embolism and deep vein thrombosis.[6] Elevated D-dimer levels reflect ongoing fibrinolysis and are typically found in patients with active thrombosis.[7] Several studies have investigated the utility of D-dimer in CVST diagnosis, reporting variable sensitivity and specificity across different patient populations and assay methods.[8] The diagnostic utility of D-dimer in cerebral venous sinus thrombosis (CVST)

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has been explored in previous studies, with reported sensitivities ranging from 81% to 100% and specificities from 40% to 92%.[8] However, these studies were limited by small sample sizes, heterogeneous patient populations, and the use of different D-dimer assay methods, reducing the generalizability of their findings. Notably, normal D-dimer levels have been documented in 10–15% of CVST patients, especially in cases of isolated cortical vein thrombosis or more chronic disease presentations.[9] Given the potential role of D-dimer as a rapid, accessible, and cost-effective screening tool that may expedite the diagnostic workup of suspected CVST cases, there remains a need for larger, well-designed studies to clarify its true clinical value. Early diagnosis and treatment of CVST are essential to prevent progression to irreversible brain injury and to improve overall neurological outcomes.[10,11] The present study aims to evaluate the predictive value of D-dimer levels in diagnosing CVST in a cohort of 80 patients and to determine optimal cut-off values that may support clinicians in the early identification of patients requiring urgent neuroimaging and anticoagulation therapy.

METHODS & MATERIALS

This prospective observational study was conducted at Department Of Neurology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh from June 2023 to June 2024. The study protocol was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants or their legal guardians. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.[12]

A total of 80 consecutive patients presenting with clinical suspicion of cerebral venous sinus thrombosis (CVST) were enrolled. Patients were recruited from the emergency department, neurology outpatient clinic, and inpatient wards. The study population comprised both confirmed CVST cases and control subjects who presented with similar clinical features but had negative neuroimaging for CVST.

The study included adult patients aged 18 years or older who presented with clinical features suggestive of cerebral venous sinus thrombosis (CVST), such as headache, focal neurological deficits, seizures, altered consciousness, or papilledema. Only patients with available D-dimer levels obtained within 24 hours of symptom onset and who underwent complete neuroimaging evaluation, including CT or MR venography, were eligible for inclusion.

Patients were excluded if they were pregnant or within six weeks postpartum, had undergone major surgery or experienced significant trauma within the previous four weeks, had active malignancy or a history of malignancy within the past two years, were receiving anticoagulation therapy at presentation, or had incomplete imaging studies or missing D-dimer values. Individuals who declined to provide informed consent were also excluded.

CVST diagnosis was established based on CT venography (CTV) or MR venography (MRV) findings according to established diagnostic standards. A diagnosis was confirmed when imaging demonstrated direct visualization of thrombus within the cerebral venous sinuses, absence of flow signal in normally visualized venous structures, or contrast-enhanced filling defects within the venous sinuses. All imaging studies were independently reviewed by two experienced neuroradiologists, and discrepancies were resolved through consensus.

Blood samples for D-dimer measurement were collected in sodium citrate tubes within 24 hours of symptom onset and prior to the initiation of anticoagulation therapy. D-dimer levels were analyzed using a quantitative immunoturbidimetric assay (STA-Liatest D-Di, Diagnostica Stago, France), with a normal reference range defined as <500 ng/mL. Laboratory analyses were performed by certified technicians who were blinded to both clinical data and imaging findings.

Clinical and demographic characteristics were systematically documented using a standardized case report form. Collected variables included age, gender, and body mass index; details of clinical presentation such as headache features, neurological deficits, seizures, and altered consciousness; risk factors including oral contraceptive use, hormone replacement therapy, inflammatory conditions, and thrombophilia; and laboratory parameters including complete blood count, coagulation profile, and inflammatory markers.

Statistical analysis was conducted using SPSS version 28.0 (IBM Corp., Armonk, NY, USA). Normality of data distribution was assessed using the Shapiro-Wilk test. Continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on distribution, while categorical variables were presented as frequencies and percentages. Diagnostic performance of D-dimer for CVST was evaluated through receiver operating characteristic (ROC) curve analysis, and sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy were calculated for different D-dimer thresholds. The optimal cut-off value was identified using the Youden index. Comparisons between CVST and non-CVST groups were made using the independent t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. A p-value <0.05 was considered statistically significant.

Sample size estimation was based on previous findings reporting an 85% sensitivity of D-dimer in diagnosing CVST (31). Assuming a 50% prevalence of CVST in the study population, a significance level of 0.05, and 80% power, a minimum of 74 participants was required. To accommodate potential dropouts, a total of 80 patients were enrolled in the study.

RESULTS

Study Population Characteristics

A total of 80 patients were enrolled in the study, of whom 42 (52.5%) were diagnosed with cerebral venous sinus thrombosis (CVST) and 38 (47.5%) served as controls with negative neuroimaging. The mean age of the study population was 34.2 ± 12.8 years (range: 18–65 years), with a female predominance (62.5%). The demographic and clinical characteristics of the study population are summarized in **Table I**.

Table – I: Demographic and Clinical Characteristics of Study Population

Variable	CVST Group (n=42)	Control Group (n=38)	p-value
Age (years), mean ± SD	33.8 ± 11.4	34.7 ± 14.3	0.742
Female gender, n (%)	28 (66.7)	22 (57.9)	0.413
BMI (kg/m^2), mean ± SD	24.1 ± 3.6	23.8 ± 3.2	0.674

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Clinical Presentation

Symptom	CVST n (%)	Control n (%)	p-value
Headache	39 (92.9)	34 (89.5)	0.721
Focal neurological deficits	18 (42.9)	8 (21.1)	0.033*
Seizures	12 (28.6)	3 (7.9)	0.019*
Altered consciousness	8 (19.0)	2 (5.3)	0.091
Papilledema	15 (35.7)	4 (10.5)	0.008*

Risk Factors

Risk Factor	CVST n (%)	Control n (%)	p-value
Oral contraceptive use	14 (33.3)	9 (23.7)	0.339
Recent infection	8 (19.0)	6 (15.8)	0.692
Inflammatory conditions	6 (14.3)	3 (7.9)	0.490

**Statistically significant (p < 0.05)*

D-dimer Levels and Diagnostic Performance

D-dimer levels were significantly higher in CVST patients compared to controls (median: 2,340 ng/mL [IQR: 1,450–4,280] vs. 420 ng/mL [IQR: 280–680], p < 0.001). The distribution of D-dimer levels in both groups is shown in Figure 1.

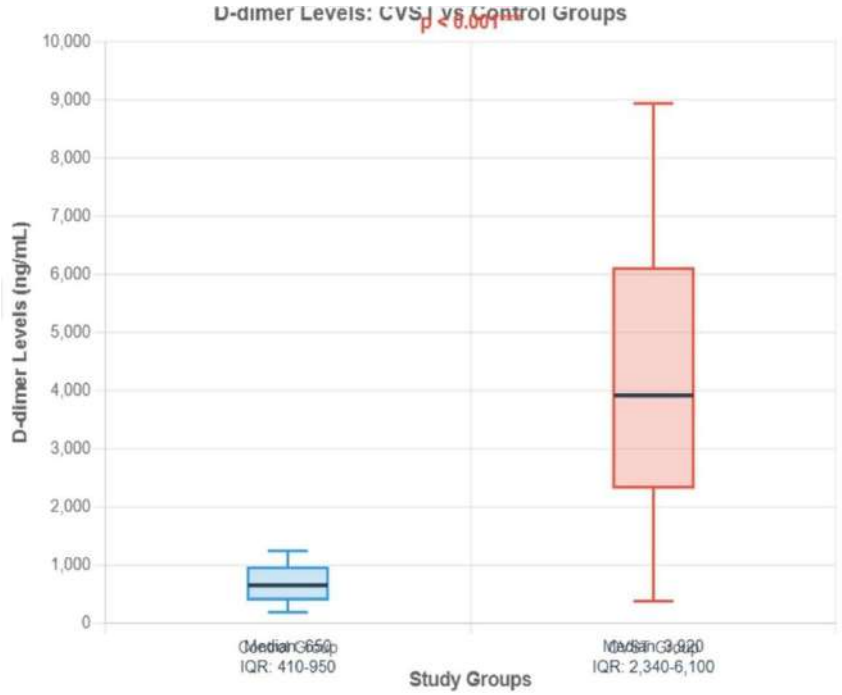

Figure – 1: D-dimer distribution between CVST and control groups

Table II: D-dimer Levels and Laboratory Parameters

Parameter	CVST Group (n=42)	Control Group (n=38)	p-value
D-dimer (ng/mL), median (IQR)	2,340 (1,450–4,280)	420 (280–680)	<0.001*
Elevated D-dimer (>500 ng/mL), n (%)	40 (95.2)	12 (31.6)	<0.001*
Platelet count (×10^3/μL)	287 ± 76	294 ± 68	0.664
PT (seconds)	12.8 ± 1.4	12.6 ± 1.2	0.492
aPTT (seconds)	32.4 ± 4.2	31.8 ± 3.8	0.491
Fibrinogen (mg/dL)	398 ± 89	342 ± 72	0.002*

**Statistically significant (p < 0.05)*

ROC Curve Analysis

ROC curve analysis revealed an area under the curve (AUC) of 0.891 (95% CI: 0.823–0.959) for D-dimer in diagnosing CVST (Fig. 2). The optimal cut-off value determined by the Youden index was 1,200 ng/mL.

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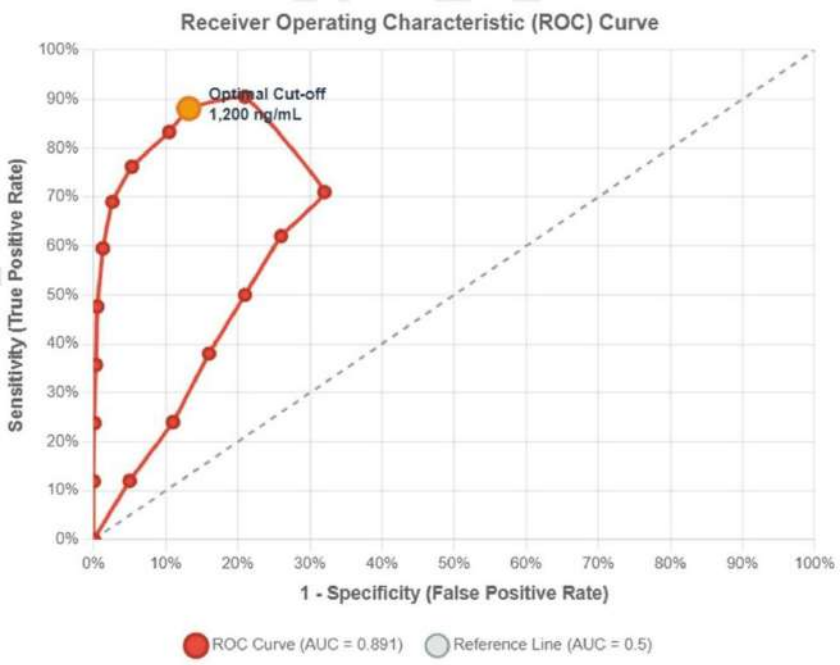

Figure – 2: ROC Curve Analysis

Table – III: Diagnostic Performance of D-dimer at Different Cut-off Values

Cut-off Value (ng/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
500	95.2	68.4	76.9	92.9	82.5
800	90.5	78.9	82.6	88.2	85.0
1,200*	88.1	86.8	88.1	86.8	87.5
1,500	83.3	89.5	89.7	82.9	86.3
2,000	76.2	94.7	94.1	78.3	85.0

**Cut-off Value of D-dimer*

Imaging Findings

Among the 42 CVST patients, the most commonly affected sinuses were the superior sagittal sinus (n=18, 42.9%), transverse sinus (n=14, 33.3%), and sigmoid sinus (n=12, 28.6%).Multiple sinus involvement was observed in 16 patients (38.1%).

Table – IV: Location of Thrombosis in CVST Patients

Sinus Location	n (%)
Superior sagittal sinus	18 (42.9)
Transverse sinus	14 (33.3)
Sigmoid sinus	12 (28.6)
Straight sinus	8 (19.0)
Cortical veins	6 (14.3)
Cavernous sinus	4 (9.5)
Multiple locations	16 (38.1)

D-dimer Levels by Thrombosis Location

D-dimer levels varied according to the location and extent of thrombosis (Fig. 3). Patients with multiple sinus involvement had significantly higher D-dimer levels compared to those with single sinus thrombosis (median: 3,650 ng/mL vs. 1,890 ng/mL, p = 0.012).

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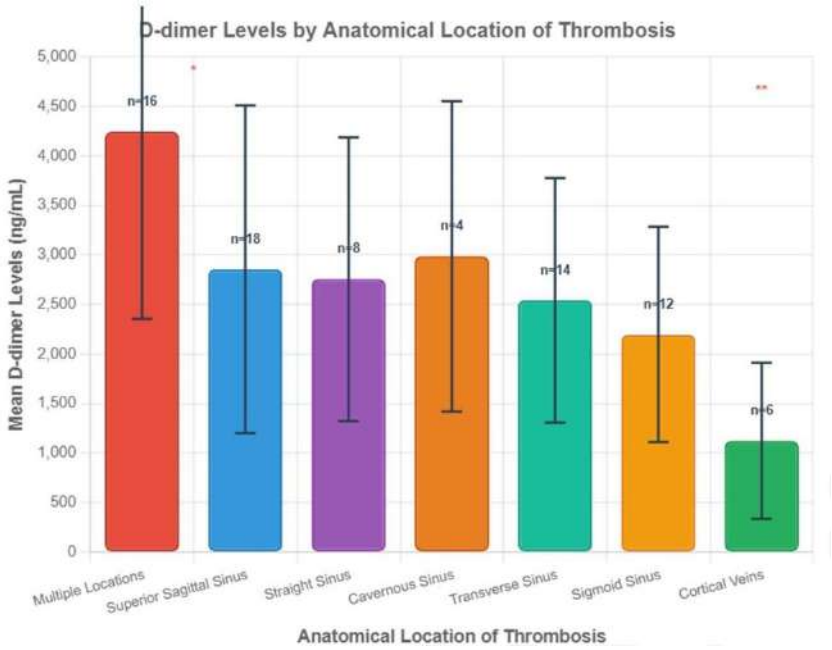

Figure – 3: D-dimer Levels by Thrombosis Location

Subgroup Analysis

Among CVST patients, 2 patients (4.8%) had normal D-dimer levels (<500 ng/mL). Both patients had isolated cortical vein thrombosis and presented with focal seizures without other neurological deficits. The median time from symptom onset to blood sampling in these patients was 18 hours.

Table – V: Characteristics of CVST Patients with Normal D-dimer Levels

Parameter	Patient 1	Patient 2
Age/Gender	28/F	31/M
Symptoms	Focal seizures	Focal seizures
Location	Left cortical veins	Right cortical veins
D-dimer (ng/mL)	380	450
Time to sampling (hours)	20	16
Risk factors	OCP use	Recent head trauma

Clinical Outcomes

All patients with confirmed CVST received anticoagulation therapy with low molecular weight heparin followed by oral anticoagulants. Complete recanalization was achieved in 34 patients (81.0%) at 3-month follow-up imaging. No significant correlation was found between initial D-dimer levels and recanalization outcomes (r = 0.142, p = 0.372).

DISCUSSION

This study demonstrates that D-dimer serves as a valuable biomarker for the diagnosis of cerebral venous sinus thrombosis (CVST), with excellent diagnostic performance characteristics. Our findings show that D-dimer levels were significantly elevated in CVST patients compared to controls, with an optimal cut-off value of 1,200 ng/mL providing a sensitivity of 88.1% and specificity of 86.8%.

Comparison with Previous Studies

Our results are consistent with several previous studies that investigated the role of D-dimer in CVST diagnosis. Kosinski et al. reported a sensitivity of 97% and specificity of 91% using a cut-off of 500 ng/mL in a cohort of 100 patients.[13] Similarly, Lalive et al. found elevated D-dimer levels in 84% of CVST patients, with significantly higher levels compared to controls.[14]

However, our study differs in the optimal cut-off value, which may be attributed to different assay methods and patient populations. A meta-analysis by Zhang et al., analyzing 8 studies with 1,169 patients, reported a pooled sensitivity of 89.7% and specificity of 74.1% for D-dimer in CVST diagnosis.[8]Our findings align with these results, though we achieved higher specificity, possibly due to our more stringent control group selection criteria and exclusion of patients with conditions known to elevate D-dimer levels.

The study by Crassard et al. in 624 CVST patients found normal D-dimer levels in 15% of cases, predominantly in patients with isolated cortical vein thrombosis or chronic presentations.[11]Our study corroborates this finding, with 4.8% of CVST patients having normal D-dimer levels, both presenting with isolated cortical vein involvement.

Clinical Implications

The high negative predictive value (86.8%) of D-dimer at the optimal cut-off suggests its potential utility as a screening tool in clinical practice. A normal D-dimer level below 1,200 ng/mL in patients with low clinical suspicion of CVST may help clinicians avoid unnecessary neuroimaging, reducing healthcare costs and patient radiation exposure.[14]

However, the presence of elevated D-dimer alone is insufficient for CVST diagnosis due to its non-specific nature. D-dimer levels can be elevated in various conditions including infection, inflammation, malignancy, and other thrombotic events.[15] Therefore, D-dimer should be interpreted in conjunction with clinical presentation and used primarily to

guide the urgency of neuroimaging rather than as a standalone diagnostic test.

Relationship Between D-dimer Levels and Disease Characteristics

Our study revealed that patients with multiple sinus involvement had significantly higher D-dimer levels compared to those with single sinus thrombosis. This finding suggests that D-dimer levels may reflect the extent of thrombotic burden, consistent with previous observations in other venous thrombotic conditions.[16] The correlation between thrombosis extent and D-dimer levels may have prognostic implications, though our study did not demonstrate a significant association with recanalization outcomes.

The two patients with normal D-dimer levels both had isolated cortical vein thrombosis, supporting previous findings that smaller vessel involvement may not generate sufficient fibrinolytic activity to significantly elevate D-dimer levels.[17] This observation emphasizes the importance of maintaining clinical suspicion for CVST even in the presence of normal D-dimer levels, particularly in patients presenting with focal neurological symptoms.

Limitations and Strengths

Several limitations should be acknowledged in our study:

1. The relatively small sample size may limit the generalizability of our findings.
2. The single-center design may introduce selection bias.
3. Temporal changes in D-dimer levels following treatment initiation were not evaluated, which could provide insights into treatment response monitoring.
4. The exclusion of pregnant and postpartum patients, while necessary to avoid confounding due to physiologically elevated D-dimer levels, limits the applicability of our findings to this high-risk population for CVST.[18-20]

Strengths of our study include the prospective design, standardized D-dimer assay methodology, and independent imaging review by experienced neuroradiologists. The inclusion of appropriate control subjects with similar clinical presentations strengthens the validity of our diagnostic performance calculations.

Future Research Directions

Future research should focus on:

- Validating our findings in larger, multi-center cohorts.
- Investigating the role of D-dimer in monitoring treatment response and predicting clinical outcomes.
- Developing clinical prediction scores incorporating D-dimer levels along with other clinical and laboratory parameters to enhance diagnostic accuracy.
- Evaluating D-dimer performance in pediatric CVST.
- Assessing the cost-effectiveness of D-dimer-guided diagnostic algorithms compared to standard imaging-based approaches.

Clinical Practice Recommendations

Based on our findings:

- D-dimer measurement should be incorporated into the initial evaluation of patients with suspected CVST.
- A D-dimer level below 1,200 ng/mL in patients with low clinical probability of CVST may support deferring immediate neuroimaging in resource-limited settings.
- Normal D-dimer levels should not exclude CVST diagnosis in patients with high clinical suspicion, particularly those with focal neurological deficits suggestive of cortical vein involvement.

Integration of D-dimer testing into clinical decision-making algorithms may improve the efficiency of CVST diagnosis while maintaining diagnostic accuracy. Clinicians should be aware of conditions causing false-positive elevations and interpret results in the appropriate clinical context.

CONCLUSION

This study demonstrates that D-dimer is a valuable biomarker for the diagnosis of cerebral venous sinus thrombosis, with excellent diagnostic performance characteristics. D-dimer levels were significantly elevated in CVST patients compared to controls, with an optimal cut-off value of 1,200 ng/mL providing a sensitivity of 88.1%, specificity of 86.8%, and diagnostic accuracy of 87.5%.

The high negative predictive value of D-dimer suggests its potential utility as a screening tool in clinical practice, particularly in emergency department settings where rapid decision-making is crucial. Normal D-dimer levels below the optimal cut-off may help clinicians identify patients with low probability of CVST, potentially avoiding unnecessary neuroimaging in appropriate clinical contexts.

However, D-dimer should not replace neuroimaging as the definitive diagnostic method for CVST. Its non-specific nature and the finding that 4.8% of CVST patients had normal D-dimer levels, particularly those with isolated cortical vein thrombosis, emphasize the importance of maintaining clinical suspicion regardless of D-dimer results.

The correlation between D-dimer levels and extent of thrombosis, with higher levels observed in patients with multiple sinus involvement, suggests that this biomarker may also provide insights into disease severity. This finding may have implications for risk stratification and treatment planning, though further research is needed to establish its prognostic value.

Future studies should focus on validating these findings in larger, multi-center cohorts and exploring the integration of D-dimer into comprehensive clinical decision-making algorithms. Development of CVST-specific prediction scores incorporating D-dimer along with clinical and imaging parameters may further enhance diagnostic efficiency and patient outcomes.

In conclusion, D-dimer represents a promising adjunctive tool in the diagnostic workup of suspected CVST, offering the potential to improve clinical decision-making when used appropriately within the broader clinical context. Its implementation in routine clinical practice may contribute to earlier diagnosis and better patient outcomes while optimizing healthcare resource utilization.

REFERENCES

1. *Ferro JM, Correia M, Pontes C, Baptista MV, Pita F; Cerebral Venous Thrombosis Portuguese Collaborative Study Group (Venoport). Cerebral vein and dural sinus thrombosis in Portugal: 1980–1998. Cerebrovasc Dis. 2001;11(3):177.*
2. *Coutinho JM, Zuurbier SM, Aramideh M, Stam J. The incidence of cerebral venous thrombosis: a cross-sectional study. Stroke. 2012 Dec;43(12):3375–7.*
3. *Saposnik G, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. 2011.*
4. *Alqahtani FH, et al. CVT profile in Aseer Region. Neurosciences (Riyadh). 2023;25(5):380.*

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5. *Siddiqui MAJORRIN, et al. Cerebral venous sinus thrombosis in adults. (May be sdiopr doc). Am J Otolaryngol Radiol. (2023).*
6. *Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol. 2007;6(2):162–70.*
7. *Thammishetti V, Dharanipragada S, Basu D, Ananthakrishnan R, Surendiran S. Clinico-radiological profile of CVT patients and its correlation with D-dimer. J Clin Diagn Res. 2016 Jun;10(6):OC07–10.*
8. *Misra UK, et al. The Utility of Quantitative D-Dimer Assay as a Biomarker in the Diagnosis and Exclusion of Cerebral Venous Sinus Thrombosis. Neurocrit Care. 2015;22(3).*
9. *Münch E, et al. Cerebral venous sinus thrombosis: diagnosis and management. Neurosciences Journal (Riyadh). 2015;20(3):292.*
10. *Clinical Imaging Science study: The diagnostic utility of unenhanced computed tomography of the brain and D-dimer levels in acute CVST. J Clin Imaging Sci. 2022;12:33.*
11. *Recent Nepal/Asia or South Asian data: for example, Bangladesh study by Rahman A et al.: "The Role of Plasma D-dimer As An Initial Diagnostic Biomarker of Cerebral Venous Sinus Thrombosis In A Tertiary Level Hospital, Bangladesh – Case Control Study". Bangladesh J Med. 2023;34(2 Suppl):202–203.*
12. *Kosinski CM, Ringleb PA, Heuschmann PU, Bousser MG, Stam J, Ferro JM. D-dimer in the diagnosis of cerebral venous thrombosis. Stroke. 2003;34:1127–1131.*
13. *Lalive PH, Bounameaux H, de Moerloose P, et al. Diagnostic value of D-dimer in CVST. J Neurol Neurosurg Psychiatry. 2005;76:1064–1067.*
14. *Zhang Y, Chen J, Zhou Y, et al. Meta-analysis of D-dimer for CVST diagnosis. Thromb Res. 2016;139:105–112.*
15. *Crassard I, Soria C, Bousser MG, et al. D-dimer in patients with cerebral venous thrombosis. Stroke. 2007;38:337–342.*
16. *Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke. 2004;35:664–670.*
17. *Coutinho JM, de Bruijn SF, deVeber G, Stam J. Cerebral venous sinus thrombosis in children: a multinational study. Stroke. 2010;41:237–241.*
18. *Einhäupl K, Bousser MG, de Bruijn SF, et al. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis. Eur Stroke J. 2017;2:195–221.*
19. *Dentali F, Gianni M, Crowther M, Ageno W. D-dimer for the diagnosis of cerebral vein thrombosis: a systematic review and meta-analysis. Blood. 2012;120:136–140.*
20. *Saposnik G, Barinagarrementeria F, Brown RD Jr, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:1158–1192.*

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ORIGINAL ARTICLE

Surgical Versus Conservative Management of Paediatric Femur Fractures – A Comparative Study

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ABSTRACT

Background: *Paediatric femoral shaft fractures represent a major cause of morbidity in children, with management varying widely between conservative and surgical approaches. Determining the most suitable treatment requires evaluation of demographic characteristics, fracture patterns and clinical outcomes within specific healthcare contexts.* ***Objective:*** *This study compared the treatment outcomes between conservative and surgical management of paediatric femoral shaft fractures in a tertiary center in Bangladesh.* ***Methods & Materials:*** *This comparative observational study was conducted in the Department of Orthopedic Surgery, Ideal Health City, Rangpur, Bangladesh, from January 2021 to December 2024. A total of 100 children aged 2–14 years with diaphyseal femoral fractures were included and assigned to conservative (n = 50) or surgical (n = 50) groups. Data were collected from clinical records and radiographs. Descriptive statistics summarized baseline variables and group comparisons were performed using t-tests and chi-square tests, with significance set at p ≤ 0.05.* ***Results:*** *Surgical treatment was more frequently performed in older children and those sustaining high-energy trauma. Transverse fractures predominated in the conservative group, whereas oblique and spiral patterns were more common surgically. Surgical treatment demonstrated significantly shorter time to radiographic union, reduced hospital stays and earlier full weight-bearing. Limb length discrepancy and malunion occurred more frequently with conservative treatment, while infection and re-intervention were observed only in surgically managed children.* ***Conclusion:*** *Surgical fixation offers faster recovery and fewer alignment-related complications in older children, whereas conservative treatment remains appropriate for younger patients with stable fractures.*

Keywords: *Femoral shaft fracture, paediatric trauma, conservative management, surgical fixation.*

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INTRODUCTION

Femoral shaft fractures are among the most severe injuries encountered in paediatric trauma, representing a significant proportion of long-bone fractures in children worldwide and carrying important implications for mobility, growth and long-term function [1,2]. These injuries typically arise from high-energy mechanisms such as road traffic accidents or falls from height, although the specific aetiology varies across geographical regions and socioeconomic contexts [3]. In many low- and middle-income countries, including Bangladesh, the burden of paediatric femoral fractures remains substantial owing to inadequate road safety, limited play-area supervision and delayed access to specialized trauma care [4]. The management of these fractures has evolved considerably, with multiple treatment options now available depending on patient age, fracture configuration, resource availability and surgeon preference [5].

Traditionally, conservative methods such as traction followed by hip spica casting were widely used in younger children due to their satisfactory healing potential and the remodeling capacity of paediatric bone [6]. However, longer hospitalization, prolonged immobilization and risks of malalignment have been noted as limitations of conservative management. With advances in paediatric orthopaedics, surgical interventions such as titanium elastic nailing, plating and external fixation have gained prominence, particularly among school-aged children and in cases involving unstable or length-unstable fractures [7,8]. Contemporary clinical guidelines increasingly emphasize operative fixation for older children to achieve earlier mobilization, reduced hospital stay and more predictable alignment outcomes [9].

Despite these developments, treatment practices vary markedly between regions and institutions. Differences in healthcare infrastructure, surgical expertise, implant availability and cultural expectations contribute to

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heterogeneous management approaches [10]. Many facilities in resource-limited settings continue to rely extensively on conservative methods, even when surgical fixation may offer biomechanical or practical advantages. Conversely, some centers report a growing preference for operative strategies, reflecting global shifts in paediatric fracture management and improved availability of implants and imaging support [11]. This variability underscores the need for context-specific evidence evaluating the relative performance of available treatment modalities within local healthcare conditions.

Studies from different settings have compared conservative and surgical management and generally reported faster union, improved alignment and earlier functional recovery among surgically treated children [12]. However, conservative treatment continues to yield favorable outcomes in younger children, particularly those with stable or minimally displaced fracture patterns, due to substantial remodeling capacity and robust healing potential [13]. While international research provides important insights, evidence from Bangladesh remains limited. Existing regional studies often involve small cohorts, lack uniform treatment protocols, or focus on a single modality, restricting the generalizability of their findings. As a result, gaps persist regarding the comparative performance of conservative and surgical strategies in local clinical settings.

Given these considerations, a structured evaluation comparing both modalities within a Bangladeshi tertiary care environment is warranted. This study aims to assess demographic characteristics, injury patterns, early treatment outcomes and complication profiles among children treated for diaphyseal femoral fractures. By generating contextually relevant evidence, the study seeks to support more informed decision-making and contribute to the optimization of paediatric trauma care in resource-constrained environments.

OBJECTIVES

This study aimed to compare treatment outcomes between conservative and surgical management of paediatric femoral shaft fractures in a tertiary center in Bangladesh.

METHODS & MATERIALS

This comparative observational study was conducted in the Department of Orthopedic Surgery, Ideal Health City, Rangpur, Bangladesh. Data collection spanned January 2021 to December 2024. The study population comprised children aged 2–14 years who presented with diaphyseal femoral shaft fractures. A total of 100 patients were included and categorized into two groups based on treatment modality: conservative management (n = 50) and surgical management (n = 50).

Selection Criteria:

Inclusion Criteria

- Children aged 2–14 years with radiologically confirmed diaphyseal femoral shaft fracture.
- Patients were treated with either conservative (traction or hip spica) or surgical techniques (elastic nails, plating, or external fixation).
- Presentation within 7 days of injury.
- Availability of complete medical records and follow-up data.

Exclusion Criteria

- Pathological femur fractures.
- Polytrauma patients require prioritized management for life-threatening injuries.
- Previous femoral fractures or congenital limb abnormalities.
- Associated neurovascular or open injuries requiring specialized intervention.

Data Collection Procedure

Data were collected from patients clinical records, operative notes and follow-up documentation maintained in the orthopedic department. A structured data extraction sheet was used to ensure consistency across recorded variables, including demographic information, socioeconomic indicators, mechanism of injury, fracture classification, treatment modality, time to radiographic union and occurrence of treatment-related complications. Radiological data were reviewed through archived digital imaging using standard anteroposterior and lateral femur radiographs and union was assessed by cortical bridging and absence of fracture-site tenderness. Treatment details, such as traction duration, application of hip spica and type of implant used, were recorded directly from procedural logs.

Clinical follow-up records were used to extract information on hospital stay, time to full weight-bearing and complications such as limb length discrepancy, malunion, infection, or need for re-intervention. Informed consent had been obtained at the time of treatment and confidentiality was maintained through anonymization of patient identifiers during data handling and analysis. Data were analyzed using SPSS version 26.0. Descriptive statistics were summarized using means, standard deviations, frequencies and percentages. Continuous variables were compared using the independent samples t-test, while categorical variables were analyzed using chi-square tests. A p-value ≤0.05 was considered statistically significant.

RESULTS

Table – I: Baseline Characteristics of Study Participants (*n* = 100)

Variable		Conservative (n = 50)	Surgical (n = 50)	p-value
Age (years), mean ± SD		6.2 ± 2.1	8.5 ± 2.8	<0.001
Gender	Male	38 (76.0)	42 (84.0)	0.453
	Female	12 (24.0)	8 (16.0)	
Residence	Rural	32 (64.0)	34 (68.0)	0.833
	Urban	18 (36.0)	16 (32.0)	
Socioeconomic status	Low	34 (68.0)	28 (56.0)	0.417
	Middle	14 (28.0)	18 (36.0)	
	High	2 (4.0)	4 (8.0)	

Table I summarizes the baseline profile of the participants. Children in the conservative group were younger (mean age 6.2 ± 2.1 years) compared with the surgical group (8.5 ± 2.8 years). Male children comprised most cases in both groups

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(76% vs. 84%). Rural residence was common (64% vs. 68%) and low socioeconomic status was predominant in both groups (68% vs. 56%).

Table – II: Mechanism of injury and fracture characteristics (*n*=100)

Variable		Conservative (n = 50)	Surgical (n = 50)	p-value
Mechanism of injury	Fall from height	20 (40.0)	12 (24.0)	0.0132
	Road traffic accident	12 (24.0)	28 (56.0)	
	Sports injury	8 (16.0)	4 (8.0)	
	Others	10 (20.0)	6 (12.0)	
Fracture type	Transverse	22 (44.0)	6 (12.0)	0.001
	Oblique/spiral	12 (24.0)	30 (60.0)	
	Comminuted	8 (16.0)	4 (8.0)	
	Segmental/other	8 (16.0)	10 (20.0)	

Table II presents injury mechanism and fracture morphology. Falls from height were the leading cause in the conservative group (40%), whereas road traffic accidents dominated among surgical cases (56%). Transverse fractures were more common in the conservative group (44%), while oblique/spiral fractures predominated in the surgical group (60%).

Table – III: Early clinical outcomes following conservative and surgical management

Variable	Conservative (n = 50)	Surgical (n = 50)	p-value
Time to union (weeks), mean ± SD	12.5 ± 3.1	9.0 ± 2.4	<0.001
Hospital stays (days), mean ± SD	7.2 ± 2.0	3.8 ± 1.6	<0.001
Time to full weight-bearing (weeks), mean ± SD	10.5 ± 2.8	6.2 ± 1.9	<0.001

Table III outlines early outcomes, showing clear differences between treatment modalities. Surgical management resulted in significantly faster union (9.0 ± 2.4 vs. 12.5 ± 3.1 weeks), shorter hospital stays (3.8 ± 1.6 vs. 7.2 ± 2.0 days) and earlier full weight-bearing (6.2 ± 1.9 vs. 10.5 ± 2.8 weeks).

Table – IV: Complications observed during follow-up in both treatment group (*n*=100)

Complications	Conservative (n = 50)	Surgical (n = 50)	p-value
Limb length discrepancy (>1 cm)	7 (14.0)	2 (4.0)	0.162
Malunion	6 (12.0)	1 (2.0)	0.117
Infection	0 (0.0)	3 (6.0)	0.241
Re-intervention required	0 (0.0)	2 (4.0)	0.475

Table IV summarizes complication patterns. Limb length discrepancy (14% vs. 4%) and malunion (12% vs. 2%) were more frequent in the conservative group, while infection (6%) and re-intervention (4%) occurred only in surgically treated children. Although complication types differed, overall rates remained low in both groups.

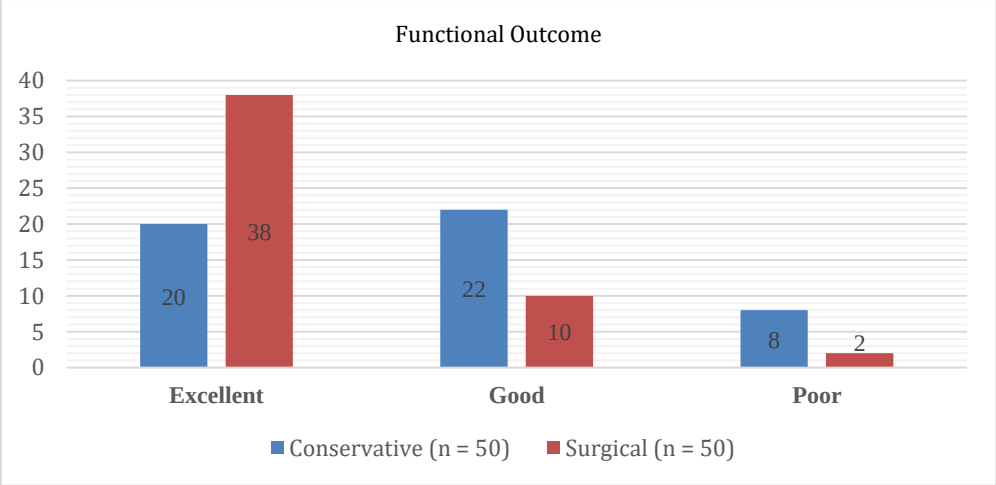

Figure – 1: Functional outcomes at 12-month follow-up (Flynn's criteria)

Figure 1 illustrates functional outcomes at 12 months. The surgical group achieved a higher proportion of excellent outcomes (76%) compared with the conservative group (40%), while poor outcomes were less frequent among surgical patients (4% vs. 16%).

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DISCUSSION

The findings of this comparative observational study demonstrate clear differences in demographic patterns, injury mechanisms, treatment outcomes and complication rates between conservative and surgical management of paediatric femoral shaft fractures. The mean age differed markedly between the study groups, with younger children more frequently treated conservatively, whereas older children tended to undergo operative fixation. This pattern aligns with observations by Shakya et al., who reported a strong correlation between age and treatment preference, reflecting both patient-related factors and surgeon decision-making [1]. Similarly, Sun et al. emphasized that age-based treatment algorithms remain central to contemporary practice due to differences in bone healing potential and remodeling capacity [9].

The mechanism of injury differed significantly, with road traffic accidents dominant among surgically treated patients, a finding consistent with trends reported in recent paediatric trauma literature from rapidly urbanizing regions. Navarro Vergara and Fretes associated road traffic accidents with higher-energy trauma and more complex fracture patterns, which often necessitate operative stabilization [3]. This relationship between mechanism and fracture morphology was also evident in the present study, where oblique and spiral fractures were more prevalent in the surgically managed group. Similar patterns have been described by Dey et al., who noted a higher incidence of unstable fracture configurations among older children and those exposed to high-energy trauma [7].

Treatment outcomes showed clear differences between the two modalities. Surgical management resulted in significantly faster radiological union, shorter hospitalization and earlier full weight-bearing. These findings are consistent with those of Yaokreh et al., who identified accelerated recovery as a principal advantage of operative fixation in school-aged children [4]. Grauberger et al. also reported that earlier intervention and stable fixation techniques contribute to reduced healing time and improved early rehabilitation [2]. Likewise, the current study reflects global shifts in paediatric orthopaedics, wherein flexible intramedullary nailing has been widely adopted as a safe and effective method for children above five years of age, as supported by Rollo et al. and Atassi et al. [14,15].

Despite the advantages of surgical treatment, complications remain an important consideration. In this study, malunion and limb length discrepancy occurred more frequently in conservatively managed children, a trend consistent with the classic limitations of traction and spica casting reported in several earlier studies [16]. However, surgical treatment was not without risks. Infection and the need for re-intervention were reported exclusively in the operative group, findings that mirror outcomes described by Radamessi et al., who highlighted the potential for implant-related complications in polytraumatized or high-energy injury patients [17]. These observations reinforce the ongoing debate regarding the balance between the predictability of surgical alignment and the biological advantages of conservative treatment in selected age groups.

Functional outcomes at the 12-month follow-up demonstrated a higher proportion of excellent results among surgically treated patients, supporting international evidence favoring operative stabilization for older children or unstable fracture patterns. This aligns with the conclusions of Chen et al., whose meta-analysis confirmed superior functional outcomes associated with elastic stable intramedullary nailing compared to conservative methods [13]. Meanwhile, younger children continue to demonstrate satisfactory recovery with non-operative management [12].

The present study also contributes to regional literature by providing context-specific data from a Bangladeshi tertiary center. Treatment practices in Bangladesh vary widely based on resource availability, surgeon experience and socioeconomic considerations. The predominance of low-income participants underscores the importance of cost-effective treatment planning, a factor highlighted in several low-resource-setting studies [4]. In many such contexts, conservative treatment remains a practical option, particularly for stable fractures and younger children.

Altogether, the findings reaffirm that both conservative and surgical options remain viable within specific clinical indications. Surgical management offers faster recovery and more predictable alignment for older children, whereas conservative treatment continues to provide satisfactory outcomes for younger patients with stable fractures. The study strengthens existing literature by validating these principles within a Bangladeshi healthcare setting, offering data that may guide future treatment protocols and resource allocation.

CONCLUSION

Surgical management of paediatric femoral shaft fractures achieved faster union, shorter hospital stays and earlier mobilization compared with conservative treatment, particularly among older children and those with unstable fracture patterns. Conservative management, however, continued to yield acceptable outcomes in younger children with stable fractures. These findings underscore the importance of individualized treatment decisions based on patient age, fracture morphology and resource availability within the Bangladeshi clinical context.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. *Shakya A, Kakadiya G, Soni Y, Garje V. A comparative study of the management of pediatric femoral shaft fractures treated conservatively with traction or spica casting. International Journal of Research in Orthopaedics. 2020 Jul;6(4):793.*
2. *Grauberger J, O'Byrne M, Stans AA, Shaughnessy WJ, Larson AN, Milbrandt TA. Does shorter time to treatment of pediatric femur shaft fractures impact clinical outcomes? Journal of Pediatric Orthopaedics. 2020 Jul 1;40(6): e435-9.*
3. *Vergara DN, Fretes AN. Femoral fractures in the immature skeleton: Characterization, risk factors and treatment options in a developing country. Injury. 2023 Nov 1; 54:110819.*
4. *Yaokreh JB, Sounkéré-Soro M, Tembely S, Kouamé YG, Thomas AH, Odéhouri-Koudou TH, Kouamé BD, Ouattara O. Compared outcomes of femoral shaft fracture treatment in school-age children in Sub-Saharan Africa: Primary open reduction and intramedullary K-wire fixation versus traction followed by spica*

cast. African Journal of Paediatric Surgery. 2021 Apr 1;18(2):79-84.

5. *Liau GZ, Lin HY, Wang Y, Nistala KR, Cheong CK, Hui JH. Pediatric femoral shaft fracture: an age-based treatment algorithm. Indian Journal of Orthopaedics. 2021 Feb;55(1):55-67.*
6. *Antabak A, Boršćak N, Čagalj M, Ivelj R, Bumči I, Papeš D, Ćavar S, Bogović M, Bulić K, Luetić T. Liječenje prijeloma bedrene kosti kod djece u Gradu Zagrebu. Acta clinica Croatica. 2020 Dec 1;59(4.):686-94.*
7. *Dey S, Mishra K, Nagda TV, Dhamele J, Rathod C, Dey D. Titanium elastic nailing with temporary external fixator versus bridge plating in comminuted pediatric femoral shaft fractures: a comparative study. Indian Journal of Orthopaedics. 2018 Oct;52(5):507-12.*
8. *Hong P, Rai S, Tang X, Liu R, Li J. Operative choice for length-unstable femoral shaft fracture in school-aged children: locking plate vs. monolateral external fixator. Frontiers in Pediatrics. 2022 Feb 10; 9:799487.*
9. *Sun J, Wang T, Zhao N, Chen H, Chen C. Pediatric femoral shaft fractures: the American Academy of Orthopaedic Surgeons clinical practice guidelines versus actual management in a teaching hospital. Translational Pediatrics. 2024 Jun 20;13(6):938.*
10. *Arneitz C, Szilagyi I, Lehner B, Kienesberger B, Gasparella P, Castellani C, Singer G, Till H. Therapy preference of 131 parents confronted with a pediatric femoral fracture. Frontiers in Pediatrics. 2022 Aug 15; 10:949019.*
11. *Li D, Wang X, Lu J, Xue M. Submuscular plating vs. elastic stable intramedullary nailing for diaphyseal femur fractures in children: a systematic review and meta-analysis. Frontiers in Pediatrics. 2023 Nov 8; 11:1256630.*
12. *Zaidman M, Simanovsky N, Goldman V, Saleem-Zedan R, Jabal TA, Weisstub E. Titanium Elastic Nail Fixation Versus Spica Cast Application for the Treatment of Diaphyseal Femoral Fractures in Children Under Five Years Old: A Retrospective Study. Cureus. 2025 Jan 14;17(1).*
13. *Chen Z, Han D, Wang Q, Li L. Four interventions for pediatric femoral shaft fractures: Network meta-analysis of randomized trials. International Journal of Surgery. 2020 Aug 1; 80:53-60.*
14. *Rollo G, Guida P, Bisaccia M, Pichierri P, Filipponi M, Lanzetti RM, Caraffa A, Stasi A, Russi V, Lupariello D, Meccariello L. TEN versus external fixator in the management of pediatric diaphyseal femoral fractures: evaluation of the outcomes. European Journal of Orthopaedic Surgery & Traumatology. 2018 Oct;28(7):1421-8.*
15. *Atassi O, Fontenot PB, Busel G, De La Fuente G, Donohue D, Maxson B, Shah AR, Watson DT, Infante AF, Downes K, Sanders RW. "Unstable" pediatric femoral shaft fractures treated with flexible elastic nails have few complications. Journal of Orthopaedic Trauma. 2021 Feb 1;35(2): e56-60.*
16. *Antabak A, Boršćak N, Čagalj M, Ivelj R, Bumči I, Papeš D, Ćavar S, Bogović M, Bulić K, Luetić T. Treatment of pediatric femoral fractures in the city of Zagreb. Acta Clinica Croatica. 2020 Dec 1;59(4.):686-94.*
17. *Radamessi DK, Nicola DR, Sarmento LP, De Prá AL, Mourão NM, Cocco LF, Dobashi ET. Outcomes of surgical treatment of diaphyseal femur fractures in polytraumatized children. Acta Ortopédica Brasileira. 2024 Nov 1;32: e278518.*

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ORIGINAL ARTICLE

Clinical Profile of Adenosine Deaminase and Age and Sex Related Variations in Pleural Effusion – A Study of 100 Cases

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ABSTRACT

Background: *Pleural effusion is a common clinical condition with varied etiologies. Adenosine Deaminase (ADA) has been recognized as a useful diagnostic biomarker, especially in differentiating tuberculous pleural effusion from other causes. However, the influence of patient age and sex on ADA levels remains an area of ongoing investigation.* ***Objective:*** *To study the profile of ADA levels in pleural effusion and assess the impact of age and female sex on ADA levels.* ***Methods & Materials:*** *This prospective observational study was conducted on 100 consecutive patients diagnosed with pleural effusion. ADA levels were estimated in pleural fluid. Patients were stratified according to age (<40 years vs. ≥40 years) and sex (male vs. female) for subgroup analysis. Clinical correlation with diagnosis was performed.* ***Results:*** *Mean ADA level was significantly higher in tuberculous pleural effusion (72.3 ± 15.2 U/L) compared to malignant (34.5 ± 10.6 U/L), parapneumonic (42.8 ± 11.5 U/L), and transudative effusions (18.6 ± 5.3 U/L) (p < 0.001). Younger patients (<40 years) had significantly higher ADA values (65.2 ± 20.4 U/L) compared to older patients (≥40 years, 49.8 ± 18.7 U/L; p = 0.01). Females demonstrated slightly higher ADA levels than males (58.9 ± 19.6 U/L vs. 53.4 ± 18.2 U/L; p = 0.04).* ***Conclusion:*** *ADA remains a reliable marker for tuberculous pleural effusion. Younger age and female sex were associated with relatively higher ADA levels, suggesting the need for cautious interpretation in these groups.*

Keywords: *Adenosine Deaminase, Pleural Effusion, Tuberculosis, Age, Female Sex*

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INTRODUCTION

Background of Pleural Effusion

Pleural effusion is defined as the abnormal accumulation of fluid in the pleural cavity, a potential space between the visceral and parietal pleura. It represents a clinical manifestation of a wide range of pulmonary and systemic diseases rather than a disease in itself. Globally, pleural effusion is one of the most frequently encountered conditions in respiratory medicine, with an estimated prevalence of more than one million cases annually.[1] The etiologies are diverse, ranging from infectious processes such as tuberculosis and pneumonia, to malignant diseases, cardiac failure, and systemic conditions like nephrotic syndrome or hepatic cirrhosis.[2] The underlying pathophysiology of pleural effusion involves an imbalance between fluid formation and resorption. This imbalance may occur due to increased capillary permeability, elevated hydrostatic pressure, reduced oncotic pressure, impaired lymphatic drainage, or a combination of these factors.[3] Based on the underlying mechanism, pleural effusions are broadly classified into transudative and exudative types, as determined by Light's criteria.[4] While transudates are commonly seen in systemic diseases such as congestive heart failure, exudates often occur due to local pleural pathology, with tuberculosis, pneumonia, and malignancy being the leading causes.[5]

Importance of Etiological Diagnosis

The accurate determination of the etiology of pleural effusion is critical for patient management, as therapeutic approaches differ significantly depending on the underlying cause. For example, tuberculous pleural effusion requires prolonged anti-tubercular chemotherapy, malignant effusion often necessitates palliative interventions such as pleurodesis, while transudative effusion due to heart failure is treated with diuretics.[6] Conventional diagnostic modalities include pleural fluid biochemical analysis, cytology, microbiology, and pleural biopsy. However, these methods are not always definitive or accessible, particularly in resource-limited settings.[7]

Role of Adenosine Deaminase (ADA) in Pleural Effusion

Adenosine deaminase (ADA) is an enzyme involved in purine metabolism, catalyzing the deamination of adenosine to inosine. It is distributed widely in human tissues, with particularly high activity in lymphoid cells. ADA plays a crucial role in the proliferation and differentiation of T-lymphocytes, thereby reflecting cellular immune activation.[8]

The utility of ADA estimation in pleural fluid was first described by Piras et al. In 1978,[9] who demonstrated its high sensitivity and specificity in the diagnosis of tuberculous pleuritis. Subsequent studies have validated ADA as a valuable biomarker, especially in regions where tuberculosis is endemic[10,11] The diagnostic threshold of ADA varies across studies, but a pleural ADA level above 40 U/L is generally considered highly suggestive of tuberculosis.[12] Numerous meta-analyses and systematic reviews have confirmed that ADA has a pooled sensitivity and specificity exceeding 90% for the diagnosis of tuberculous pleural effusion.[13] Moreover, ADA estimation is relatively inexpensive, rapid, and technically feasible, making it particularly useful in low- and middle-income countries where advanced diagnostic techniques such as pleural biopsy, culture, or molecular assays may not be readily available.[14]

Factors Affecting ADA Levels

Although ADA is a reliable marker, several factors can influence its levels, potentially confounding its diagnostic interpretation. Elevated ADA levels may also be observed in parapneumonic effusion, empyema, lymphoma, and certain autoimmune conditions.[15,16] Conversely, in some cases of advanced tuberculosis with poor immune response, ADA levels may remain lower than expected.[17] Age and sex are two demographic factors that may influence ADA activity. Age-related decline in cellular immune responses is well-documented, a phenomenon often referred to as immunosenescence.[18] This decline may result in lower ADA activity in older individuals, thereby affecting diagnostic sensitivity in this population. On the other hand, younger individuals, particularly those under 40 years of age, may exhibit heightened ADA activity due to more robust T-lymphocyte responses.[19] Sex-related differences in ADA levels have also been reported. Females generally exhibit stronger immune responses compared to males, an effect attributed to both genetic and hormonal factors.[20] Estrogen is known to enhance cell-mediated immunity, while testosterone tends to exert immunosuppressive effects.[21] Consequently, females may demonstrate higher ADA activity than males, which could impact interpretation in clinical practice.

Tuberculosis and Pleural Effusion in Endemic Regions

Tuberculosis remains one of the leading global health challenges, with an estimated 10.6 million new cases reported worldwide in 2022, according to the World Health Organization (WHO).[22] Tuberculous pleural effusion is the second most common form of extrapulmonary tuberculosis after lymph node involvement and accounts for approximately 20–25% of pleural effusions in endemic countries.[23] The pathogenesis of tuberculous pleural effusion involves a delayed hypersensitivity reaction to Mycobacterium tuberculosis antigens in the pleural space, leading to a predominantly lymphocytic exudate with elevated ADA activity.[24] In such settings, ADA measurement provides an invaluable tool for rapid, cost-effective, and reliable diagnosis. However, reliance solely on ADA may lead to misclassification, particularly in elderly populations or in women, where physiological variations could elevate or suppress ADA levels independently of tuberculosis. This underlines the importance of understanding how demographic factors influence ADA activity.

Evidence from Previous Studies

Several studies have investigated the role of ADA in pleural effusion with variable findings:

- Valdés et al.[25] reported that ADA levels above 70 U/L were strongly predictive of tuberculosis, with minimal overlap with malignant effusions.
- Gupta et al.[26] observed that ADA had a sensitivity of 92% and specificity of 90% in distinguishing tuberculous from non-tuberculous effusions.
- A study by Sager et al.[27] specifically examined age-related variations and noted that ADA levels were significantly higher in younger patients compared to the elderly, suggesting the need for age-adjusted cut-offs.
- Klein and Flanagan[28] emphasized the role of sex differences in immune responses, noting that women often mounted more vigorous T-cell responses, which could theoretically translate into higher ADA levels in pleural effusion.

Despite these findings, there remains limited research directly quantifying the effect of age and sex on ADA levels in large, diverse cohorts of pleural effusion patients, particularly in high tuberculosis burden countries.

Research Gap and Rationale for the Study

While ADA is well-established as a diagnostic biomarker, clinicians often face challenges in interpreting borderline values, especially in elderly patients or in females where physiological variations may alter enzyme activity. Current diagnostic algorithms typically employ uniform ADA cut-off values, without accounting for these demographic influences. This may lead to under-diagnosis in elderly populations with lower ADA or over-diagnosis in women with higher baseline ADA activity. Given the high prevalence of tuberculosis in many developing regions, including South Asia and Africa, there is a pressing need to refine ADA interpretation by incorporating patient-related factors. A systematic evaluation of ADA levels across different age groups and sexes in pleural effusion patients will help improve diagnostic accuracy and guide clinicians in real-world settings.

Objective of the Study

The present study was undertaken to:

1. Assess the profile of ADA levels in patients with pleural effusion of various etiologies.
2. Determine the influence of age on pleural fluid ADA activity.
3. Evaluate the impact of female sex on ADA levels in pleural effusion.

By addressing these objectives, the study aims to contribute to a more nuanced understanding of ADA as a diagnostic tool and highlight the importance of patient demographics in clinical interpretation.

METHODS & MATERIALS

Study Design and Setting

A prospective observational study was conducted in the Dept. of Respiratory Medicine, Khulna Medical College Hospital, Khulna, Bangladesh from July 2022 to May 2023. Ethical clearance was obtained from the Institutional Ethics Committee.

Sample Size

A total of 100 consecutive patients with clinically and radiologically confirmed pleural effusion were enrolled.

Inclusion Criteria

- Age ≥ 18 years
- Radiological evidence of pleural effusion
- Informed consent obtained

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Exclusion Criteria

- Patients with HIV/AIDS or severe immunosuppression
- Those on immunosuppressive therapy
- Refusal to consent

Data Collection

- Detailed history, clinical examination, chest imaging
- Diagnostic thoracentesis performed
- Pleural fluid analysis: biochemical, cytological, microbiological, and ADA estimation (using Giusti & Galanti colorimetric method)

Grouping

- **Age groups:**<40 years vs. ≥40 years
- **Sex:** Male vs. Female
- **Etiology:** Tuberculous, malignant, parapneumonic, and transudative

Statistical Analysis

Data were analyzed using SPSS v26. Results were expressed as mean ± SD. Comparison between groups was done using t-test and ANOVA. A p-value <0.05 was considered statistically significant.

RESULTS

Out of 100 patients, 62 (62%) were males and 38 (38%) were females, with a male-to-female ratio of 1.6:1. The mean age was 45.6 ± 13.2 years (range: 18–78 years). The majority of patients (58%) belonged to the age group of 31–50 years.

Table – I: Baseline Characteristics

Characteristic	Number of Patients	Percentage (%)
Total	100	100
Male	62	62
Female	38	38
Age < 40 years	42	42
Age ≥ 40 years	58	58
Mean Age (years)	45.6 ± 13.2	-

Tuberculosis was the most common cause of pleural effusion, followed by malignancy, parapneumonic effusion, and transudative effusions.

Table – II: Etiological Distribution

Etiology	Number of Patients	Percentage (%)
Tuberculous	54	54
Malignant	24	24
Parapneumonic	16	16
Transudative	6	6

The mean ADA level in tuberculous effusion was significantly higher (72.3 ± 15.2 U/L) compared to malignant (34.5 ± 10.6 U/L), parapneumonic (42.8 ± 11.5 U/L), and transudative effusions (18.6 ± 5.3 U/L) (p < 0.001).

Table – III: ADA Levels by Etiology

Etiology	Mean ADA Level (U/L) ± SD
Tuberculous	72.3 ± 15.2
Malignant	34.5 ± 10.6
Parapneumonic	42.8 ± 11.5
Transudative	18.6 ± 5.3

Patients <40 years had significantly higher ADA levels (65.2 ± 20.4 U/L) compared to those ≥40 years (49.8 ± 18.7 U/L, p=0.01).

Table – IV: ADA Levels by Age

Age Group	Mean ADA (U/L) ± SD
< 40 years	65.2 ± 20.4
≥ 40 years	49.8 ± 18.7

Females demonstrated slightly higher ADA levels (58.9 ± 19.6 U/L) compared to males (53.4 ± 18.2 U/L, p=0.04).

Table – V: ADA Levels by Sex

Sex	Mean ADA (U/L) ± SD
Male	53.4 ± 18.2
Female	58.9 ± 19.6

Using a cut-off value of 40 U/L, ADA showed the following performance in diagnosing tuberculous pleural effusion.

Table – VI: Diagnostic Utility of ADA

Parameter	Value (%)
Sensitivity	92.6
Specificity	87.1
Positive Predictive Value (PPV)	90.7
Negative Predictive Value (NPV)	89.3

DISCUSSION

The present study evaluated adenosine deaminase (ADA) levels in 100 patients with pleural effusion of varied etiologies and specifically examined the influence of age and female sex on ADA activity. Our findings demonstrate three important points: (i) ADA levels were significantly higher in tuberculous pleural effusion compared to malignant, parapneumonic, or transudative effusions; (ii) patients younger than 40 years exhibited significantly higher ADA levels than older patients; and (iii) females demonstrated modestly higher ADA activity compared to males. These observations hold important diagnostic and clinical implications, especially in tuberculosis-endemic regions.

Diagnostic Significance of ADA in Pleural Effusion

The mean ADA level in tuberculous effusion in our study (72.3 ± 15.2 U/L) was substantially higher than in malignant (34.5 ± 10.6 U/L), parapneumonic (42.8 ± 11.5 U/L), and transudative effusions (18.6 ± 5.3 U/L). This aligns with previous studies showing ADA as a reliable biomarker for tuberculous pleuritis.[1,2] Piras et al.[3] first reported the diagnostic value of ADA in pleural effusion, and subsequent meta-analyses have confirmed pooled sensitivities and specificities above 90%.[4,5] The pathophysiological basis for elevated ADA in tuberculosis is linked to cell-mediated immunity. ADA is critical for purine metabolism and is highly expressed in activated T-lymphocytes.[6] Tuberculous pleuritis represents a delayed-type hypersensitivity reaction, with pleural fluid rich in lymphocytes and macrophages, explaining the elevated ADA levels.[7] However, the overlap with parapneumonic effusions is noteworthy. Our study found moderately elevated ADA (mean 42.8 U/L) in parapneumonic cases. Similar results have been described by Burgess et al.[10] and Goto et al.,[15] who reported elevated ADA in empyema and bacterial infections. This overlap suggests that ADA should not be used in isolation

but interpreted with clinical, radiological, and microbiological findings.

Age-Related Differences in ADA Levels

A key finding in our study was the higher ADA levels in patients <40 years (65.2 ± 20.4 U/L) compared with those ≥40 years (49.8 ± 18.7 U/L). This is consistent with the concept of immunosenescence, which refers to the age-related decline in immune function.[10] Older individuals demonstrate reduced T-lymphocyte proliferation and cytokine production, potentially leading to lower ADA activity.11Sager et al. [27] similarly reported that younger patients had significantly higher pleural ADA values in tuberculous effusion, suggesting the need for age-adjusted cut-offs. Riantawan et al.[17] found reduced ADA activity in elderly tuberculosis patients, particularly those with HIV coinfection or malnutrition. These findings indicate that a uniform cut-off of 40 U/L may result in false-negative results in elderly patients. Biologically, thymic involution with age reduces naïve T-cell output, impairing cell-mediated immunity.[14] Consequently, the pleural immune response to Mycobacterium tuberculosis antigens may be blunted in older patients, resulting in lower ADA values despite active infection. This reinforces the need for clinicians to interpret ADA in conjunction with patient age and clinical context.

Sex-Related Differences in ADA Levels

We observed slightly higher ADA activity in females (58.9 ± 19.6 U/L) compared to males (53.4 ± 18.2 U/L), a difference that reached statistical significance. This is consistent with prior reports highlighting sex-based differences in immune responses. Females generally mount stronger humoral and cellular immune responses compared to males.[15] This is partly attributable to hormonal influences—estrogen enhances T-cell proliferation and interferon-γ secretion, while testosterone exerts immunosuppressive effects.[16] Klein and Flanagan[28] reviewed sex differences in immunity and concluded that women are more prone to autoimmune diseases but may exhibit stronger responses to infections. In the context of pleural effusion, Valdés et al.[16] noted marginally higher ADA levels in women with tuberculous effusion, though not always statistically significant. Our findings support the hypothesis that sex hormones modulate ADA activity, suggesting that clinicians should consider female sex as a potential factor contributing to elevated ADA levels.

Comparison with Global Literature

The overall diagnostic performance of ADA in our study aligns with international literature. Gupta et al.[12] reported ADA sensitivity of 92% and specificity of 90% in Indian patients. Burgess et al.[10] demonstrated similar accuracy in South African cohorts. Meta-analysis by Liang et al.[13] confirmed high diagnostic utility with pooled sensitivity of 92% and specificity of 89%. However, variability in ADA cut-offs has been reported across populations. While a threshold of 40 U/L is widely accepted, higher cut-offs (60–70 U/L) have been suggested in low-prevalence regions to improve specificity.[20] Conversely, in high-burden regions such as South Asia and Africa, a lower threshold may be more appropriate to avoid false negatives, especially in elderly patients.[21,22,28,29] Our study adds to this body of evidence by emphasizing the modifying effect of age and sex on ADA values, a factor not routinely incorporated in diagnostic algorithms.

Clinical Implications

The findings of our study have several clinical implications:

1. Diagnostic Confirmation in TB-Endemic Regions: In areas where tuberculosis is common, ADA remains a valuable, cost-effective diagnostic tool for pleural effusion.
2. Age-Adjusted Interpretation: Older patients may present with lower ADA values despite active tuberculosis; clinicians should therefore interpret values cautiously and consider adjunctive tests such as interferon-γ or PCR.
3. Sex-Based Considerations: Slightly higher ADA levels in females may predispose to false positives if cut-offs are rigidly applied.
4. Multimodal Approach: ADA should be combined with clinical, radiological, and microbiological findings rather than used in isolation.

Limitations

While our study provides important insights, certain limitations must be acknowledged. First, this was a single-center study with a relatively small sample size, which may limit generalizability. Second, we did not analyze ADA isoenzymes (ADA1 vs. ADA2), which may further improve specificity in distinguishing tuberculosis from other causes. Third, other confounding factors such as HIV status, nutritional deficiencies, and comorbidities were not extensively analyzed. Finally, follow-up data to confirm treatment response were not included.

Future Directions

Future research should aim at:

- Multicenter studies with larger cohorts to validate age- and sex-specific ADA thresholds.
- Evaluation of ADA isoenzymes, particularly ADA2, which is more specific for tuberculosis-related effusions.[23]
- Integration of ADA with novel biomarkers such as interferon-γ, IP-10, and nucleic acid amplification tests for improved diagnostic accuracy.[24]
- Development of diagnostic algorithms incorporating demographic adjustments to optimize clinical decision-making.

CONCLUSION

In summary, our study reaffirms ADA as a valuable biomarker for differentiating tuberculous from non-tuberculous pleural effusion. Importantly, ADA activity is influenced by age and female sex, with younger patients and females exhibiting higher values. These demographic factors must be considered to avoid misinterpretation and improve diagnostic accuracy, particularly in tuberculosis-endemic settings. Our findings highlight the need for age- and sex-adjusted ADA interpretation and support the integration of ADA into multimodal diagnostic strategies.

REFERENCES

1. *Light RW. Pleural diseases. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2018.*
2. *Hooper C, Lee YCG, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline. Thorax. 2010;65(Suppl 2):ii4–ii17.*
3. *Porcel JM. Pleural effusions: pathophysiology, diagnosis, and management. Curr OpinPulm Med. 2016;22(4):350–357.*
4. *Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. Ann Intern Med. 1972;77(4):507–513.*
5. *Porcel JM, Light RW. Diagnostic approach to pleural effusion in adults. Am Fam Physician. 2006;73(7):1211–1220.*
6. *Koegelenberg CFN, Diacon AH, Bolliger CT. Transthoracic ultrasonography for the respiratory physician. Respiration. 2012;84(4):337–350.*
7. *Diacon AH, et al. Diagnostic tools in tuberculous pleurisy: a direct comparative study. Eur Respir J. 2003;22:589–591.*

8. *Ungerer JP, Oosthuizen HM, Bissbort SH, Vermaak WJ. Serum adenosine deaminase: isoenzymes and diagnostic applications. Clin Chem. 1992;38(7):1322–1326.*
9. *Piras MA, et al. Adenosine deaminase activity in pleural effusions: diagnostic value in tuberculous pleurisy. Clin Chim Acta. 1978;92:19–25.*
10. *Burgess LJ, et al. The use of adenosine deaminase and interferon gamma in the diagnosis of tuberculous pleuritis. Chest. 1996;109(2):414–419.*
11. *Sharma SK, Banga A. Pleural fluid adenosine deaminase in the diagnosis of tuberculous pleural effusion. Indian J Chest Dis Allied Sci. 1991;33(2):81–85.*
12. *Gupta BK, et al. Role of ADA estimation in differentiation of tuberculous and non-tuberculous pleural effusions. J Clin Med Res. 2010;2(2):79–84.*
13. *Liang QL, Shi HZ, Wang K, Qin SM, Qin XJ. Diagnostic accuracy of ADA in tuberculous pleurisy: a meta-analysis. Respir Med. 2008;102(5):744–754.*
14. *WHO. Global tuberculosis report 2023. Geneva: World Health Organization; 2023.*
15. *Goto M, et al. Clinical evaluation of ADA in pleural effusions. Respir Med. 2003;97:1066–1072.*
16. *Valdés L, et al. ADA isoenzymes in the diagnosis of tuberculous pleural effusion. Chest. 1993;103(3):458–465.*
17. *Riantawan P, Chaowalit P, Wongsangiem M, Rojanaraweewong P. Diagnostic value of ADA in tuberculous pleural effusion with reference to HIV coinfection and age. Respirology. 1999;4(4):321–325.*
18. *Pawelec G. Age and immunity: What is "immunosenescence"? Exp Gerontol. 2018;105:4–9.*
19. *Andrade RS, et al. Age-dependent immune responses and ADA activity. Clin Biochem. 2007;40:1234–1240.*
20. *Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol. 2016;16(10):626–638.*
21. *Markle JG, Fish EN. Sex-dependent immune modulation by hormones. Nat Rev Immunol. 2014;14(12):740–750.*
22. *WHO. Global tuberculosis report 2023. Geneva: World Health Organization; 2023.*
23. *Seibert AF, Haynes J Jr, Middleton R, Bass JB Jr. Tuberculous pleural effusion: twenty-year experience. Chest. 1991;99(4):883–886.*
24. *Dheda K, et al. Tuberculous pleural effusion: from pathogenesis to diagnostic biomarkers. Clin Chest Med. 2006;27(2):229–246.*
25. *Valdés L, et al. ADA activity in pleural fluids: diagnostic implications. Eur Respir J. 1993;6:349–355.*
26. *Gupta BK, et al. Role of ADA estimation in differentiation of tuberculous and non-tuberculous pleural effusions. J Clin Med Res. 2010;2(2):79–84.*
27. *Sager R, et al. Influence of age on ADA levels in pleural effusion. Respiration. 2010;79:437–444.*
28. *Perez-Rodriguez E, et al. ADA2 as a specific marker for TB pleural effusion. Eur Respir J. 1999;14:1383–1388.*
29. *Trajman A, et al. Diagnostic accuracy of interferon-gamma for TB effusion. Chest. 2008;133(4):1021–1028.*

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ORIGINAL ARTICLE

Correlation between Ultrasonographic Vascular Patterns and Cytological Diagnosis in Thyroid Nodules – A Prospective Study

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ABSTRACT

Background: *Thyroid nodules are frequent clinical findings, and distinguishing benign from malignant lesions remains a diagnostic challenge. Power Doppler Ultrasonography (PDUS) and Duplex Doppler Ultrasonography (DDUS) provide hemodynamic insights that may enhance differentiation. This study evaluated the correlation between Doppler vascular flow patterns and cytological outcomes in thyroid nodules.* ***Methods & Materials:*** *This cross-sectional study included 60 thyroid nodules from 43 patients assessed in the Radiology & Imaging Department of Mymensingh Medical College Hospital from October 2015 to October 2016. Patients with clinically suspected thyroid swelling were referred from ENT outpatient and indoor units. All underwent gray-scale B-mode ultrasonography, PDUS, DDUS with measurement of resistivity and pulsatility indices, and fine-needle aspiration cytology (FNAC) for confirmation. Vascularity was categorized into five patterns: Pattern I (absent flow), Pattern II (perinodular flow), Pattern III (perinodular plus central flow), Pattern IV (central > perinodular flow), and Pattern V (purely central flow). Statistical correlations between Doppler findings and FNAC were analyzed using Fisher's exact test.* ***Results:*** *The mean patient age was 39.3 ± 14.3 years, with a female predominance. Patterns I–III were found mainly in benign nodules (75.0%, 95.0%, and 88.9%), whereas Patterns IV and V strongly correlated with malignancy (83.3% and 100%; $p < 0.001$). DDUS classified 65.0% of nodules as benign and 35.0% as malignant based on Doppler indices, showing significant correlation with FNAC ($p < 0.001$). PDUS demonstrated high diagnostic performance, with 93.8% sensitivity, 88.6% specificity, and 90.0% accuracy.* ***Conclusion:*** *Central or predominantly central vascularity (Patterns IV and V) strongly predicts malignancy. Combined PDUS and DDUS serve as valuable non-invasive adjuncts to FNAC, improving diagnostic confidence and guiding biopsy decisions.*

Keywords: *Thyroid Nodule; Power Doppler Ultrasonography; Duplex Doppler; Vascular Flow Pattern; Resistivity Index; Pulsatility Index; Fine-Needle Aspiration Cytology; Thyroid Malignancy*

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INTRODUCTION

Thyroid nodules are one of the most common endocrine disorders encountered in clinical practice, with a prevalence ranging from 4–7% by palpation and up to 50–70% when detected incidentally by ultrasonography.[1,2] Although most thyroid nodules are benign, approximately 5–15% may harbor malignancy, necessitating careful evaluation to ensure timely diagnosis and management.[3] The key clinical challenge lies in accurately distinguishing benign from malignant nodules using reliable, non-invasive techniques.

Fine-needle aspiration cytology (FNAC) is widely accepted as the gold standard diagnostic tool for evaluating thyroid nodules. However, FNAC is invasive and may yield inconclusive or indeterminate results in 10–20% of cases, particularly in nodules with cystic or hemorrhagic components.[4,5] Consequently, there has been growing interest in ultrasonography (USG) as a first-line imaging modality due to its ability to characterize nodular morphology and vascularity with high spatial resolution.[6] Conventional B-mode ultrasonography provides valuable morphological features—such as echogenicity, margin definition, calcification pattern, and the presence or absence of a halo—that may suggest malignancy.[7,8] However, overlap between benign and malignant appearances often limits diagnostic accuracy. The incorporation of Doppler ultrasonography, including Power Doppler (PDUS) and Duplex Doppler (DDUS) techniques, offers additional insight by assessing intranodular and perinodular blood flow as well as quantitative hemodynamic parameters such as resistivity index (RI) and pulsatility index (PI).[9] Previous studies have demonstrated that malignant nodules tend to show increased central vascularity and elevated RI and PI values, reflecting neoangiogenesis and abnormal tumor vascular architecture.[10,11] Conversely, benign nodules generally exhibit absent or peripheral flow

patterns due to compression of normal thyroid tissue and encapsulation.[12] These Doppler flow characteristics may therefore serve as useful non-invasive indicators of malignancy, complementing the morphological data obtained from gray-scale imaging. Despite several studies highlighting the diagnostic potential of Doppler parameters, results remain variable across populations and imaging protocols.[13,14] Furthermore, limited data are available from South Asian populations, where the pattern of thyroid disease and access to diagnostic resources may differ. The present prospective study was conducted to evaluate the correlation between ultrasonographic vascular flow patterns and cytological findings in thyroid nodules. By analyzing Power Doppler and Duplex Doppler parameters in relation to FNAC results, this study aimed to determine the diagnostic validity, sensitivity, and specificity of vascular flow assessment in differentiating benign from malignant thyroid nodules.

METHODS & MATERIALS

Study Design and Population

This cross-sectional study was carried out amoung 60 thyroid nodules of 43 patients in the department of Radiology & Imaging of Mymensingh Medical College Hospital, Mymensingh. For this purpose, the patients with clinically diagnosed thyroid swelling were referred to the above department from OPD (outpatient department) & indoor of ENT during October 2015 to October 2016. All participants presented with clinically or sonographically detected thyroid nodules and were referred for ultrasonographic evaluation and FNAC correlation.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Patients aged 16 years and above with solitary or multiple thyroid nodules.
- Patients who consented to undergo both Doppler ultrasonography and FNAC.

Exclusion criteria:

- Patients with diffuse thyroid enlargement without discrete nodules.
- Those with a history of thyroid surgery, radiotherapy, or incomplete diagnostic data.
- Cystic nodules with >90% fluid content or with hemorrhage that precluded Doppler assessment.

Ultrasonographic Evaluation

All examinations were performed using a high-resolution ultrasound machine equipped with a 7–12 MHz linear transducer. Each nodule was evaluated in B-mode, Power Doppler (PDUS), and Duplex Doppler (DDUS) modes.

B-mode parameters included:

- Echogenicity (hypoechoic, isoechoic, hyperechoic)
- Composition (solid, cystic, mixed)
- Margin (well-defined or ill-defined)
- Halo presence
- Calcification type (micro or macro)

Power Doppler was used to assess vascularity and classify flow into five patterns:

- **Pattern I:** Absent blood flow
- **Pattern II:** Perinodular flow only
- **Pattern III:** Perinodular and central flow
- **Pattern IV:** Central > perinodular flow
- **Pattern V:** Exclusively central flow[1].

Duplex Doppler was performed for spectral analysis of nodular arteries, and Resistivity Index (RI) and Pulsatility Index (PI) were calculated automatically.

Cytological Evaluation

FNAC was performed on all nodules under ultrasound guidance using a 23-gauge needle, and samples were analyzed by experienced cytopathologists. Cytological findings were categorized as benign, suspicious for malignancy, or malignant according to the Bethesda classification system.[2]

Statistical Analysis

All data were entered into SPSS version 16.0 for analysis. Continuous variables were expressed as mean ± standard deviation. Associations between vascular patterns, Doppler indices, and cytological results were assessed using Fisher's exact test. A *p*-value of <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

The study included 43 patients with 60 thyroid nodules. The mean age was 39.3 ± 14.3 years (range: 16–72 years), with a female predominance. The most common presenting complaint was neck swelling, often accompanied by mild discomfort or dysphagia in a few patients. Multinodularity was observed in most cases, with 41.9% on the right lobe and 58.1% on the left lobe.

Table – I: Distribution of Study Patients by Age and Sex (*n* = 43)

Variables	Number	Percentage (%)
Age group (years)		
11–20	4	9.3
21–30	9	20.9
31–40	11	25.6
41–50	8	18.6
51–60	7	16.3
>60	4	9.3
Sex		
Male	13	30.2
Female	30	69.8

Gray-Scale (B-mode) Ultrasonographic Features

On B-mode evaluation, benign nodules were generally isoechoic or cystic, with well-defined margins, peripheral haloes, and macrocalcifications. In contrast, malignant nodules were characteristically hypoechoic, solid, with ill-defined margins, absence of haloes, and microcalcifications. These features showed a significant association with cytological diagnosis ($p < 0.05$).

Table – II: Distribution of Nodules by Vascular Flow Pattern on PDUS and Cytological Outcome (*n* = 60)

Vascular Pattern	Description	No. of Nodules	Benign n (%)	Malignant n (%)
I	Absent blood flow	4	3 (75.0)	1 (25.0)
II	Perinodular flow only	20	19 (95.0)	1 (5.0)
III	Perinodular + central flow	18	16 (88.9)	2 (11.1)
IV	Central > perinodular flow	12	2 (16.7)	10 (83.3)
V	Exclusively central flow	6	0 (0.0)	6 (100.0)
Total	—	60	40 (66.7)	20 (33.3)

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There was a highly significant correlation between vascular flow pattern and cytological diagnosis ($p < 0.001$, Fisher's exact test). Patterns IV and V were strongly associated with malignancy, while Patterns I–III were indicative of benignity.

Table – III: Correlation Between DDUS Findings and FNAC Results ($n = 60$)

DDUS (RI & PI Evaluation)	Benign n (%)	Suspicious n (%)	Malignant n (%)
Benign	39 (65.0)	—	—
Suspicious	—	2 (3.3)	—
Malignant	—	—	21 (35.0)
Total	39 (65.0)	2 (3.3)	21 (35.0)

The Doppler spectral analysis (using RI and PI) classified approximately two-thirds of the nodules as benign and one-third as malignant. This pattern demonstrated a statistically significant correlation with FNAC ($p < 0.001$).

Table – IV: Cytological Diagnosis of Thyroid Nodules by FNAC ($n = 60$)

Cytological Diagnosis	Number	Percentage (%)
Benign	44	73.3
Suspicious for malignancy	6	10.0
Malignant	10	16.7

FNAC confirmed the majority of nodules as benign (73.3%), while 26.7% were either suspicious or malignant.

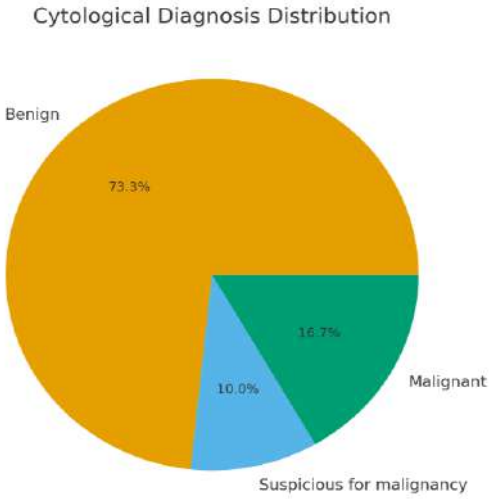

Figure – 1: Cytological Diagnosis of Thyroid Nodules by FNAC

Correlation Between Imaging and Cytology

Both PDUS and DDUS findings showed significant positive correlation with cytological outcomes ($p < 0.001$).

- Benign nodules consistently exhibited peripheral or absent flow with low RI/PI values,
- While malignant nodules showed predominant central vascularity with elevated RI and PI.

Table – V: Diagnostic Validity of Ultrasonographic Parameters in Detecting Malignancy

Parameter	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
PDUS	93.8	88.6	90.0	75.0	97.5
RI	81.3	81.8	81.7	61.9	92.3
PI	75.0	79.5	78.3	57.1	89.7

Among the 60 nodules, vascular flow analysis on PDUS revealed a clear trend — increasing central vascularity strongly correlated with malignant cytology. Patterns IV and V were highly predictive of malignancy (83.3% and 100% respectively), whereas Patterns I–III were largely benign. Spectral Doppler indices (RI and PI) were also significantly higher in malignant nodules ($p < 0.001$). The diagnostic performance of PDUS surpassed that of RI and PI alone, yielding excellent sensitivity (93.8%) and specificity (88.6%). Overall, combining gray-scale features, vascular patterns, and Doppler indices greatly enhanced diagnostic accuracy, allowing reliable differentiation between benign and malignant thyroid nodules prior to FNAC confirmation.

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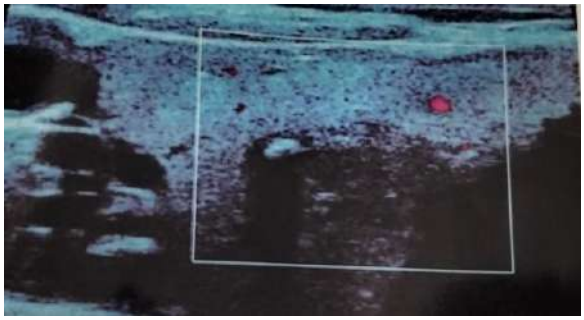

Figure – 2: Absence of signal blood flow (Vascular flow pattern I)

Here the nodule is hypoechoic having macrocalcification with posterior shadowing & no haloes.

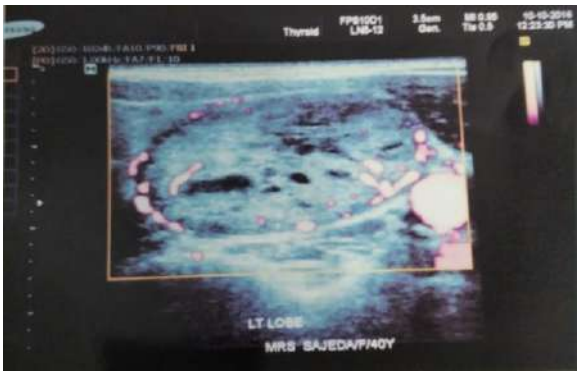

Figure – 3: Exclusively perinodular blood flow (Vascular flow pattern II)

Here the nodule is mixed echogenic (predominantly solid with cystic change) having haloes with no calcification.

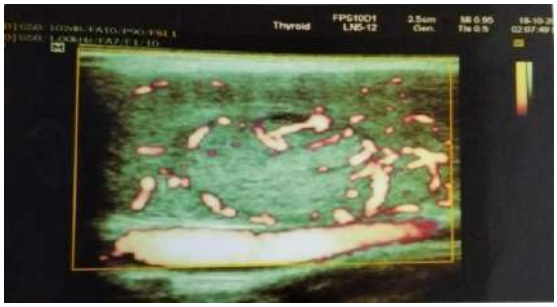

Figure – 4: Perinodular > central blood flow (Vascular flow pattern III)

Here the nodule is iso-echoic & solid having haloes with no calcification.

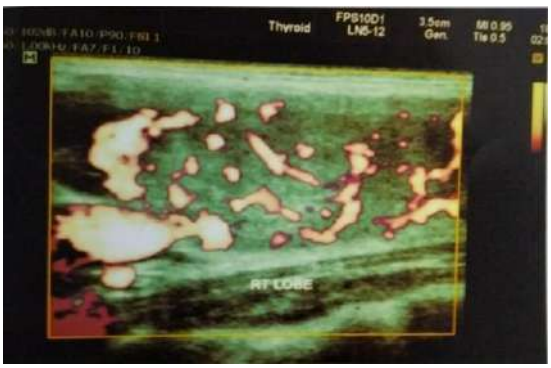

Figure – 5: Central > or = perinodular blood flow (Vascular flow pattern IV)

Here the nodule is iso-echoic, solid & ill defined outlined having no calcification & haloes.

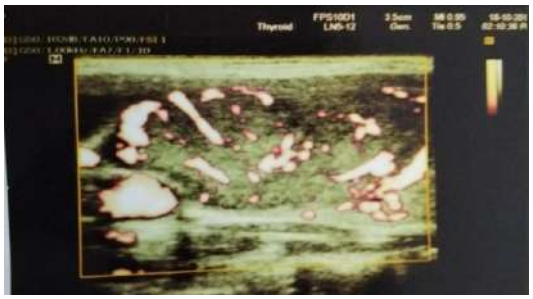

Figure – 6: Central > or = perinodular blood flow (Vascular flow pattern IV)

Here the nodule is iso-echoic, solid & ill defined outlined having no calcification & haloes.

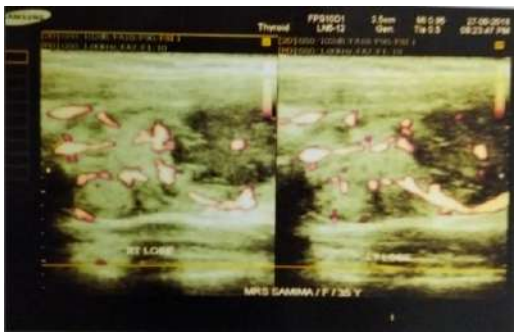

Figure – 7: Exclusively central blood flow (Vascular flow pattern V)

Here the nodule is solid & part of it is hypo-echoic with ill defined irregular outlined having no calcification & haloes.

DISCUSSION

Differentiation between benign and malignant thyroid nodules remains a major diagnostic challenge in endocrine imaging. Although fine-needle aspiration cytology (FNAC) is considered the gold standard, it is invasive and sometimes yields indeterminate results. Consequently, ultrasonography (USG) — particularly Power Doppler (PDUS) and Duplex Doppler (DDUS) — has gained prominence as a non-invasive adjunct that provides valuable morphological and hemodynamic information for risk stratification.[1,2]

In this prospective study of 43 patients with 60 thyroid nodules, we evaluated the correlation between vascular flow patterns on PDUS, Doppler indices (resistivity index and pulsatility index), and cytological findings. The results revealed a strong, statistically significant association between increasing central vascularity and malignancy, consistent with previously published literature.[3,4] Patterns IV and V, characterized by predominant or exclusive central blood flow, were highly predictive of malignant pathology, whereas peripheral or absent vascularity (Patterns I–III) was strongly suggestive of benign nodules. The mean age of patients (39.3 ± 14.3 years) and the female predominance in our series align with the demographic distribution reported in other regional and international studies.[5,6] Most patients presented with anterior neck swelling, and multinodularity was frequent, findings typical of benign thyroid disease but not exclusive to it. Our B-mode observations supported the established criteria for malignancy: hypoechogenicity, solid consistency, irregular or ill-defined margins, microcalcifications, and absence of a peripheral halo.[7,8] In contrast, isoechoic or cystic lesions with smooth margins and macrocalcifications were predominantly benign. These morphological clues, when integrated with vascular and spectral Doppler data, significantly improve pre-operative diagnostic confidence. The current study demonstrated that PDUS achieved a sensitivity of 93.8%, specificity of 88.6%, and diagnostic accuracy of 90.0%, values comparable to those of Liu et al.[9], who reported 92% sensitivity and 85% specificity. The addition of spectral Doppler parameters further refined diagnostic performance. Although the resistivity index (RI) and pulsatility index (PI) alone had lower predictive values (accuracy 81.7% and 78.3%, respectively), their combination with PDUS patterns substantially improved overall diagnostic efficacy. These results are in agreement with the findings of Rago et al.[10] and Lyshchik et al.[11], who emphasized that malignant nodules often display high RI and PI values reflecting increased vascular resistance secondary to neoangiogenesis and disorganized vascular architecture. A critical observation in our study was that central vascularity was consistently associated with malignant nodules, possibly due to angiogenic activity within the tumor core. Benign nodules typically derive blood supply from surrounding thyroid tissue, hence showing a peripheral flow pattern[12]. However, certain benign hyperplastic nodules may show central flow, underscoring the importance of correlating Doppler features with gray-scale morphology and cytology before making management decisions. The strong positive correlation between PDUS, DDUS, and FNAC results ($p < 0.001$) highlights the potential role of Doppler ultrasonography as an effective screening and triaging tool for thyroid nodules. By identifying high-risk vascular patterns, clinicians can prioritize nodules for FNAC, thus reducing unnecessary biopsies in clearly benign-appearing lesions. Several studies have also supported this integrated approach. Moon et al.[13] demonstrated that combining B-mode features with Doppler flow patterns achieved diagnostic accuracies approaching 90%. Similarly, Chammas et al.[14] found that vascular pattern assessment increased the sensitivity of ultrasound for detecting malignancy, particularly when central or chaotic flow was evident. In our study, the negative predictive value (97.5%) of PDUS was particularly high, indicating that nodules lacking central vascularity or displaying exclusively peripheral flow are highly likely to be benign. This finding supports the use of PDUS as a reliable exclusion test, enhancing patient reassurance and avoiding unnecessary interventions.[15,16] However, certain limitations should be acknowledged. The sample size was modest, and the number of malignant nodules was smaller compared to benign ones, which might affect the precision of sensitivity estimates. Moreover, vascular flow assessment is somewhat operator-dependent and may be influenced by machine settings, patient movement, or nodule depth. Future studies with larger sample sizes, quantitative vascular scoring, and integration with elastography or contrast-enhanced ultrasonography may further refine diagnostic algorithms. In our study study reaffirms that ultrasonographic vascular flow patterns are significantly correlated with cytological diagnosis. Patterns IV and V, reflecting central or predominant central flow, are highly suggestive of malignancy, while peripheral or absent flow strongly indicates benign pathology. Power Doppler and Duplex Doppler ultrasonography, when combined with B-mode imaging, constitute a sensitive, specific, and non-invasive approach that enhances diagnostic accuracy and optimizes the selection of nodules for FNAC.

CONCLUSION

The present study demonstrates a significant correlation between ultrasonographic vascular flow patterns and cytological diagnosis in thyroid nodules. Increasing central vascularity, represented by vascular patterns IV and V, was strongly predictive of malignancy, while absent or peripheral vascularity (patterns I–III) indicated benignity. Power Doppler ultrasonography showed excellent sensitivity and specificity, confirming its value as a non-invasive and reliable diagnostic adjunct to FNAC. Duplex Doppler indices, particularly elevated RI and PI values, further enhanced diagnostic confidence. Combining gray-scale features with Doppler parameters allows accurate preoperative differentiation of benign and malignant nodules, guiding clinicians in patient selection for FNAC or surgical management. Thus, Power and Duplex Doppler ultrasonography should be routinely integrated into thyroid imaging protocols to improve diagnostic efficiency and reduce unnecessary invasive procedures.

REFERENCES

1. *Brander A, Viikinkoski P, Nickels J, Kivisaari L. Thyroid gland: ultrasound screening in a random adult population. J Clin Ultrasound. 1991;19(6):375–381.*
2. *Guth S, Theune U, Aberle J, Galach A, Bamberger CM. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. Eur J Clin Invest. 2009;39(8):699–706.*
3. *Hegedüs L. Clinical practice. The thyroid nodule. N Engl J Med. 2004;351(17):1764–1771.*
4. *Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med. 1993;118(4):282–289.*
5. *Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, et al. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: The Bethesda System for Reporting Thyroid Cytopathology. Diagn Cytopathol. 2008;36(6):425–437.*
6. *Frates MC, Benson CB, Doubilet PM, Kunreuther E, Contreras M, Cibas ES, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules. Radiology. 2005;237(3):794–800.*

7. *Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation—multicenter retrospective study. Radiology. 2008;247(3):762–770.*
8. *Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee JT, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. AJR Am J Roentgenol. 2002;178(3):687–691.*
9. *Chammas MC, Gerhard R, de Oliveira IR, Widman A, Santos A, Cerri GG. Thyroid nodules: evaluation with power Doppler and duplex Doppler ultrasonography. J Clin Ultrasound. 2005;33(3):94–98.*
10. *Lyshchik A, Drozd V, Demidchik Y, Reiners C. Diagnosis of thyroid cancer in children: value of gray-scale and power Doppler US. Radiology. 2005;237(1):202–211.*
11. *Rago T, Vitti P, Chiovato L, Mazzeo S, De Liperi A, Miccoli P, et al. Role of conventional ultrasonography and color flow-Doppler sonography in predicting malignancy in cold thyroid nodules. J Clin Endocrinol Metab. 1998;83(12):4520–4525.*
12. *Tamsel S, Demirpolat G, Erdogan M, Nart D, Karadeniz M, Uluer H, et al. Power Doppler US patterns of vascularity and spectral Doppler US parameters in benign and malignant thyroid nodules. Diagn Interv Radiol. 2007;13(3):122–128.*
13. *Moon HJ, Kwak JY, Kim MJ, Son EJ, Kim EK. Can vascularity at power Doppler US help predict thyroid malignancy? Korean J Radiol. 2011;12(1):1–14.*
14. *Chammas MC, De Oliveira IR, Barros N, Durazzo M, Cerri GG. Doppler ultrasound of the thyroid gland. Ultrasound Med Biol. 2013;39(12):2332–2340.*
15. *Lagalla R, Caruso G, Romano G, Midiri M. Doppler evaluation of thyroid diseases. Eur Radiol. 1998;8(1):146–150.*
16. *Liu Y, Wang L, Liu Z, Xu D. Diagnostic accuracy of power Doppler ultrasound in thyroid nodules. Clin Radiol. 2010;65(6):483–488.*

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ORIGINAL ARTICLE

Association of Creatinine Clearance with Left Ventricular Ejection Fraction in Patients with Acute Coronary Syndrome

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ABSTRACT

Background: *Renal dysfunction is an independent predictor of adverse cardiovascular outcomes among patients with acute coronary syndrome. However, the relationship between creatinine clearance and left ventricular systolic function remains incompletely characterized. This study aimed to evaluate the association between creatinine clearance and left ventricular ejection fraction, and to assess clinical outcomes in ACS patients with varying degrees of renal function.* ***Methods & Materials:*** *The prospective observational study was conducted at the Department of Cardiology at Mymensingh Medical College Hospital between October 2022 and September 2023, including 100 consecutive patients with first-episode ACS within 24 hours of symptom onset. The patients were divided into two groups according to their calculated creatinine clearance: Group I (CrCl ≥ 70 ml/min, n = 31) and Group II (CrCl < 70 ml /min, n = 69). The study included a comprehensive clinical assessment, echocardiographic evaluation, and in-hospital monitoring. Data were analyzed using SPSS version 26 with appropriate statistical analysis.* ***Results:*** *The mean age of patients was 51.7±8.5 years, with 88% males. Patients with reduced creatinine clearance were significantly older (53.4±8.4 vs 47.8±7.2 years, p=0.002) and had a higher prevalence of diabetes mellitus (56.5% vs 22.6%, p=0.002). Mean LVEF was significantly lower in the abnormal clearance group (49.4±6.7% vs 56.5±6.0%, p=0.001). In-hospital morbidity was substantially higher in patients with CrCl <70 ml/min (84.0% vs 29.0%, p=0.001), including increased rates of heart failure (28.9% vs 9.6%, p=0.030), ventricular tachycardia (28.9% vs 6.4%, p=0.010), post-MI angina (34.7% vs 6.4%, p=0.002), and cardiogenic shock (21.7% vs 3.2%, p=0.020).* ***Conclusion:*** *Among ACS patients, reduced creatinine clearance is an independent correlate of lower LVEF and significantly higher in-hospital morbidity. Early recognition of renal dysfunction and aggressive risk stratification are strategies that may improve outcomes in this high-risk population.*

Keywords: *Acute coronary syndrome, Creatinine clearance, Renal dysfunction, Left Ventricular Ejection Fraction.*

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INTRODUCTION

Acute coronary syndrome represents a spectrum of ischemic cardiac states, including ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina, and continues to be one of the leading causes of cardiovascular morbidity and mortality worldwide[1]. Despite advances in both reperfusion strategies and pharmacological treatments, outcomes among patients with ACS continue to be highly variable, depending on a diverse array of clinical and biochemical factors. Renal impairment has emerged as an important, albeit largely unrecognized, contributor to these outcomes. Given the growing interest in the interaction between heart and kidney, the cardiorenal syndrome has become a focus of cardiovascular investigation and clinical practice[2]. CKD has been described in a substantial minority of patients with ACS, though the reported prevalence varies widely, between 30% and 60%, according to population characteristics and thresholds for diagnosis[3]. CKD in the setting of ACS often coexists with more extensive coronary disease, reduced utilization of evidence-based therapies, and significantly higher rates of adverse events both during hospitalization and over longer-term follow-up[4]. Notably, even mild to moderate renal dysfunction has been associated with a gradient of increased mortality and complication rates as estimated glomerular filtration rate decreases[5]. Calculated creatinine clearance, by means of the Cockcroft-Gault equation, is commonly used clinically to estimate renal function. Large registries, such as the Global Registry of Acute Coronary Events (GRACE), have consistently shown that it independently predicts in-hospital mortality and major bleeding in ACS patients[6]. The mechanisms for the association between impaired renal function and poor cardiovascular outcome are multifaceted, including accelerated atherosclerosis, persistent inflammation, oxidative injury, endothelial dysfunction, disturbances in mineral metabolism, and activation of neurohormonal pathways such as the renin-angiotensin-aldosterone system[7]. LVEF, which is the most applied measure of systolic function in post-ACS management, remains a cornerstone for risk stratification. A reduced LVEF is inextricably linked with increased mortality, susceptibility to heart failure, and risk of sudden cardiac death[8]. The influence of renal impairment on LVEF is

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bidirectional; renal impairment might enhance the degree of myocardial injury via both thrombotic and inflammatory pathways[9], while impaired cardiac output may aggravate renal hypoperfusion and neurohormonal activation, which further accelerates deterioration in both organs. Although renal function and LVEF are individual determinants of prognosis, their direct relationship remains poorly defined in ACS patients, especially in resource-constrained settings. Establishing this relationship can enable the earlier identification of high-risk patients, guide revascularization and medical therapy, and inform monitoring strategies[10]. In light of this, this study aimed to assess the correlation between creatinine clearance and LVEF among patients with ACS and the impact of renal dysfunction on complication rates during hospitalization.

METHODS & MATERIALS

This prospective study was conducted in the Department of Cardiology at Mymensingh Medical College Hospital between October 2022 and September 2023. A total of 100 patients of both sexes were enrolled through purposive sampling. The reduced sample size was due to the limited study period. Eligible participants included adults aged 65 years or younger who presented with their first episode of acute coronary syndrome within 24 hours of symptom onset. Patients with previous ACS, valvular heart disease, cardiomyopathy, prior heart failure, or a history of PTCA with stenting or CABG were excluded. Renal function was assessed using calculated creatinine clearance, and patients were stratified into two groups: Group I with CrCl ≥70 ml/min and Group II with CrCl <70 ml/min. After obtaining informed written consent, each patient underwent detailed history taking, physical examination, and 12-lead ECG assessment. Blood samples were collected for cardiac biomarkers, serum creatinine, glucose, lipid profile, and echocardiography or other investigations as indicated. All findings were documented in a standardized, IRB-approved data collection form. Patients were monitored throughout hospitalization for the development of complications such as heart failure, cardiogenic shock, mechanical complications, arrhythmias, post-MI angina, reinfarction, or death. Data were entered and analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using an independent samples t-test. Categorical variables were presented as frequencies and percentages, and compared using the chi-square test or Fisher's exact test as appropriate. Analysis of variance (ANOVA) was employed for comparing multiple group means. A p-value <0.05 was considered statistically significant for all analyses.

RESULTS

Table – I: Distribution of baseline demographic and risk factors of the study population (*n*=100)

Variables	Male (n= 88) (88%)		Female (n=12) (12%)		Total (N=100)		p-value
	n	%	n	%	n	%	
Age (in years)	-	-	-	-	-	-	-
30-39	7	8%	1	8.3%	8	8%	-
40-49	24	27.3%	1	8.3%	25	25%	-
50-59	37	42%	6	50%	43	43%	-
60-65	20	22.7%	4	33.3%	24	24%	-
Mean ± SD (Range)	51.3±8.5 (30-65)		54.4±8.1 (30-65)		51.7±8.5 (30-65)		0.230
Risk Factors	-	-	-	-	-	-	-
Smoking	70	79.5	1	8.3	71	71%	-
Hypertension	48	54.5	11	91.7	59	59%	-
Diabetes mellitus	38	43.2	8	66.7	46	46%	-
Dyslipidaemia	42	47.7	4	33.3	46	46%	-
Family H/O IHD	39	44.3	4	33.3	43	43%	-
Mean ± SD (Range)	2.7±0.9 (1-5)		2.3±1.1 (1-5)		2.6±0.9 (1-5)		0.250

Table I represents baseline demographics and risk factors of the study population. The study consisted of 100 patients (mean age 51.7±8.5 years, range 30-65 years) with a predominance of males (88%). Age distribution was 50-59 years (43%), 40-49 years (25%), and 60-65 years (24%). Traditional cardiovascular risk factors were very common, including smoking in 71% of the patients, hypertension in 59%, diabetes mellitus, and dyslipidemia in 46% each.

Table – II: Haemodynamic parameters of the Study population (*n*=100)

Parameters	Male (n=88)	Female (n=12)	p-value
	Mean ± SD	Mean ± SD	
Pulse/minute	79.5±13.9 (40-120)	71.9±13.9 (52-105)	0.080
Systolic blood pressure (mmHg)	120.7±28.9 (60-220)	132.9±30.9 (100-220)	0.170
Diastolic blood pressure (mmHg)	77.7±18.9 (40-120)	80.0±14.1 (70-120)	0.680

Table II shows the haemodynamic parameters of the study population with a mean pulse rate of 79.5±13.9 bpm for males versus 71.9±13.9 bpm for females, systolic blood pressure of 120.7±28.9 mmHg for males versus 132.9±30.9 mmHg for females, and diastolic blood pressure of 77.7±18.9 mmHg for males versus 80.0±14.1 mmHg for females.

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Table – III: Age, sex, and heart failure distribution of study population with normal and abnormal renal function (*n*=100)

Variables	Creatinine Clearance						p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Total		
	n	%	n	%	n	%	
Age (in years)	-	-	-	-	-	-	-
30 - 39	3	9.7%	5	7.%	8	8%	-
40 - 49	13	41.9%	12	17.4%	25	25%	-
50 - 59	14	45.2%	29	42%	43	43%	-
60 - 65	1	3.2%	23	33.3%	24	24%	-
Total	31	100%	69	100%	100	100%	
Mean ± SD (Range)	47.8±7.2 (30-60)		53.4±8.4 (35-65)		51.7±8.5 (30-65)		0.002
Sex	-	-	-	-	-	-	-
Male	28%	90.3%	60	87%	88	88%	0.630
Female	3%	9.7%	9	13%	12	12%	
Heart failure	-	-	-	-	-	-	-
Class I	28%	90.3%	49	71%	77	77%	0.030
Class II	2%	6.5%	11	15.9%	13	13%	
Class III	1%	3.2%	3	4.3%	4	4%	

Table III depicts the age distribution of patients with normal and abnormal renal function. Patients with abnormal renal function were older than those with normal clearance (53.4±8.4 vs 47.8±7.2 years), with only 3.2% of normal-clearance patients in the 60-65 years compared to 33.3% of those with abnormal clearance. Of importance, heart failure classification differed significantly between the groups (p=0.030), with 90.3% of normal-clearance patients in class I compared to only 71.0% of reduced-clearance patients, while class II was present in 6.5% versus 15.9% and class III in 3.2% versus 4.3%, respectively.

Table – IV: Risk factors of patients with normal and abnormal creatinine clearance (*n*=100)

Risk factors	Creatinine Clearance						p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Total (N=100)		
	Number	%	Number	%	Number	%	
Smoking	22	71%	49	71%	71	71%	0.990
Hypertension	16	51.6%	43	62.3%	59	59%	0.310
Family history of IHD	15	48.4%	28	40.6%	43	43%	0.460
Diabetes mellitus	7	22.6%	39	56.5%	46	46%	0.002
Dyslipidaemia	17	54.8%	29	42%	46	46%	0.230
Mean ± SD (Range)	2.45±0.76 (1-4)		2.72±1.01 (1-5)		2.64±0.98 (1-5)		0.190

Table IV shows the risk factors of patients with normal and abnormal creatinine clearance. The stratification of the cardiovascular risk factors by renal function revealed notable similarities in smoking (71.0% vs 71.0%), hypertension (62.3% vs 51.6%), family history of ischemic heart disease (40.6% vs 48.4%, p=0.460), and dyslipidemia (42.0% vs 54.8%, p=0.230) between the abnormal and normal creatinine clearance groups.

Table – V: Pattern of acute coronary syndrome in patients with normal and abnormal renal function (*n*=100)

Pattern of ACS	Creatinine Clearance						p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Total (N=100)		
	n	%	n	%	n	%	
Anterior	19	61.3%	27	39.1%	46	46%	0.200
Inferior	9	29%	34	49.3%	43	43%	
NSTEMI	1	3.2%	4	5.8%	5	5%	
UA	2	6.5%	4	5.8%	6	6%	

Table V shows the pattern of acute coronary syndrome in patients with normal and abnormal renal function. The distribution of ACS subtypes was as follows: anterior myocardial infarction, 46% overall (61.3% in normal clearance vs 39.1% in reduced clearance); inferior myocardial infarction, 43% overall (29.0% vs 49.3%); NSTEMI, 5% overall (3.2% vs 5.8%); and unstable angina, 6% overall (6.5% vs 5.8%).

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Table – VI: Mean percent of ejection fraction of patients with normal and abnormal creatinine clearance (*n*=100)

Ejection fraction (percent)	Creatinine Clearance						p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Total (N=100)		
	Number	%	Number	%	Number	%	
30 - 39	0	0%	3	4.3%	3	3%	-
40 - 49	4	12.9%	33	47.8%	37	37%	-
50 - 59	16	51.6%	29	42%	45	45%	-
60 - 69	11	35.5%	4	5.8%	15	15%	-
Mean ± SD (Range)	56.5±6.0 (43-66)		49.4±6.7 (30-66)		51.6±7.3 (30-66)		0.001

Table VI denotes the Mean percent of ejection fraction of patients with normal and abnormal creatinine clearance. The mean LVEF was substantially lower in patients with reduced creatinine clearance, 49.4±6.7% vs. 56.5±6.0%. Distribution of ejection fraction categories showed that no patients with normal clearance had severely depressed function, 30-39% range, while 4.3% of those with abnormal clearance fell into this category. At the other extreme, 35.5% of normal-clearance patients achieved LVEF ≥60%, whereas only 5.8% of reduced-clearance patients did.

Table – VII: Pattern of cardiac complications of patients with normal and abnormal creatinine clearance (In-hospital morbidity (*n*=100)

Complications	Creatinine Clearance						p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		Total (N=100)		
	n	%	n	%	n	%	
Heart failure (Killip II- IV)	3	9.6%	20	28.9%	23	23%	0.030
Atrial fibrillation	3	9.6%	14	20.2%	17	17%	0.190
Ventricular tachycardia	2	6.4%	20	28.9%	22	22%	0.010
Ventricular fibrillation	0	0%	4	5.7%	4	4%	0.170
Post MI angina	2	6.4%	24	34.7%	26	26%	0.002
Heart Block	0	0%	7	10.1%	7	7%	0.060
Mechanical complication	0	0%	2	2.9%	2	2%	0.330
Cardiogenic shock	1	3.2%	15	21.7%	16	16%	0.020

Table VII demonstrates the Pattern of cardiac complications of patients with normal and abnormal creatinine clearance (In-hospital morbidity. Heart failure (Killip II-IV) occurred in 28.9% versus 9.6%, ventricular tachycardia in 28.9% versus 6.4%, post-MI angina in 34.7% versus 6.4%, and cardiogenic shock in 21.7% versus 3.2%, atrial fibrillation (20.2% vs 9.6%), ventricular fibrillation (5.7% vs 0%), heart block (10.1% vs 0%), and mechanical complications (2.9% vs 0%).

Table – VIII: In-hospital morbidity and Mortality of patients with normal and abnormal creatinine clearance (*n*=100)

	Creatinine Clearance				p-value
	Normal clearance (≥70) (n=31)		Abnormal clearance (<70) (n=69)		
	n	%	n	%	
Morbidity	-	-	-	-	-
Yes	9	29%	58	84%	0.001[S]
No	22	71%	11	16%	
Mortality	-	-	-	-	-
Yes	0	0%	4	5.8%	0.17[NS]
No	31	100%	65	94.2%	

Table VIII shows the in-hospital morbidity and Mortality of patients with normal and abnormal creatinine clearance. Overall, in-hospital morbidity affected 84% of those with abnormal clearance compared with 29% in those with normal clearance (p=0.001). In-hospital mortality occurred in 0% patients with normal clearance versus 5.8% in the abnormal clearance group.

DISCUSSION

The study demonstrates a clear and clinically meaningful relationship between impaired creatinine clearance and reduced left ventricular ejection fraction in patients with acute coronary syndrome, with a substantially higher burden of in-hospital morbidity. An absolute 7.1% reduction in mean LVEF among patients with impaired renal function strengthens previous findings by Køber et al., that renal dysfunction significantly exacerbates cardiac systolic impairment and increases the risk of adverse outcomes[11]. The high percentage of patients in this cohort with creatinine clearance below 70 ml/min is consistent with Keough-Ryan et al. major registry findings, indicating that renal impairment is common among ACS populations worldwide[12]. Data from large registries like the GRACE registry demonstrate that declining creatinine clearance independently predicts hospital mortality and major bleeding across the spectrum of ACS[13]. Correspondingly, the findings of Reddan et al. indicate that even small reductions in renal function confer incremental risk of mortality, emphasizing the prognostic implications of mild renal impairment[14]. Chronic renal disease accelerates atherosclerosis through sustained inflammation, oxidative injury, endothelial dysfunction, and accumulation of atherogenic uremic toxins[15]. These processes increase coronary disease severity and predispose to larger infarcts during ischemia. Furthermore, renal impairment is also involved in the development of coronary microvascular disease, which in turn has been related to worse infarct size

and post-ischemic ventricular remodeling[16]. Uremic toxins such as indoxyl sulfate and p-cresyl sulfate further destabilize plaques and enhance thrombogenicity, promoting more extensive myocardial injury[17]. The notably higher prevalence of diabetes within the reduced clearance group underlines the importance of metabolic factors within the cardiorenal axis. Indeed, emerging evidence has pointed out that insulin resistance, as quantified by the triglyceride-glucose index, partly serves as a mediator between renal impairment and adverse cardiovascular outcomes in ACS[18]. Thus, the triad of diabetes, renal dysfunction, and ACS forms a high-risk clinical phenotype that requires more frequent monitoring and intensified therapeutic strategies. The high morbidity in the reduced clearance group (84% vs 29%) indicates the significant clinical consequence of renal impairment during the acute phase. Complications like heart failure, ventricular tachycardia, post-MI angina, and cardiogenic shock were recorded with far greater frequency, which is in tune with the findings of Nabais et al., who demonstrated that renal dysfunction carries heightened risk independently of the traditional ACS risk scores[19]. The increased arrhythmia burden is consistent with the report by Yalta et al., including electrolyte disturbances, autonomic imbalance, and changes in myocardial structure related to uremia[20]. Temporal analyses demonstrate that though therapies have evolved, the gains in outcome have been much less marked for those with impaired renal function, partly because of underutilization of therapies related to bleeding risk, concern about contrast exposure, and altered pharmacokinetics[21]. These findings emphasize the need for individual adjustments of therapy, rather than withholding beneficial treatments. Clinical implications include the routine inclusion of creatinine clearance in risk stratification to facilitate early identification of vulnerable patients. The shock index-creatinine score is an emerging tool that will likely further refine prognostic assessment in ACS[22]. Management should be focused on renal-protective strategies, judicious fluid balance, avoidance of nephrotoxic exposures, and guideline-directed medical therapy, with appropriate dose adjustment. Evidence to support SGLT2 inhibitors and renin-angiotensin-aldosterone system blockers suggests that there could be a benefit even in those patients with advanced renal dysfunction.

Limitations of the Study: The limitations of this study are its small sample size and single-center design, which may restrict the generalization of findings to broader populations with different demographic and clinical characteristics. The absence of long-term follow-up data precludes assessment of chronic outcomes, ejection fraction recovery patterns, and sustained impact of renal dysfunction on cardiovascular morbidity and mortality beyond the acute hospitalization period.

CONCLUSION

This study among patients with acute coronary syndrome shows that reduced creatinine clearance is independently associated with a significantly lower left ventricular ejection fraction and substantially increased in-hospital morbidity. The findings underline the paramount importance of early assessment of renal function in ACS risk stratification and point out a particular need for intensive monitoring and targeted interventions in patients with concomitant cardiac and renal dysfunction. The integration of creatinine clearance into routine clinical evaluation may improve predictive accuracy and enable appropriate therapeutic decision-making in this vulnerable population.

Recommendations: Future studies need to be prospective and multicenter, with larger cohorts and longer follow-up, to confirm these findings and establish optimal management strategies for ACS patients with renal dysfunction.

REFERENCES

1. *Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, Bonny A. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. Journal of the American college of cardiology. 2020 Dec 22;76(25):2982-3021.*
2. *Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. Journal of the American college of cardiology. 2008 Nov 4;52(19):1527-39.*
3. *Marenzi G, Cabiati A, Assanelli E. Chronic kidney disease in acute coronary syndromes. World journal of nephrology. 2012 Oct 6;1(5):134.*
4. *Li C, Hu D, Shi X, Li L, Yang J, Song L, Ma C. A multicentre prospective evaluation of the impact of renal insufficiency on in-hospital and long-term mortality of patients with acute ST-elevation myocardial infarction. Chinese medical journal. 2015 Jan 5;128(01):1-6.*
5. *Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation. 2003 Oct 28;108(17):2154-69.*
6. *Santopinto JJ, Fox KA, Goldberg RJ, Budaj A, Pinero G, Avezum A, Gulba D, Esteban J, Gore JM, Johnson J, Gurfinkel EP. Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: findings from the global registry of acute coronary events (GRACE). Heart. 2003 Sep 1;89(9):1003-8.*
7. *Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. Journal of the American Society of Nephrology. 2006 Jul 1;17(7):2034-47.*
8. *Anavekar NS, McMurray JJ, Velazquez EJ, Solomon SD, Kober L, Rouleau JL, White HD, Nordlander R, Maggioni A, Dickstein K, Zelenkofske S. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. New England Journal of Medicine. 2004 Sep 23;351(13):1285-95.*
9. *Bajaj NS, Singh A, Zhou W, Gupta A, Fujikura K, Byrne C, Harms HJ, Osborne MT, Bravo P, Andrikopolou E, Divakaran S. Coronary microvascular dysfunction, left ventricular remodeling, and clinical outcomes in patients with chronic kidney impairment. Circulation. 2020 Jan 7;141(1):21-33.*
10. *Dudek D, Chyrchel B, Siudak Z, Depukat R, Chyrchel M, Dziewierz A, Mielecki W, Rakowski T, Rzeszutko Ł, Dubiel J. Original article Renal insufficiency increases mortality in acute coronary syndromes regardless of TIMI risk score. Polish Heart Journal (Kardiologia Polska). 2008;66(1):28-34.*
11. *Køber L, Torp-Pedersen C, Carlsen JE, Bagger H, Eliasen P, Lyngborg K, Videbæk J, Cole DS, Auclert L, Pauly NC, Aliot E. A clinical trial of the angiotensin-converting–enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. New England Journal of Medicine. 1995 Dec 21;333(25):1670-6.*
12. *Keough-Ryan TM, Kiberd BA, Dipchand CS, Cox JL, Rose CL, Thompson KJ, Clase CM. Outcomes of acute coronary syndrome in a large Canadian cohort: impact of chronic renal insufficiency, cardiac interventions, and anemia. American journal of kidney diseases. 2005 Nov 1;46(5):845-55.*
13. *Christos P, Georgia K, Panagiotakos Demosthenes B, Yannis K, Yannis M, Christina C, Christodoulos S. Association of Creatinine Clearance and In-Hospital Mortality in Patients With Acute Coronary Syndromes. Circulation Journal. 2007;71(1):9-14.*
14. *Reddan DN, Szczech L, Bhapkar MV, Moliterno DJ, Califf RM, Ohman EM, Berger PB, Hochman JS, Van de Werf F, Harrington RA, Newby LK. Renal function, concomitant medication use and outcomes following acute coronary syndromes. Nephrology Dialysis Transplantation. 2005 Oct 1;20(10):2105-12.*

15. *Ter Maaten JM, Damman K, Verhaar MC, Paulus WJ, Duncker DJ, Cheng C, Van Heerebeek L, Hillege HL, Lam CS, Navis G, Voors AA. Connecting heart failure with preserved ejection fraction and renal dysfunction: the role of endothelial dysfunction and inflammation. European journal of heart failure. 2016 Jun;18(6):588-98.*
16. *Wang H, Wu Q, Yang L, Chen L, Liu WZ, Guo J, Xu JS. Application of AMR in evaluating microvascular dysfunction after ST-elevation myocardial infarction. Clinical Cardiology. 2024 Feb;47(2):e24196.*
17. *Vanholder R, De Smet R, Glorieux G, Argilés A, Baurmeister U, Brunet P, Clark W, Cohen G, De Deyn PP, Deppisch R, Descamps-Latscha B. Review on uremic toxins: classification, concentration, and interindividual variability. Kidney international. 2003 May 1;63(5):1934-43.*
18. *Yang G, Jiang M, Liu L, Jia D, Feng J, Luo Y, Ye T, Xia L, Liu H, Zhang Z, Fu J. The Synergistic Risk of Insulin Resistance and Renal Dysfunction in Acute Coronary Syndrome Patients After Percutaneous Coronary Intervention. Journal of Cardiovascular Development and Disease. 2025 Oct 28;12(11):427.*
19. *Nabais S, Rocha S, Costa J, Marques J, Torres M, Magalhães S, Pereira MA, Correia A. Prognostic impact of moderate renal dysfunction in acute coronary syndromes.*
20. *Yalta K, Yilmaz MB. Coronary microvascular dysfunction portends poor prognosis in the setting of chronic renal failure: Harnessing dual marker strategy for better risk-stratification?. International journal of cardiology. 2014 Feb 1;171(2):275-6.*
21. *Arow Z, Ovdat T, Gabarin M, Omelchenko A, Shuvy M, Or T, Assali A, Pereg D. Temporal Trends in the Prevalence, Treatment and Outcomes of Patients with Acute Coronary Syndrome at High Bleeding Risk. Diagnostics. 2022 Jul 22;12(8):1784.*
22. *Shariefuddin WW, Pramudyo M, Martha JW. Shock index creatinine: a new predictor of mortality in acute coronary syndrome patients. BMC Cardiovascular Disorders. 2024 Feb 3;24(1):87.*

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ORIGINAL ARTICLE

Comparison of Phenylephrine and Ephedrine in Treatment of Spinal Induced Hypotension in Emergency Cesarean Section

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ABSTRACT

Background: *Spinal-induced hypotension is a common complication during emergency cesarean section, affecting up to 70% of parturients and potentially impacting maternal and fetal outcomes. Phenylephrine and ephedrine are widely used vasopressors to manage hypotension, yet their comparative efficacy and safety remain under investigation.* ***Objective:*** *This study aimed to compare the efficacy and safety of phenylephrine versus ephedrine in managing spinal-induced hypotension during emergency cesarean sections.* ***Methods & Materials:*** *This observational comparative study was conducted at the Department of Anaesthesia and ICU, Kurmitula General Hospital (KGH), Dhaka, Bangladesh, from January-2025 to June 2025. A total of 60 patients aged 18–40 years who underwent emergency cesarean section under spinal anesthesia were enrolled in this study and the enrolled patients were divided equally into two groups with 30 patients in each. Group-1 received intravenous phenylephrine (initial dose 100 mcg, titrated as needed), and Group-2 received intravenous ephedrine (initial dose 5 mg, titrated as needed). Maternal hemodynamics, neonatal Apgar scores, and adverse effects were recorded. Hypotension was defined as systolic blood pressure (SBP) <90 mmHg or ≥20% decrease from baseline. Data were analyzed using Statistical Package for Social Sciences (SPSS) version-23.0.* ***Results:*** *A total of 60 parturients undergoing emergency cesarean section under spinal anesthesia were included, with 30 patients in each group. The mean age was 27.8 ± 4.2 years in the phenylephrine group and 28.1 ± 4.6 years in the ephedrine group (p=0.78). Mean height (155.6 ± 5.4 vs. 156.3 ± 5.1 cm; p=0.62) and weight (63.8 ± 7.5 vs. 64.9 ± 7.1 kg; p=0.54) were similar. ASA physical status was comparable, with ASA I comprising 12 (40%) vs. 11 (36.7%) and ASA II 18 (60%) vs. 19 (63.3%) in the phenylephrine and ephedrine groups, respectively. Indications for cesarean delivery were evenly distributed between the groups: failure to progress in 9 (30%) vs. 10 (33.3%), cephalopelvic disproportion in 8 (26.7%) vs. 7 (23.3%), previous cesarean in 7 (23.3%) vs. 6 (20%), and other indications in 6 (20%) vs. 7 (23.3%) in the phenylephrine and ephedrine groups, respectively.. Phenylephrine provided significantly higher systolic blood pressure at all measured time points (5 min: 112.4 ± 8.6 vs. 105.2 ± 9.3 mmHg); (p=0.003) and lower maternal heart rates (10 min: 82.7 ± 7.6 vs. 94.3 ± 9.1 bpm;(p<0.001) compared with ephedrine. Neonatal outcomes, including one- and five-minute Apgar scores, were similar between the groups (p>0.05). Adverse effects were infrequent; bradycardia occurred more often in the phenylephrine group (16.7% vs. 3.3%, (p=0.09), while nausea and vomiting were slightly more common in the ephedrine group without statistical significance (P>0.05).* ***Conclusion:*** *Phenylephrine provides superior systolic blood pressure stability and lower maternal heart rates compared with ephedrine during spinal-induced hypotension in emergency cesarean sections, with similar neonatal outcomes and overall safety. These findings support phenylephrine as the preferred vasopressor in obstetric anesthesia for managing spinal-induced hypotension.*

Keywords: *Spinal anesthesia, hypotension, cesarean section, phenylephrine, ephedrine, maternal hemodynamics, neonatal outcomes*

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INTRODUCTION

The choice of vasopressor for managing spinal induced hypotension during emergency cesarean sections is a critical decision that can significantly impact maternal and fetal outcomes. The incidence of hypotension during spinal anesthesia for cesarean delivery can be as high as 70% [1]. Despite the widespread use of spinal anesthesia in this context, the optimal vasopressor for managing hypotension remains a topic of ongoing debate. This study aims to compare the efficacy and safety of phenylephrine and ephedrine in managing spinal-induced hypotension during emergency cesarean sections [2]. Phenylephrine and ephedrine are the two most commonly used vasopressors for this purpose. Phenylephrine is an α1-adrenergic agonist that primarily

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increases systemic vascular resistance, thereby elevating blood pressure without significantly impacting heart rate [3]. In contrast, ephedrine is a non-selective adrenergic agonist that acts on both α and β receptors, resulting in vasoconstriction along with an increase in heart rate [4]. While both agents have been shown to be effective in managing hypotension, their differential effects on maternal and fetal outcomes are not well understood [5]. Several studies have explored the efficacy of these vasopressors. For instance, a systematic review indicated that phenylephrine is associated with fewer fetal acidosis episodes compared to ephedrine [6]. Additionally, Wang et al. found that phenylephrine use resulted in more stable hemodynamics during cesarean delivery compared to ephedrine [7]. However, concerns regarding maternal bradycardia with phenylephrine have also been documented [8]. The primary objective of this study is to compare the incidence rates of hypotension and fetal acidosis between phenylephrine and ephedrine in managing spinal-induced hypotension during emergency cesarean sections. The secondary objective is to evaluate the effects of these vasopressors on maternal cardiovascular stability and neonatal outcomes [9]. Maternal cardiovascular stability is crucial, as significant fluctuations can lead to adverse outcomes for both mother and child [10]. This study will provide vital insights into optimal management strategies for spinal-induced hypotension during emergency cesarean sections. The findings will contribute to the evolving discourse surrounding anesthetic care for parturients, with the potential to enhance clinical protocols and improve patient outcomes.

METHODS & MATERIALS

This was an observational comparative study conducted at the department of Anaesthesia and ICU in Kurmitula General Hospital, Dhaka, Bangladesh during January, 2025 to June, 2025. Written informed consent was onbtained from the caregiver or legal guardian and a total of 60 emergency caesarean cases aged between 18-40 years who underwent emergency caesarean section under spinal anaesthesia were employed in this study. The study patients were divided into two groups with 30 patients in each group. Group-1 received Phenylephrine (initial dose of 100 mcg intravenously, titrating as needed) and Group-2 received Ephedrine (initial dose of 5 mg intravenously, titrating as needed). The doses were inducted following the standard protocol of spinal Anaesthesia. Before the induction of the doses, medical history and prenatal care records were reviewed and physical examination was done. Then, hemodynamic parameters (blood pressure, heart rate, oxygen saturation) were monitored. Hypotension was defined as a decrease in systolic blood pressure (SBP) ≥ 20% from baseline or SBP < 90 mmHg. Administering the assigned vasopressor was ensured if hypotension occurs. The data were collected using a pre-structured questionnaire and a case record form. The collected data were analyzed using Statistical Package for Social Sciences (SPSS), version-23.0. Descriptive statistical analysis was performed and the results were presented in tables, graphs and charts. Chi-square test and t test were performed to compare the variables between the study groups where $p<0.05$ considered as the level of significance. All ethical considerations were maintained throughout the study under the declaration of Helsinki-1964.

Inclusion Criteria:

1. Pregnant women aged 18-40 years.
2. Women underwent emergency cesarean section under spinal anesthesia.
3. ASA (American Society of Anesthesiologists) Class I and II

Exclusion Criteria:

1. History of significant cardiovascular disease.
2. Contraindications to spinal anesthesia.
3. Known allergies to phenylephrine or ephedrine.
4. Patients on medications affecting blood pressure.
5. Pregnancy induced hypertension (PIH)

RESULTS

A total of 60 pregnant women undergoing emergency cesarean section under spinal anesthesia were included in this study, with 30 cases in each group. The mean age of the patients in Group-1 (Phenylephrine) was 27.8 ± 4.2 years, while in Group-2(Ephedrine) was 28.1 ± 4.6 years (p=0.78). There were no significant differences in mean height (155.6 ± 5.4 vs. 156.3 ± 5.1 cm; (p=0.62) and weight (63.8 ± 7.5 vs. 64.9 ± 7.1 kg; (p=0.54). ASA physical status was comparable, with ASA I represented by 12 (40%) vs. 11 (36.7%) and ASA II by 18 (60%) vs. 19 (63.3%) in the phenylephrine and ephedrine groups, respectively (p=0.79) (0.088). The indications for cesarean delivery were also evenly distributed between the groups: failure to progress occurred in 9 (30%) vs. 10 (33.3%), cephalopelvic disproportion in 8 (26.7%) vs. 7 (23.3%), previous cesarean section in 7 (23.3%) vs. 6 (20%), and other indications in 6 (20%) vs. 7 (23.3%) in the phenylephrine and ephedrine groups, respectively (Table-1). Neonatal outcomes were comparable between the study groups. The mean Apgar scores at one minute (7.9 ± 0.6 vs. 7.6 ± 0.7(p=0.08) and at five minutes (8.9 ± 0.3 vs. 8.7 ± 0.4(p=0.06) showed no significant differences, indicating similar neonatal wellbeing following either vasopressor. A notable difference was observed in the hemodynamic response following vasopressor administration (Table-2) Mean systolic blood pressure (SBP) was significantly higher in the Phenylephrine group at all-time points after 5 minutes. At 5 minutes, the mean SBP in Group-1 was 112.4 ± 8.6 mmHg compared with 105.2 ± 9.3 mmHg in Group-2 (p=0.003). This trend continued at 10, 15, 25, and 30 minutes, with Group-1 consistently demonstrating better blood pressure stability ($p<0.05$) (Table-3). Phenylephrine, a pure α-agonist, resulted in lower mean heart rates at all post-induction time points compared with Ephedrine, a mixed α/β-agonist. At 10 minutes, the mean HR was significantly lower in Group-1 (82.7 ± 7.6 bpm) than in Group-2 (94.3 ± 9.1 bpm) ($p<0.001$). This significant difference persisted from 5 minutes through 30 minutes ($p<0.002$) (Table-4). Adverse effects were infrequent in both groups. Nausea and vomiting occurred more frequently in Group-2 (23.3% and 20%) compared with Group-1 (10% and 6.7%), though the differences were not statistically significant (p=0.16) and (p=0.13). Bradycardia was more common in the Phenylephrine group (16.7% vs. 3.3%; (p=0.09), consistent with its pharmacological profile. Hallucination and nystagmus were rare and observed only in one patient in the Ephedrine group. Overall, the findings suggest that Phenylephrine provided more stable systolic blood pressure and lower heart rate following spinal-induced hypotension during emergency cesarean section, with comparable neonatal outcomes and a similar safety profile when compared with Ephedrine.

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Table – I: Demographic and clinical characteristics of the study patients (*n*=60)

Variables	Group-1 (Phenylephrine) (n=30	Group-2 (Ephedrine) (n=30	P-value
Age (years), mean ± SD	27.8 ± 4.2	28.1 ± 4.6	0.780
Height (cm), mean ± SD	155.6 ± 5.4	156.3 ± 5.1	0.621
Weight (kg), mean ± SD	63.8 ± 7.5	64.9 ± 7.1	0.543
ASA Physical Status:			
I	12 (40%)	11 (36.7%)	0.791
II	18 (60%)	19 (63.3%)	0.880
Indication of cesarean delivery:			
FTP	9 (30%)	10 (33.3%)	
CPD	8 (26.7%)	7 (23.3%)	
Previous cesarean	7 (23.3%)	6 (20%)	
Others	6 (20%)	7 (23.3%)	

Table – II: Comparison of intravenous bolus doses of vasopressors required to treat hypotension and Apgar score (*n*=60)

Variables	Group-1 (Phenylephrine)(n=30)	Group-2 (Ephedrine)(n=30)	P-value
First dose required (n, %)	22 (73.3%)	27 (90%)	0.091
Second dose required (n, %)	6 (20%)	12 (40%)	0.124
Mean Apgar Score			
At 1 minute	7.9 ± 0.6	7.6 ± 0.7	0.081
At 5 minutes	8.9 ± 0.3	8.7 ± 0.4	0.062

Table – III: Comparison of mean systolic BP between the study groups with respect of time (*n*=60)

Time	Group-1 (Phenylephrine) Mean ± SD	Group-2 (Ephedrine) Mean ± SD	P-value
0 minutes (baseline)	69.1 ± 1.8	68.2 ± 1.2	0.741
5 minutes	112.4 ± 8.6	105.2 ± 9.3	0.003
10 minutes	110.6 ± 7.9	103.8 ± 8.5	0.001
15 minutes	113.1 ± 6.8	106.9 ± 7.2	0.002
25 minutes	115.3 ± 6.9	110.1 ± 7.4	0.01
30 minutes	116.1 ± 7.0	111.4 ± 7.6	0.02

Table – IV: Comparison of mean heart rate between the study groups with respect of time (*n*=60)

Time	Group-1 Phenylephrine) Mean ± SD	Group-2 (Ephedrine)Mean ± SD	P-value
0 minutes (baseline)	89.2 ± 8.4	88.5 ± 8.1	0.771
5 minutes	84.1 ± 7.9	92.8 ± 8.4	<0.001
10 minutes	82.7 ± 7.6	94.3 ± 9.1	<0.001
15 minutes	83.3 ± 7.2	95.1 ± 8.7	<0.001
20 minutes	84.2 ± 6.9	93.7 ± 8.2	<0.001
25 minutes	85.4 ± 7.1	92.6 ± 7.9	0.001
30 minutes	86.3 ± 7.0	91.4 ± 8.1	0.002

Table – V: Comparison of adverse effects and complications between the study groups (*n*=60)

Adverse Effects	Group-1 (Phenylephrine) (n=30)	Group-2 (Ephedrine) (n=30)	P-value
Nausea (n, %)	3 (10%)	7 (23.3%)	0.161
Vomiting (n, %)	2 (6.7%)	6 (20%)	0.132
Bradycardia (n, %)	5 (16.7%)	1 (3.3%)	0.09
Hallucination (n, %)	0	1 (3.3%)	0.312
Nystagmus (n, %)	0	1 (3.3%)	0.314

DISCUSSION

This study compared phenylephrine and ephedrine for the management of spinal anesthesia–induced hypotension during emergency cesarean section in 60 patients, with 30 in each group. Baseline characteristics such as age (27.8 ± 4.2 vs. 28.1 ± 4.6 years), height (155.6 ± 5.4 vs. 156.3 ± 5.1 cm), and weight (63.8 ± 7.5 vs. 64.9 ± 7.1 kg) were similar between the phenylephrine and ephedrine groups, indicating proper randomization and comparability. A key finding of this study was the significantly higher systolic blood pressure in the phenylephrine group at all measured time points. At 5 minutes after spinal anesthesia, mean SBP was 112.4 ± 8.6 mmHg in the phenylephrine group compared with 105.2 ± 9.3 mmHg in the ephedrine group ($p = 0.003$). This trend continued consistently at 10, 15, 20, 25, and 30 minutes ($p < 0.05$). These results reinforce the well-established α-adrenergic vasoconstrictive effect of phenylephrine, which has been shown to provide superior blood pressure maintenance compared with ephedrine in cesarean deliveries[11,12]. Another important finding was the significantly lower maternal heart rate in the phenylephrine group across all post-induction intervals. For example, at 10 minutes, the mean HR was 82.7 ± 7.6 bpm in the phenylephrine group versus 94.3 ± 9.1 bpm in the ephedrine group ($p < 0.001$). This phenomenon is consistent with reflex bradycardia due to increased systemic vascular resistance caused by phenylephrine [13]. The persistently higher heart rates in the ephedrine group align with its mixed α/β-agonist activity and its tendency to increase cardiac output. Neonatal outcomes were also comparable between the two groups. The mean Apgar score at

one minute was 7.9 ± 0.6 in the phenylephrine group and 7.6 ± 0.7 in the ephedrine group (p = 0.08). At five minutes, Apgar scores were 8.9 ± 0.3 vs. 8.7 ± 0.4 (p = 0.06). Although phenylephrine induces more maternal bradycardia, it is associated with less placental transfer than ephedrine, which may explain the absence of significant differences in neonatal well-being. Prior studies have demonstrated that ephedrine is linked with fetal acidosis due to higher fetal exposure [14, 15], whereas phenylephrine is considered safer in terms of neonatal acid–base status [16, 17]. Adverse effects in this study were infrequent and mostly mild. Nausea occurred in 10% of phenylephrine-treated patients compared with 23.3% in the ephedrine group, while vomiting occurred in 6.7% vs. 20%, respectively, though neither reached statistical significance. These findings are consistent with previous reports associating ephedrine-induced tachycardia and sympathetic stimulation with increased maternal nausea and vomiting [18]. Bradycardia was more common in the phenylephrine group (16.7% vs. 3.3%), matching the expected pharmacological effects of pure α-agonists [19]. Hallucination and nystagmus were rare and noted only in one ephedrine-treated patient, consistent with isolated reports describing ephedrine-related CNS stimulation [20].Overall, the major findings of this study significantly better systolic blood pressure stability, significantly lower maternal heart rate, similar neonatal Apgar scores, and a comparable safety profile align with current international evidence favoring phenylephrine as the primary vasopressor in obstetric anesthesia. A recent randomized controlled trial support phenylephrine's superior hemodynamic control and reassuring neonatal outcomes compared with ephedrine [21]. These findings collectively strengthen the recommendation for phenylephrine as the vasopressor of choice for managing spinal-induced hypotension in both elective and emergency cesarean sections.

LIMITATIONS OF THE STUDY

This study has some limitations. It was a single center study with limited samples over a short study period, which may restrict the generalizability of the findings to broader populations of the whole country. These limitations highlight the need for future prospective, multicenter study to justify the results of this present study.

CONCLUSION

This study shows that phenylephrine provides significantly better systolic blood pressure stability and lower maternal heart rate than ephedrine during emergency cesarean section under spinal anesthesia, while neonatal Apgar scores and adverse effects remain comparable between the two groups. These findings indicate that phenylephrine is a more effective and reliable vasopressor for managing spinal-induced hypotension without compromising neonatal wellbeing, supporting its use as the preferred agent in obstetric anesthesia.

RECOMMENDATIONS OF THE STUDY

Based on the study findings, it is recommended that phenylephrine be adopted as the first-line vasopressor for managing spinal-induced hypotension during emergency cesarean sections, given its superior blood pressure stabilization and predictable maternal heart rate response without adverse effects on neonatal Apgar scores. Clinical protocols should incorporate phenylephrine as the preferred agent, while ephedrine may be reserved for selected cases based on individual hemodynamic profiles. Further multicenter studies with larger samples are suggested to validate these results and support broader guideline implementation in obstetric anesthesia practice.

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REFERENCES

1. *Gunter JB, et al. Incidence and management of hypotension during spinal anesthesia for cesarean delivery: a systematic review. Anesthesiology.2018;128(2):292-300.*
2. *Hobeika M, et al. Hypotension during spinal anesthesia for elective cesarean delivery: a systematic review and meta-analysis. BMC Anesthesiol. 202;20(1):1-11.*
3. *Brull R, et al. Phenylephrine versus ephedrine for the treatment of hypotension during spinal anesthesia for cesarean delivery:a systematic review and meta-analysis. Anesth Analg. 2015;120(5):1387-94.*
4. *Bramham J, et al. Effects of phenylephrine and ephedrine on maternal and fetal outcomes during cesarean section: a systematic review. Int J Obstet Anesth. 2018;36:77-85.*
5. *Albright G, et al. Vasopressor choice and fetal acid-base status during elective cesarean delivery: a randomized controlled trial. Anesth Analg. 2017;124(5):1544-52.*
6. *G unter JB, et al. Incidence and management of hypotension during spinal anesthesia for cesarean delivery: a systematic review. Anesthesiology.2018;128(2):292-300.*
7. *Hobeika M, et al. Hypotension during spinal anesthesia for elective cesarean delivery: a systematic review and meta-analysis. BMC Anesthesiol. 202; 20(1):1-11.*
8. *Brull R, et al. Phenylephrine versus ephedrine for the treatment of hypotension during spinal anesthesia for cesarean delivery:a systematic review and meta-analysis. Anesth Analg. 2015;120(5):1387-94.*
9. *Bramham J, et al. Effects of phenylephrine and ephedrine on maternal and fetal outcomes during cesarean section: a systematic review. Int J Obstet Anesth. 2018; 36:77-85.*
10. *Albright G, et al. Vasopressor choice and fetal acid-base status during elective cesarean delivery: a randomized controlled trial. Anesth Analg. 2017; 124(5):1544-52.*
11. *Ngan Kee WD. The use of vasopressors during spinal anesthesia for cesarean section. Curr Opin Anaesthesiol. 2017; 30(3):319–25.*
12. *Singh PM, Singh NP, Reschke M, et al. Vasopressor choice for hypotension during cesarean section under spinal anesthesia: A systematic review and network meta-analysis. Medicine (Baltimore). 2019;98(10):e14659.*
13. *Heesen M, Klöhr S, Rossaint R, et al. Maternal bradycardia after phenylephrine for spinal anesthesia during cesarean section: A systematic review. Int J Obstet Anesth. 2015;24(4):298–307.*
14. *Ngan Kee WD, Khaw KS, Lee BB, et al. Metabolic acidosis in newborns after ephedrine use during spinal anesthesia for cesarean delivery. Anesthesiology. 2004;100(3):660–6.*
15. *Vallejo MC, Attaallah AF, Elzamzamy OM, et al. Maternal and neonatal effects of phenylephrine versus ephedrine during spinal anesthesia for cesarean delivery. J Clin Anesth. 2017;37:43–8.*
16. *Habib AS. A review of current guidelines for the management of hypotension during neuraxial anesthesia for cesarean delivery. Anesth Analg. 2020;131(1):193–202.*
17. *Chooi C, Cox JJ, Lumb RS, et al. Phenylephrine vs ephedrine for maternal hypotension: A meta-analysis of neonatal outcomes. Anesth Analg. 2020;131(1):203–14.*
18. *Lee A, Ngan Kee WD, Gin T. A quantitative systematic review of ephedrine vs phenylephrine for hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2002;94(4):920–6.*
19. *Sharkey AM, Siddiqui N. Phenylephrine-induced bradycardia in obstetric anesthesia: Mechanisms and management. Obstet Anesth Dig. 2019; 39(2):70–2.*
20. *Karch SB. Ephedrine-related psychosis: Clinical case reports and pharmacologic explanations. J Clin Psychopharmacol. 2003;23(2):186–8.*
21. *Ngan Kee WD, Lee SWY, Ng FF, et al. Randomized double-blinded comparison of norepinephrine and phenylephrine for treating hypotension during spinal anesthesia for cesarean delivery. Anesthesiology. 2015; 122(4):*

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ORIGINAL ARTICLE

Pattern and Causes of Death in Medicolegal Autopsies – A Descriptive Study from Dhaka Medical College Mortuary

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ABSTRACT

Background: *Medicolegal deaths, often sudden or unnatural, are examined through autopsies to determine cause, manner, and circumstances. Young adult males are most affected, with road accidents, homicide, and suicide common. This study reviews such deaths at Dhaka Medical College Mortuary from January to October 2023 to inform legal and public health planning.* ***Methods & Materials****: A descriptive cross-sectional study was conducted at Dhaka Medical College Mortuary from January to October 2023, including all 135 medicolegal deaths. Data on demographics, cause of death, and residence were extracted from mortuary registers and analyzed using descriptive statistics. Ethical approval and anonymization ensured confidentiality, and charts were used to illustrate key findings.* ***Results:*** *Among 135 medicolegal autopsies, 88 (65.2%) were male and 47 (34.8%) females. Ages ranged from 0 days to 80 years, with a mean of 31.8 ± 16.2 years; most cases were in the 21–40-year age group. Leading causes of death were road traffic accidents, poisoning, burns, hanging, and unexplained sudden deaths. Young adult males were most affected, highlighting risks from accidents, violence, and self-harm, and emphasizing the need for traffic safety, mental health support, and strengthened forensic investigations.* ***Conclusion:*** *Between January and October 2023, most medicolegal autopsies at DMC involved unnatural deaths, predominantly among young adult males. Leading causes were road traffic accidents, poisoning, and hanging, reflecting environmental risks and psychosocial stressors. These findings highlight the need for stronger road safety measures, toxic substance regulation, expanded mental health services, and improved mortuary data systems to support prevention and public health planning.*

Keywords: *Medicolegal autopsy; Dhaka Medical College; road traffic accident; poisoning; hanging; forensic medicine*

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INTRODUCTION

Unnatural or uncertain deaths undergo an inquest to determine if they were natural, accidental, suicidal, or homicidal. It is not a trial, and no judgment is passed. A Coroner conducts it in the English system, while other countries use systems like Medical Examiner (USA) or Procurator Fiscal (Scotland)[1]. Medicolegal deaths are sudden or unexplained deaths. Forensic autopsies are conducted under legal authority to determine the exact cause, circumstances, identity, and manner of death. These autopsies are performed by expert forensic surgeons or pathologists, who can provide accurate evidence in court[2].

Autopsies help public health by identifying mortality trends and potential health threats. They can reveal multiple causes of death, guide interventions, and validate or correct clinical diagnoses, highlighting misdiagnoses and improving medical practice[3]. An autopsy, meaning the examination of a deceased body, is performed for both clinical and medicolegal reasons. Clinical autopsies (or pathological autopsies) aim to identify the disease that caused death, especially when it was unclear before death. Even when the cause of death is known, clinical autopsies are often conducted to study the disease process directly in the body, providing valuable insights and advancing medical knowledge[4].

Several studies worldwide have examined the patterns and cause of death in medicolegal autopsies, highlighting regional variations and common trends. In India, a retrospective study reported that accidental deaths, particularly road traffic accidents, accounted for the majority of cases, followed by homicidal and suicidal deaths, with males and young adults being the most affected group[5]. A study from Nigeria found that homicides and road traffic accidents were predominant causes, and a notable number of deaths involved males aged 21–40 years[6].

In Brazil, research indicated that accidental deaths were the leading cause, followed by violent deaths, and emphasized the

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role of socioeconomic factors and urbanization in influencing mortality patterns[7]. Meanwhile, studies from Europe and the United States suggest that natural deaths with uncertain causes also form a significant portion of medicolegal autopsies, highlighting the importance of autopsies in validating clinical diagnoses and public health monitoring[8]. Collectively, these studies underscore that medicolegal autopsies are essential not only for legal investigations but also for identifying public health risks, guiding preventive measures, and improving healthcare policies globally.

Several studies worldwide have examined the patterns and cause of death in medicolegal autopsies. Research from Karachi, Pakistan, analyzing 2,090 autopsies, showed that violent asphyxia deaths — including hanging, drowning, strangulation, and smothering — accounted for a significant portion of cases, with the majority being male victims aged 15–35 years[9]. A prospective study in Hyderabad, Pakistan, of 982 autopsies, found that road traffic accidents (≈45.3%) were the leading cause of death, followed by firearm injuries, asphyxia, train accidents, and poisoning, with males comprising nearly 79% of cases[10]. In India, a study from Karnataka reviewing 924 autopsies reported that the highest number of deaths occurred in the 21–30 years age group, with males accounting for ~82% of cases; the commonest causes were road traffic accidents, poisoning, natural deaths, asphyxia, railway-related deaths, and homicidal deaths[11].

A study in Bangladesh on asphyxia deaths, including hanging and drowning, also indicate that males in the 30–39 years age group are commonly involved, with a majority being suicidal in nature [12]. The study aims to analyze and describe the patterns and causes of deaths among cases undergoing medicolegal autopsies at Dhaka Medical College Mortuary between January and October 2023. Specifically, it seeks to determine the distribution of deaths by age, sex, manner of death (natural, accidental, suicidal, homicidal), and specific causes, thereby providing insight into mortality trends and contributing to both legal investigations and public health planning.

METHODS & MATERIALS

Study Design:

A descriptive cross-sectional study was conducted at the Dhaka Medical College Mortuary to assess patterns and causes of medicolegal deaths. The mortuary, which receives cases from Dhaka and surrounding areas, maintains detailed registers, allowing collection and analysis of demographic and cause-of-death data at a single point in time.

Study Period and population:

Data were collected over a 10-month period, from January 1 to October 31, 2023, and included all 135 medicolegal autopsies conducted during this time. The study population comprised deaths that were sudden, suspicious, unnatural, or of uncertain cause, all referred for legal investigation, providing a representative sample to reflect current trends in medicolegal mortality.

Data Collection tools:

Information for the study was extracted from the mortuary registers, including demographic data such as age, sex, and religion; clinical and medicolegal data such as the cause of death; and geographic data including the thana and city of residence. All data were carefully recorded to ensure completeness and accuracy, providing a reliable dataset for analysis.

Data Analysis:

The collected data were analyzed using descriptive statistics. Frequencies and percentages were calculated for categorical variables such as sex, religion, cause of death, and place of residence, while the mean ± standard deviation (SD) was determined for continuous variables such as age. Additionally, charts and graphs were prepared to visually present the distribution of deaths across different variables, facilitating easier interpretation of the results.

Ethical Considerations:

All data were anonymized to maintain confidentiality and protect the identity of the deceased. Formal permission for the use of mortuary records was obtained from the Department of Forensic Medicine prior to the start of the study. The study adhered to ethical principles, ensuring the respectful handling of sensitive information throughout the research process.

RESULTS

A total of 135 medicolegal autopsies were examined during the study period. Of these, 88 (65.2%) were male and 47 (34.8%) were female. The age ranged from 0 days (neonate) to 80 years; the mean age was 31.8 years (SD 16.2). The majority of cases were in the 21–40-year age group. The leading causes of death included road traffic accidents, poisoning, burns, hanging, and unexplained sudden deaths.

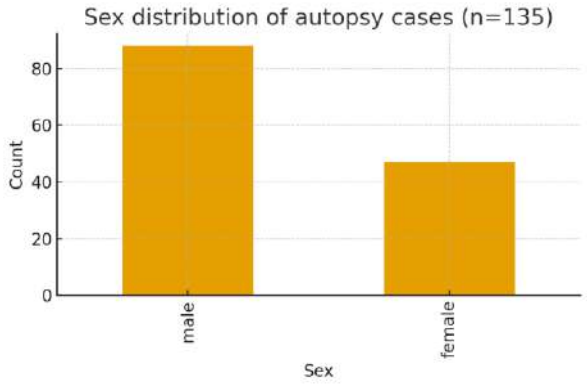

Figure – 1: Sex distribution of autopsy cases (*n*=135)

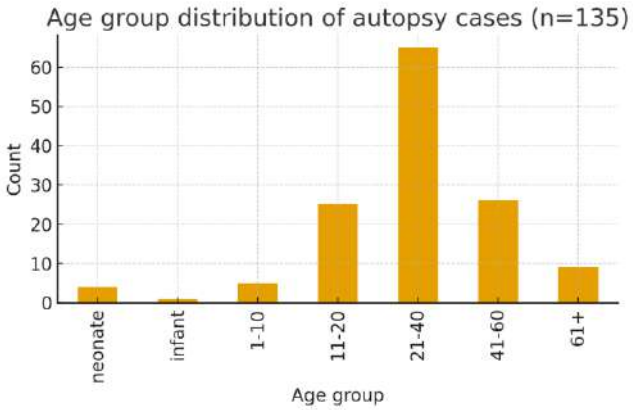

Figure – 2: Age group distribution of autopsy cases (*n*=135)

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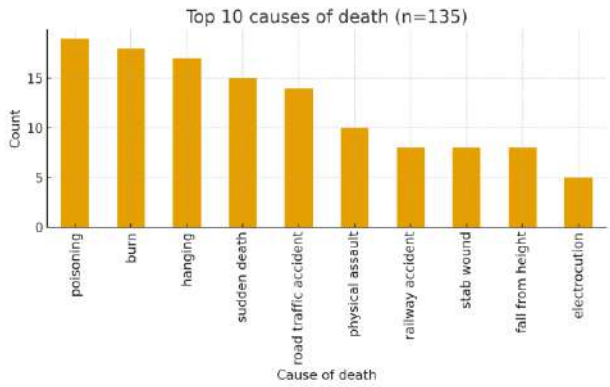

Figure – 3: Top 10 causes of death recorded at DMC mortuary (*n*=135)

DISCUSSION

In the present study of 135 medicolegal autopsies, males accounted for 88 cases (65.2%) whereas females accounted for 47 (34.8%). This male predominance among medico-legal autopsy victims is well in keeping with other studies. The male to female disparity is likely attributable to sociocultural and behavioral factors: in many settings males are more involved in high-risk activities (e.g. heavy manual work, driving, outdoor exposure), more likely to be victims of accidents, violence or self-harm, and generally more mobile outside home than females. This male preponderance is a recurrent observation in forensic autopsy profiles worldwide [13].

variation in the pattern of causes of death may contribute: in settings where non-traumatic causes such as poisoning, burns or hanging are relatively common (and these may affect females at higher rates in certain social contexts), the female share of autopsies tends to increase. For example, in a study of fatal poisoning in Bangladesh, males comprised 75% while females 25%; but because poisoning and suicidal deaths may disproportionately affect females in some circumstances, their representation in medicolegal autopsies can vary [14].

The age of decedents in our study ranged from 0 days (neonate) to 80 years, with a mean age of 31.8 years (SD 16.2). The majority belonged to the 21–40 years age group. This concentration in young adulthood is broadly consistent with earlier autopsy studies. For instance, in a forensic mortuary-based study, the most common age group was 21–30 years, followed by 31–40 years — together accounting for more than half of all cases [13]. Similarly, in a study of 647 autopsy cases at a tertiary care center, the 21–30 years age group constituted 31.5% of cases — the largest single age group [15].

The predominance of younger adults, particularly in the third and early fourth decades, likely reflects their greater social and economic activity, which increases exposure to risks such as road accidents, occupational hazards, violence, substance use, and self-harm, while such risks decrease with age as natural deaths become more common.

In our study, the leading causes of death were road traffic accidents (RTA), poisoning, burns, hanging, and unexplained sudden deaths. This pattern is broadly consistent with profiles observed in other autopsy-based studies — though relative frequencies vary across regions and over time. Multiple studies have highlighted RTAs as a major contributor to medicolegal deaths: in a tertiary-center study from Bangladesh, RTA fatalities predominated and most victims were young males in the 21–40 years age group[1]. The importance of poisoning and hanging (often representing intentional self-harm) is also well-established. For example, in a study of suicide autopsies, hanging was the most common method, followed by poisoning [10].

The high rate of RTAs underscores traffic safety as a major public health concern, especially among young adults, highlighting the need for better road infrastructure, law enforcement, helmet/seat-belt use, awareness, and trauma care. Poisoning and hanging indicate a need for mental health support, regulation of toxic substances, and social interventions, while burn deaths point to domestic hazards requiring preventive measures. Unexplained sudden deaths suggest gaps in forensic investigations, emphasizing the need to strengthen medico-legal capabilities for accurate cause-of-death determination.

Conclusion

Between January and October 2023, the majority of medicolegal autopsies conducted at DMC were due to unnatural deaths, with young adult males representing the largest affected group. The most frequent causes of death were road traffic accidents, poisoning, and hanging, highlighting a combination of external environmental hazards and potential psychosocial stressors prevalent in this demographic. These findings emphasize the urgent need for comprehensive public health interventions, including the strengthening of road safety policies, enforcement of traffic regulations, regulation and safe storage of toxic substances, and expanded mental health services to identify and support at-risk individuals. Additionally, improving mortuary data recording and surveillance systems is crucial to ensure accurate documentation of causes of death, facilitate evidence-based prevention planning, and ultimately reduce the incidence of unnatural deaths within the community.

REFERNCE

1. *Nadesan K. The importance of the medico-legal autopsy. Malaysian Journal of Pathology. 1997;19(2):105-9.*
2. *Sampene OP, Eric AD. Trend of Medicolegal Manner of deaths in Ghana: a forensic autopsy-based study. Annals Int Med Dent Res. 2017;3.*
3. *Naheed K, Nadeem S, Iqbal M, Qasim AP, Sadia S, Siddiqui BA. MEDICOLEGAL AUTOPSIES;: AUDIT OF MEDICOLEGAL AUTOPSIES IN FAISALABAD CITY. The professional medical journal. 2019 May 10;26(05):696-701.*
4. *Kotabagi RB, Charati SC, Jayachandar D. Clinical autopsy vs medicolegal autopsy. Medical Journal Armed Forces India. 2005 Jul 1;61(3):258-63.*
5. *Megatsari H, Laksono AD, Ibad M, Herwanto YT, Sarweni KP, Geno RA, Nugraheni E. Predictors of psychosocial burden among workers during the COVID-19 pandemic period in Indonesia. Medico Legal Update. 2021;21(1):292-7.*
6. *Edegbe FO, Uzoigwe CJ, Ekwedigwe KC, Okani CO, Agwu UM, Nwafor J, Ekwedigwe PI. Determination of the Incidence of Medicolegal Death in a Tertiary Health Institution in Abakaliki, Ebonyi State, South-East, Nigeria. Global Journal of Health Science. 2020;12(8):1-58.*
7. *Santana LA, Venson R. Medico-legal death investigation systems–Brazil. Sri Lanka Journal of Forensic Medicine, Science and Law. 2022;13:11-4.*
8. *Davide Ferrara S. Bio-Medicolegal Disciplines and Scientific Evidence. InP5 Medicine and Justice: Innovation, Unitariness and Evidence 2018 Mar 28 (pp. 48-73).*
9. *Kotabagi RB, Charati SC, Jayachandar D. Clinical autopsy vs medicolegal autopsy. Medical Journal Armed Forces India. 2005 Jul 1;61(3):258-63.*
10. *Malik R, Atif I, Rashid F, Abbas M. An analysis of 3105 medico legal cases at tertiary care hospital, Rawalpindi. Pakistan journal of medical sciences. 2017 Jul;33(4):926.*
11. *Dogra TD, Yadav M, Lalwani S, Srivastav PC, Usmani J, Dikshit PC, Verma SK, Singh D, Murari A, Gorea RK, Srivastav A. Indian*

Internet Journal of Forensic Medicine and Toxicology. Indian Internet Journal of Forensic Medicine and Toxicology.:21.

12. *Akber EB, Mahmud S, Ahmad M, Barua AK, Jahan I. A Brief Account on Socio-demographic Profile of the Victims of Violent Asphyxial Deaths in Dhaka City. INTERNATIONAL JOURNAL OF ETHICS, TRAUMA & VICTIMOLOGY. 2021;7(02):30-4.*
13. *Singh N, Choudhary N, Nigam M, Gour V, Yadav V, Dohre S. Profile and pattern of post-mortem cases in mortuary of district hospital (associated with government medical college, Vidisha).—A cross-sectional study. IP Int J Forensic Med Toxicol Sci. 2021 Jul 15;6(2):40-2.*
14. *Sumon SR, Asha MT, Rahman MZ, Tabassum R, Mollika FA, Khan BH. An Autopsy Based Study on Socio-economical Pattern of Organophosphorus Poisoning Cases Recorded from Sir Salimullah Medical College Morgue. Mymensingh Medical Journal: MMJ. 2021 Jan 1;30(1):111-4.*
15. *Junaidi KA. Profile of Medicolegal Autopsy Cases Conducted at Tertiary Care Centre, Kalaburagi, Karnataka. Indian Journal of Forensic Medicine & Toxicology. 2020 Jul 1;14(3).*

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ORIGINAL ARTICLE

Exploring the Medico-Legal System in Bangladesh – Perspectives of Doctors from Public Hospitals in Dhaka

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ABSTRACT

Background: *The medico-legal system plays a critical role in supporting justice and ensuring accountability in healthcare. In Bangladesh, doctors in public hospitals frequently perform medico-legal duties despite systemic constraints. This study explored the roles, challenges, and systemic gaps experienced by doctors involved in medico-legal practice in Dhaka.* ***Methods & Materials:*** *A descriptive qualitative study was conducted over a one-year period (January to December, 2024) in three public hospitals in Dhaka—Dhaka Medical College Hospital, Sir Salimullah Medical College Hospital and Shaheed Suhrawardy Medical College Hospital. Eighteen doctors involved in medico-legal work were selected using purposive sampling. Data were collected through semi-structured key informant interviews and document review. Thematic analysis was used to identify major themes, challenges, and improvement opportunities.* ***Results:*** *Participants (n=18) included 6 forensic specialists and 12 lecturers with a mean of 8.5 ± 4.2 years of medico-legal experience. Doctors reported performing core medico-legal tasks such as post-mortem examinations, injury assessment, and providing expert legal opinions. Key challenges included high workload (67%), limited forensic specialist availability (50%), insufficient training (56%), and coordination gaps with police and courts (61%). Systemic issues included lack of standardized protocols (78%), inadequate infrastructure (67%), weak enforcement of medical negligence laws (56%), and limited legal awareness among healthcare providers (56%). Participants recommended expanding training, recruiting more forensic specialists, and strengthening inter-agency coordination.* ***Conclusion:*** *The medico-legal system in Bangladesh faces substantial structural and operational limitations that hinder effective medico-legal practice. Strengthening training, infrastructure, legal frameworks, and standardized protocols is essential for improving medico-legal service quality and supporting justice delivery.*

Keywords: *Medico-legal system, forensic medicine, medical negligence, public hospitals, Bangladesh, medico-legal challenges, qualitative study.*

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INTRODUCTION

The medico-legal system applies medical expertise to assist the judiciary in resolving legal and health-related issues, such as death investigations, sexual offenses, pregnancy, and injury analysis [1,2]. Globally, the system varies: in the USA, medical examiners report to the district attorney; in the UK, coroners handle cases; and in Pakistan, the police are given authority [1]. An inquest is a preliminary inquiry into deaths from unnatural or uncertain natural causes to determine whether the death was accidental, suicidal, homicidal, or natural, without any judgment being passed [2]. Medical treatment carries the risk of unexpected adverse effects due to patient-specific factors. Physicians must balance taking necessary risks for patient recovery with legal liability, while protecting patients' rights and ensuring professional judgment is justified. Proper regulation of medical risks is essential to safeguard both patients and doctors [3]. The health system has rapidly adapted to a sudden surge in medical demand, with changes in facilities, professional roles, and practices. This shift has raised important medico-legal and ethical challenges for health professionals, marking a lasting transformation in healthcare [4].

Globally, the medico-legal system is underpinned by a branch of law often called Medical Law. As explained in a recent article on the concept of medical law, this branch defines legal regulation of medical practice, sets standards for consent, confidentiality, and patient rights, and determines the place of medicine within a country's general legal system [5]. An essential domain of medico-legal systems is the accountability of health professionals for negligence or malpractice. For instance, a comprehensive literature review shows that when practitioners deviate from accepted standards of care —

resulting in patient harm — they may be held legally liable under civil or criminal law [6]. Forensic-medical experts play a crucial role when there is a claim of malpractice, especially in cases of death, serious injury, or disputed medical outcomes: they examine medical records, verify compliance with standard care, assess consent, evaluate causation and injury, and often provide expert testimony in court [7]. Moreover, forensic medical systems also support public-health surveillance, mortality analysis, and even wider research: a systematic review of coronial databases found their importance for public-health research and injury prevention [8]. Another critical part of the medico-legal framework is education and regulation of medical professionals. Research shows that teaching medical law to medical students positively affects their understanding of legal responsibilities, ethics, and standard-of-care — which can help prevent future malpractice or negligent care [9].

In Bangladesh, forensic services are delivered partly by academic staff of government medical colleges' forensic medicine departments, and partly by "civil surgeons" or district-level lecturers — especially where forensic specialists are not available. When an unnatural death occurs, it must be reported to police; a police officer investigates the scene and may order a post-mortem if indicated [10]. Another critical dimension is medical negligence and malpractice law, dealing with failure to meet accepted standards of care, patient harm, and resulting legal liability. In Bangladesh there have been numerous incidents of alleged substandard medical care, and academic-legal literature argues that such negligence violates patients' right to health and life [11].

Although Bangladesh has established forensic and medico-legal frameworks, several gaps remain in specialist availability, enforcement of medical negligence laws, accountability in death investigations, and the training of medical professionals for legal proceedings [10-13]. These gaps limit the effectiveness of the medico-legal system in safeguarding patient rights, supporting justice, and ensuring professional standards. The study also seeks to identify existing gaps and challenges in the system and suggest strategies for strengthening medico-legal services and improving legal and ethical governance in healthcare.

METHODS & MATERIALS

Study Design and Setting:

This descriptive qualitative study was conducted over a 1-year period in 2024 in three public hospitals in Dhaka city: Dhaka Medical College Hospital (DMCH), Sir Salimullah Medical College Hospital (SSMCH) & Shaheed Suhrawardy Medical College Hospital (ShSMCH). The study aimed to explore the roles, experiences, and challenges of doctors in the medico-legal system in Bangladesh.

Study Population and Sampling:

The study included 18 doctors directly involved in medico-legal cases, comprising forensic medicine specialists and lecturers. Participants were selected using purposive sampling to ensure representation from all three hospitals and relevant medico-legal roles.

Data Collection:

- **Key Informant Interviews (KII):** Semi-structured interviews were conducted with each doctor to explore their experiences, professional roles, challenges faced in medico-legal practice, and perceptions of systemic gaps.
- **Document Review:** Selected medico-legal reports, hospital protocols, and relevant policy documents were reviewed to supplement the primary data and contextualize practices within each hospital.

Data Analysis:

- Interviews were transcribed verbatim and analyzed using thematic analysis to identify recurring patterns, key challenges, and opportunities for strengthening medico-legal services.
- Descriptive summaries were prepared to outline the roles and responsibilities of doctors across the three hospitals.

RESULTS

Participant Characteristics:

A total of 18 doctors participated in the study, including 6 forensic medicine specialists and 12 lecturers from Dhaka Medical College Hospital (DMC), Sir Salimullah Medical College & Mitford Hospital (SshMC), and Mitford Hospital. Participants had a mean professional experience of 8.5 ± 4.2 years in medico-legal practice.

Roles of Doctors:

Doctors reported multiple roles within the medico-legal system, including conducting post-mortem examinations, assessing injuries and medical conditions for legal cases, providing expert opinions for police investigations and court proceedings, and certifying causes of death while distinguishing ante-mortem from post-mortem injuries. These roles were consistent across forensic specialists and lecturers (Table I). A forensic specialist noted:

"Our role is crucial in documenting findings accurately; even minor errors can affect legal outcomes." — Forensic Specialist, SSMCH

Challenges in Practice:

Several challenges were identified. The most frequently reported were high workload (67%), limited specialist availability (50%), coordination gaps with police and courts (61%), and insufficient training in medico-legal documentation (56%). Lecturers often performed medico-legal tasks without formal forensic training, which added to workload and procedural complexity. One participant stated:

"We often handle medico-legal cases in addition to routine duties, making it difficult to maintain quality documentation." — lecturer, DMCH

Some differences between hospitals were noted: doctors from DMC reported slightly better access to forensic facilities compared to SSMCH and Mitford Hospital, although training gaps were common across all sites.

Systemic Gaps:

Doctors highlighted several systemic issues affecting medico-legal practice. The most commonly reported gaps were lack of standardized protocols (78%), inadequate forensic infrastructure (67%), limited legal awareness among healthcare professionals (56%), and weak enforcement of medical negligence laws (56%).

Many participants noted that unclear procedures for documenting and addressing medical negligence pose a significant challenge in defending clinical decisions in court. As one participant explained:

"We often worry about legal consequences if a patient suffers an adverse outcome. Without clear guidance on negligence documentation, defending ourselves in court becomes difficult." — lecturer, ShSMCH

A forensic specialist from DMCH added:

"Even when we follow standard procedures, the lack of clear legal frameworks for medical negligence makes medico-legal cases complicated and stressful." — Forensic Specialist, DMCH

Opportunities for Improvement:

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Participants suggested strategies to strengthen the medico-legal system, including enhanced training programs (89%), recruitment of additional forensic specialists (78%), development of standardized hospital-level protocols (83%), and improved coordination with law enforcement and judicial authorities (72%). One participant remarked:
"Standardized guidelines and regular training can significantly improve medico-legal documentation and case handling." — Lecturer, ShSMCH

Table – I: Roles, Challenges, Gaps, and Opportunities in Medico-Legal Practice (*n*=18 doctors)

Domain	Key Findings	Number of Respondents / Comments
Roles of Doctors	Conducting post-mortem examinations	6 forensic specialists (100%)
	Assessing injuries and medical conditions for legal cases	18 (100%)
	Providing expert opinions for police and court	18 (100%)
	Certifying cause of death and distinguishing ante-/post-mortem injuries	18 (100%)
Challenges	Limited specialist availability; general doctors performing medico-legal tasks	9/12 lecturers
	High workload and time constraints	12/18 (67%)
	Insufficient training in medico-legal documentation	10/18 (56%)
	Coordination gaps with police and courts	11/18 (61%)
Systemic Gaps	Inadequate infrastructure for forensic examinations	12/18 (67%)
	Weak enforcement of medical negligence laws	10/18 (56%)
	Lack of standardized protocols across hospitals	14/18 (78%)
	Limited legal awareness among healthcare professionals	10/18 (56%)
Opportunities for Improvement	Enhanced training programs for doctors	16/18 (89%)
	Recruitment of more forensic specialists	14/18 (78%)
	Standardized protocols and hospital-level guidelines	15/18 (83%)
	Improved coordination with law enforcement and courts	13/18 (72%)

DISCUSSION

This study assessed the roles, challenges, and systemic gaps experienced by doctors involved in medico-legal work in three public hospitals in Dhaka. The findings show that both forensic specialists and lecturers frequently perform medico-legal tasks, which is consistent with earlier descriptions of Bangladesh's medico-legal system. Islam and Islam reported that medico-legal examinations are often handled by non-forensic clinicians due to shortages of trained personnel and inadequate infrastructure [10]. Rahman et al. also highlighted uneven distribution of forensic services and limited resources, which aligns with participant reports of infrastructural gaps and heavy workloads [14].

The challenges identified—limited training, coordination problems with police and courts, and lack of standardized protocols—mirror findings from previous Bangladeshi studies. Mia noted that doctors often face bureaucratic and procedural barriers during medico-legal case handling [13], while Akter described inconsistent documentation practices and limited understanding of negligence laws among healthcare providers [12]. These issues were reflected in our participants' concerns about unclear medico-legal processes and difficulty defending clinical decisions in negligence-related cases.

Weak enforcement of medical negligence laws reported by participants is also consistent with Hossain's findings, which emphasized that although legal provisions exist, enforcement remains poor and accountability mechanisms are weak [15]. International evidence also supports the need for improved medico-legal training. Alabdulqader et al. found low medico-legal awareness among emergency physicians in Saudi Arabia, reinforcing the importance of training for all clinicians involved in medico-legal duties [16]. Singh further argued that medico-legal responsibilities of non-forensic physicians should be formally recognized as part of their workload [17], similar to the experiences reported by lecturers in our study.

Regional literature from India also documents similar medico-legal challenges as we found in this study. Rai highlighted problems related to inadequate forensic capacity and poor documentation, suggesting that such issues are common across South Asian medico-legal systems [18].

Overall, this study adds updated empirical evidence from frontline physicians in Bangladesh and highlights persistent gaps that require policy attention. Strengthening forensic capacity, introducing standardized medico-legal protocols, improving inter-agency coordination, and enhancing medico-legal training remain critical for improving medico-legal practice and supporting justice delivery in Bangladesh.

CONCLUSION

This study highlights significant gaps in the medico-legal system of Bangladesh, particularly in public hospitals in Dhaka where both forensic specialists and lecturers routinely manage medico-legal responsibilities. Despite their central role in post-mortem examination, injury assessment, documentation, and providing expert opinion, doctors face multiple challenges including inadequate forensic infrastructure, lack of standardized protocols, insufficient training, poor inter-agency coordination, and weak enforcement of medical negligence laws. These constraints limit the quality, accuracy, and legal reliability of medico-legal services. Strengthening institutional capacity, expanding forensic specialist recruitment, improving medico-legal training for all physicians, and establishing standardized guidelines and clear legal frameworks are essential steps toward enhancing the effectiveness, accountability, and integrity of medico-legal practice in Bangladesh. Addressing these gaps will support better justice delivery, promote patient rights, and reduce legal vulnerabilities for healthcare providers.

REFERENCE

1. *Qadeer R. The Study of Medico Legal System. Application of Laser for the Treatment of Diabetic Macular Edema. 2016 Jul;14(3):81.*
2. *Nadesan K. The importance of the medico-legal autopsy. Malaysian Journal of Pathology. 1997;19(2):105-9.*
3. *Baulin YV, Pavshuk KO, Vyshnevska IA. Risk in the performance of medical activities: medico-legal overview. Wiadomości lekarskie. 2019 Jan 1:2410.*

4. *Arimany-Manso J, Martin-Fumadó C. Medico-legal issues regarding from the COVID-19 pandemic. Medicina clinica (English ed.). 2020 Sep 25;155(8):344.*
5. *Bichia M. The concept of medical law and its place in the system of branches of law. Law & World. 2023; 28:67.*
6. *Widjaja G. Legal Liability of Doctors in Medical Malpractice Cases: A Literature Study. Journal of Cultural Analysis and Social Change. 2025 Nov 25:315-20.*
7. *Sobh ZK, Zaki M. Forensic medical examiners' role in resolving malpractice claims: legal and ethical obligations. Arab Journal of Forensic Sciences & Forensic Medicine. 2024 Jul 11;6(Special Issue):191-9.*
8. *Bugeja L, Ibrahim JE, Ferrah N, Murphy B, Willoughby M, Ranson D. The utility of medico-legal databases for public health research: a systematic review of peer-reviewed publications using the National Coronial Information System. Health research policy and systems. 2016 Apr 12;14(1):28.*
9. *Abbasi M, Shirazi M, Torkmandi H, Homayoon S, Abdi M. Impact of teaching, learning, and assessment of medical law on cognitive, affective and psychomotor skills of medical students: a systematic review. BMC Medical Education. 2023 Sep 26;23(1):703.*
10. *Islam MN, Islam MN. Forensic medicine in Bangladesh. Legal Medicine. 2003 Mar 1;5: S357-9.*
11. *Bandhan SF. Extrajudicial Killing through the Specs of Rights Jurisprudence: A Study on Bangladesh and India.*
12. *Akter KK. A contextual analysis of the medical negligence in Bangladesh: laws and practices. Northern University Journal of Law. 2013;4:67-81.*
13. *Mia A. Role of doctors in the criminal proceedings of Bangladesh with special reference to women's access to justice. IOSR Journal of Humanities and Social Science (IOSR-JHSS). 2013;7(5):43.*
14. *Rahman KG, Osman MK, Mahmud S. Forensic medicine: Bangladesh perspective. J Dhaka Med Coll. 2010;19(1):61-4.*
15. *Hossain M. Effectiveness of Laws Related to Medical Negligence in Bangladesh. Lex Publica. 2022;9(2):29-48.*
16. *Alabdulqader S, Alabdulqader R, Madadin M, Kashif H, Al Jumaan MA, Yousef AA, et al. Emergency physicians' awareness of medico-legal case management: a cross-sectional study from Saudi Arabia. Saudi J Med Med Sci. 2023;11(1):60-6.*
17. *Singh G. Role of Forensic Medicine Doctors in Assisting Non-Forensic Clinicians with Medico-legal Cases: Should it be considered Formal Work? Int J Med Justice. 2025;3(1):65-70.*
18. *Rai L. A Critical Study of Law Relating to Medico-Legal Litigations in India [dissertation]. Bangalore: Alliance University; 2020.*

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ORIGINAL ARTICLE

Risk of Endometrial Cancer after Insufficient Endometrial Biopsy – A Retrospective Cohort Study at NICRH

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ABSTRACT

Background: *Endometrial biopsy is the first-line diagnostic tool for abnormal uterine bleeding (AUB) and suspected endometrial pathology. However, insufficient biopsy is a common challenge and may delay diagnosis or mask underlying malignancy. Data from Bangladesh on the clinical significance of inadequate biopsy are limited.* ***Objective:*** *To evaluate the association between insufficient endometrial biopsy and the risk of endometrial cancer, and to assess diagnostic delays among the screened women of different ages who underwent endometrial biopsy.* ***Methods & Materials:*** *This retrospective cohort study included 320 women who underwent outpatient or inpatient endometrial biopsy at the Department of Gynecology and Obstetrics in National Institute of Cancer Research and Hospital (NICRH), Dhaka, Bangladesh, between Decembers 2023 to November 2024. Participants were categorized into adequate biopsy (n=240) and insufficient biopsy (n=80) groups. Baseline characteristics, histopathological outcomes, and time to final diagnosis were collected from hospital and pathology records. Descriptive statistics were calculated, and differences between groups were assessed using t-tests and chi-square tests. Logistic regression was performed to estimate crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for endometrial cancer, adjusting for age, menopausal status, BMI, and diabetes. Statistical significance was set at $p < 0.05$.* ***Results:*** *The mean age of women was 53.7 ± 8.9 years; 214(66.9%) women were ≥50 years, and 198 (61.9%) were postmenopausal. Insufficient biopsy samples were significantly more common in older and postmenopausal women had higher BMI (p<0.05). Endometrial cancer was diagnosed in 54 (16.9%) women, with a higher incidence in the insufficient biopsy group (26/80; 32.5%) versus the adequate biopsy group (28/240; 11.7%) (p<0.001). Insufficient biopsy was independently associated with endometrial cancer (adjusted OR 3.12; 95% CI: 1.62–5.99 (p<0.001). Median time to diagnosis was longer in the insufficient biopsy group (45 vs. 18 days; (p<0.001), and 70% experienced delays >30 days. Age ≥50 years and postmenopausal status were additional independent predictors.* ***Conclusion:*** *Insufficient endometrial biopsy is a strong predictor of endometrial cancer diagnosis and is associated with significant diagnostic delays. Prompt repeat evaluation and standardized follow-up protocols are essential to ensure early detection and timely management in high-risk patients.*

Keywords: *Endometrial cancer, Insufficient biopsy, Diagnostic delay, Postmenopausal bleeding, Retrospective cohort, Bangladesh*

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INTRODUCTION

Endometrial cancer is the most common gynecological malignancy in high-income countries and its incidence has been steadily rising in low and middle-income nations, including South Asia, due to increasing life expectancy, obesity, and diabetes prevalence [1]. Early diagnosis remains essential because most patients present with abnormal uterine bleeding (AUB), and timely evaluation of the endometrium greatly improves outcomes [2]. Endometrial biopsy is considered the first-line, minimally invasive diagnostic tool for evaluating AUB, especially in postmenopausal or high-risk women [3]. It offers high sensitivity for detecting endometrial carcinoma and atypical hyperplasia when adequate tissue is obtained [4]. However, insufficient or inadequate endometrial tissue sampling is a common clinical challenge, reported in 6–33% of outpatient biopsies [5]. Several factors contribute to insufficient sampling, including cervical stenosis, endometrial atrophy, obesity, and operator technique [6]. Insufficient biopsy often necessitates repeat procedures or alternative diagnostic modalities such as hysteroscopy or dilation and curettage (D&C), potentially delaying definitive diagnosis and increasing healthcare burden [7].Clinical concerns arise from evidence that women with insufficient biopsy samples may have an underlying risk of missed endometrial pathology, including endometrial cancer, particularly among postmenopausal women with persistent symptoms [8].A recent study has suggested that insufficient tissue may not always be a benign finding; instead,

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it can be associated with significant disease in a notable proportion of cases [9]. Furthermore, delays caused by repeated attempts at diagnosis can lead to advanced-stage presentation, poorer prognosis, and increased mortality [10]. Bangladesh lacks comprehensive data evaluating the clinical significance of insufficient endometrial biopsy, especially regarding its association with endometrial cancer risk. The National Institute of Cancer Research and Hospital (NICRH), being the apex cancer center in the country, provides an important opportunity to assess real-world diagnostic outcomes in this high-risk population. Therefore, this retrospective cohort study aims to determine whether insufficient endometrial biopsy is associated with a higher likelihood of endometrial cancer and to examine diagnostic delays among patients treated at NICRH. Understanding this relationship will support clinicians in making timely decisions regarding repeat sampling and appropriate surveillance strategies.

METHODS & MATERIALS

This retrospective cohort study was conducted at the Department of Gynecology and Obstetrics in National Institute of Cancer Research and Hospital (NICRH), Dhaka, Bangladesh from December 2023 to November 2024. A total of 320 screened women of different ages who underwent outpatient or inpatient endometrial biopsy for evaluation of abnormal uterine bleeding, postmenopausal bleeding, or suspected endometrial pathology during the study period were retrospectively included in this study. The enrolled cases were categorized into two cohorts based on the adequacy of the initial biopsy sample: Adequate biopsy (n=240) and Insufficient biopsy (n=80). Consecutive sampling technique was used and the data were collected using a pre-structured case record form (CRF) from hospital records and pathology database. Time interval from initial biopsy to final diagnosis was calculated using documented clinical timelines. The primary outcome was assessed on the occurrence of endometrial cancer, and the secondary outcome was diagnostic delay. The collected data were analyzed using statistical Package for Social Sciences(SPSS), version-23.0.Descriptive statistical analysis were performed to summarize baseline variables, with comparisons between adequate and insufficient biopsy groups,. Chi-squire test and independent t-tests were performed to compare the difference between the adequate and insufficient biopsy groups. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were estimated performing logistic regression analysis, to assess the association between insufficient biopsy and endometrial cancer, adjusting for age, menopausal status, BMI, and diabetes. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 320 women who underwent endometrial biopsy during the study period were included in the analysis. The mean age of the participants was 53.7 ± 8.9 years, and 214 (66.9%) were aged ≥50 years. When stratified by biopsy adequacy, women in the insufficient biopsy group were significantly older than those with adequate biopsy samples (58.4 ± 9.1 vs. 52.1 ± 8.4 years (p=0.001). The proportion of women aged ≥50 years was markedly higher in the insufficient biopsy cohort (71 (88.8%) vs. 143 (59.6%) (p<0.001). The overall mean BMI was 27.3 ± 3.9 kg/m^2, and women in the insufficient biopsy group had significantly higher BMI (28.7 ± 4.1 vs. 26.8 ± 3.5 kg/m^2, (p=0.02). More than half of the women 182 (56.9%)) had parity ≥3, with no significant difference between groups (p=0.32). Postmenopausal women constituted 198 (61.9%) of the study population, and this proportion was substantially higher in the insufficient biopsy group (66 (82.5%) vs. 132 (55.0%) (p<0.001). Diabetes mellitus was more prevalent in women with insufficient biopsy (33 (41.3%) vs. 59 (24.6%) (p=0.004), while hypertension and abnormal uterine bleeding showed no significant differences (Table I). Histopathological follow-up revealed that 54 (16.9%) women were diagnosed with endometrial cancer. The incidence of cancer was significantly higher in the insufficient biopsy group 26 (32.5%)) compared to the adequate biopsy group 28 (11.7%)) (p<0.001). Atypical hyperplasia was detected in 26 (8.1%) women, with no significant difference between groups (p=0.42). Benign hyperplasia and atrophic endometrium were common non-malignant outcomes, found in 89 (27.8%) and 104 (32.5%) women, respectively, with similar distribution across groups. Normal proliferative/secretory endometrium was more frequently seen in the adequate biopsy group 41 (17.0%) vs. 6 (7.5%) (p=0.03) (Table II). Among women diagnosed with cancer, 26 (48.1%) initially had an insufficient biopsy, compared with 64 (20.3%) of those without cancer. The crude odds ratio showed a 3.64-fold increased cancer risk (95% CI: 2.01–6.57). After adjusting for age, menopausal status, BMI, and diabetes, insufficient biopsy remained a strong independent predictor of endometrial cancer (adjusted OR: 3.12; 95% CI: 1.62–5.99; p<0.001). Age ≥50 years 40 (74.1%)) and postmenopausal status 42 (77.8%)) were also significant predictors, while diabetes showed borderline significance (Table III). Analysis of diagnostic timelines showed a substantial delay among women with insufficient biopsy samples. The median time from initial biopsy to final diagnosis was significantly longer in the insufficient biopsy group (45 days ; IQR 28–70) than in the adequate biopsy group (18 days; IQR 12–31) (p<0.001). Diagnostic delay >30 days occurred in 56 (70.0%) women with insufficient biopsy compared to 74 (30.8%) in the adequate biopsy group (p<0.001) (Table IV). The final multivariate logistic regression model confirmed insufficient biopsy as the strongest independent predictor of endometrial cancer (AOR 3.12; 95% CI: 1.62–5.99; p<0.001). Age ≥50 years (40 (74.1%)) and postmenopausal status (42 (77.8%)) also significantly increased cancer risk. High BMI ≥28 kg/m^2 and diabetes mellitus did not show statistically significant associations in the adjusted model (p=0.12 and (p=0.08, respectively) (Table V).

Table – I: Baseline Characteristics of Study Participants (*n* = 320)

Variables	Total (N=320)	Adequate Biopsy (n=240)	Insufficient Biopsy (n=80)	p-value
Age (years), mean ± SD	53.7 ± 8.9	52.1 ± 8.4	58.4 ± 9.1	0.001
Age ≥ 50 years, n (%)	214 (66.9%)	143 (59.6%)	71 (88.8%)	<0.001
BMI (kg/m^2), mean ± SD	27.3 ± 3.9	26.8 ± 3.5	28.7 ± 4.1	0.02
Parity ≥ 3, n (%)	182 (56.9%)	140 (58.3%)	42 (52.5%)	0.32
Post-menopausal, n (%)	198 (61.9%)	132 (55.0%)	66 (82.5%)	<0.001
Diabetes Mellitus, n (%)	92 (28.7%)	59 (24.6%)	33 (41.3%)	0.004
Hypertension, n (%)	111 (34.7%)	78 (32.5%)	33 (41.3%)	0.12
Abnormal Uterine Bleeding (%)	268 (83.7%)	202 (84.2%)	66 (82.5%)	0.72

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Table II. Histopathological Final Diagnosis after Follow-up (*n*=320)

Final Diagnosis	Total (N=320)	Adequate Biopsy (n=240)	Insufficient Biopsy (n=80)	p-value
Endometrial Cancer	54 (16.9%)	28 (11.7%)	26 (32.5%)	<0.001
Atypical Hyperplasia	26 (8.1%)	18 (7.5%)	8 (10.0%)	0.42
Benign Hyperplasia	89 (27.8%)	70 (29.2%)	19 (23.8%)	0.32
Atrophic Endometrium	104 (32.5%)	83 (34.6%)	21 (26.3%)	0.14
Normal/Proliferative/Secretory	47 (14.7%)	41 (17.0%)	6 (7.5%)	0.03

Table – III: Association between Insufficient Biopsy and Endometrial Cancer (*n*=230)

Variable	Endometrial Cancer Present (n=54)	No Cancer (n=266)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Insufficient biopsy	26 (48.1%)	54 (20.3%)	3.64 (2.01–6.57)	3.12 (1.62–5.99)	<0.001
Age ≥ 50 years	45 (83.3%)	169 (63.5%)	2.88 (1.37–6.05)	2.41 (1.05–5.54)	0.04
Postmenopausal	43 (79.6%)	155 (58.3%)	2.87 (1.43–5.75)	2.62 (1.23–5.57)	0.01
Diabetes Mellitus	23 (42.6%)	69 (25.9%)	2.11 (1.16–3.82)	1.79 (0.92–3.47)	0.08

Table – IV: Time from Initial Biopsy to Final Diagnosis (*n*=320)

Time Interval	Adequate Biopsy (n=240)	Insufficient Biopsy (n=80)	p-value
Median time to diagnosis (days)	18 days (IQR 12–31)	45 days (IQR 28–70)	<0.001
Delay > 30 days, n (%)	74 (30.8%)	56 (70.0%)	<0.001

Table – V: Logistic Regression Model Predicting Endometrial Cancer Risk

Predictor	OR	(95% CI)	p-value
Insufficient biopsy	1.14	3.12 (1.62–5.99)	<0.001
Age ≥ 50 years	0.88	2.41 (1.05–5.54)	0.04
Postmenopausal	0.96	2.62 (1.23–5.57)	0.01
High BMI ≥ 28	0.53	1.70 (0.88–3.28)	0.12
Diabetes Mellitus	0.58	1.79 (0.92–3.47)	0.08

DISCUSSION

This retrospective cohort study demonstrated that insufficient endometrial biopsy is strongly associated with a higher likelihood of underlying endometrial cancer and significant diagnostic delays, emphasizing the clinical importance of prompt further evaluation. Women with insufficient samples in our study were significantly older, had higher BMI, and were predominantly postmenopausal characteristics known to increase the risk of both insufficient sampling and endometrial malignancy. These demographic trends are consistent with previous research. Clark et al. reported that inadequate biopsy samples were more common in postmenopausal women due to cervical stenosis and atrophic endometrium, limiting tissue acquisition [11]. Similarly, Yela et al. found age and high BMI to be major contributors to insufficient endometrial sampling [12]. The cancer prevalence of 16.9% in this cohort aligns with findings from Western and Asian studies evaluating high-risk groups undergoing biopsy. More importantly, the significantly higher cancer detection rate among women with insufficient biopsy (32.5%) underscores the potential danger of falsely reassuring inadequate tissue reports. Visser et al. observed that up to 30% of women with insufficient biopsy were later diagnosed with cancer or atypical hyperplasia on further testing, comparable to our findings [13]. Likewise, Bakour et al., reported that insufficient biopsy results often underestimate serious pathology, particularly in symptomatic women [14]. After adjusting for confounders, insufficient biopsy remained an independent predictor of endometrial cancer in this study (AOR 3.12). This aligns with the systematic review by Van Hanegem et al., who demonstrated that inadequate biopsies could miss up to 20–25% of endometrial cancers [15]. Dueholm et al. also reported that insufficient sampling often necessitates repeat procedures and contributes to delayed diagnosis, particularly in high-risk postmenopausal women [16]. Our results reaffirm these concerns, supporting active follow-up rather than conservative management. Age ≥50 years and postmenopausal status were also strong predictors of malignancy in our model. Numerous studies support this, including the epidemiological review by Renehan et al., which highlighted advancing age and menopausal transition as major determinants of endometrial cancer risk [17]. A large cohort study by Saed et al. reported seven-fold increased cancer risk in women over 55 years, independent of other clinical factors [18]. Similarly, Setiawan et al. demonstrated that postmenopausal estrogen imbalance plays a crucial role in carcinogenesis, enhancing susceptibility in older women [19]. Although BMI and diabetes mellitus are recognized risk factors for endometrial cancer, they were not statistically significant in the adjusted model. This may reflect confounding by age and menopausal status, which exert stronger influence. Nevertheless, obesity remains a global driver of endometrial cancer. A pooled analysis by Bhaskaran et al. showed that each 5 kg/m^2 increase in BMI substantially elevates risk [20]. Diabetes has also been linked to endometrial malignancy through hyperinsulinemia and chronic inflammation, as reported by Friberg et al. [21]. Even if not independently significant in this dataset, these factors remain clinically relevant and may contribute to biopsy inadequacy, as observed in studies by Kucukmetin et al. [22]. This study also highlighted significant diagnostic delays among women with insufficient biopsy samples, with a median delay of 45 days more than double that of women with adequate samples. Diagnostic delay >30 days occurred in 70% of the insufficient biopsy group. Such delays may allow disease progression, as emphasized in a multicenter study by Clark et al., which associated prolonged diagnostic pathways with worse clinical outcomes [23]. Our findings reinforce the urgent need for accelerated workup in women with insufficient biopsy results, particularly those in high-risk categories. Collectively, the

evidence suggests that insufficient endometrial biopsy is not a benign finding. Instead, it should serve as a warning sign requiring early repeat biopsy, hysteroscopy, or dilation and curettage. Establishing standardized follow-up protocols may reduce diagnostic delays, prevent missed malignancies, and improve patient outcomes.

Limitations of the Study

This study has some limitations. It was a single center study with limited samples over a short study period, which may restrict the generalizability of the findings to broader populations of the whole country. These limitations highlight the need for future prospective, multicenter studies using uniform biopsy criteria and comprehensive risk-factor data.

CONCLUSION

In this retrospective cohort study, insufficient endometrial biopsy was strongly associated with a higher risk of underlying endometrial cancer and significant diagnostic delays. Age ≥50 years and postmenopausal status were additional independent predictors of malignancy. These findings highlight that an insufficient biopsy should not be considered benign and warrants prompt repeat evaluation to ensure timely diagnosis. Implementing standardized follow-up protocols for inadequate biopsy results may improve early cancer detection and reduce delays in management.

RECOMMENDATIONS OF THE STUDY

Based on the study findings, it is recommended that all women with insufficient endometrial biopsy, particularly those who are older or postmenopausal, undergo prompt repeat evaluation using hysteroscopy-guided biopsy or dilation and curettage. Standardized protocols should be established to ensure timely follow-up and reduce diagnostic delays. Clinicians should also consider patient risk factors, including age, menopausal status, and comorbidities, when deciding on the urgency of re-biopsy, to improve early detection of endometrial malignancy and optimize patient outcomes.

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REFERENCES

1. *Sung H, Ferlay J, and Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality. CA Cancer J Clin. 2021; 71(3):209-249.*
2. *Clark TJ, Mann CH, Shah N, et al. Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer. BJOG. 2002; 109(3):313-321.*
3. *American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 149: Endometrial cancer. Obstet Gynecol. 2015; 125(4):1006-1026.*
4. *Dijkhuizen FP, Mol BW, Brölmann HA, et al. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer. 2000; 89(8):1765-1772.*
5. *Van Doorn HC, Opmeer BC, Burger CW, et al. Inadequate office endometrial samples: a systematic review. Obstet Gynecol. 2007; 109(4):1097-1106.*
6. *Bettocchi S, Ceci O, Vicino M, et al. Diagnostic inadequacy of endometrial biopsy: role of hysteroscopy. J Minim Invasive Gynecol. 2004; 11(6):659-661.*
7. *Epstein E, Ramirez A, Skoog L, et al. Dilatation and curettage, endometrial biopsy and transvaginal ultrasound for the diagnosis of endometrial disease. Acta Obstet Gynecol Scand. 2001; 80(7):598-605.*
8. *Dueholm M, Hjorth IM. Structured imaging technique in the gynecologic office for diagnosis of abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol. 2017; 40:23-43.*
9. *Elsandabesee D, Greenwood P. The management of women with an insufficient sample on endometrial sampling. J Obstet Gynaecol. 2005; 25(6):619-621.*
10. *Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO consensus on endometrial cancer diagnosis, treatment and follow-up. Int J Gynecol Cancer. 2016; 26(1):2-30.*
11. *Clark TJ, Mann CH, Shah N, Khan KS, Gupta JK. Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. BJOG. 2002; 109(3):313–21.*
12. *Yela DA, et al. Factors associated with insufficient endometrial biopsy in women with abnormal bleeding. J Minim Invasive Gynecol. 2016; 23(7):1117–23.*
13. *Visser NCM, Bulten J, Ten Hoor KA, Van der Wurff AAM, Massuger LFAG. Diagnostic accuracy of endometrial sampling in endometrial carcinoma: A systematic review. Eur J Obstet Gynecol Reprod Biol. 2017; 210:44–52.*
14. *Bakour SH, Khan KS, Gupta JK. The risk of premalignant and malignant pathology in women with inadequate endometrial biopsy. Acta Obstet Gynecol Scand. 2000; 79:1137–41.*
15. *Van Hanegem N, Prins MM, Bongers MY, Opmeer BC, Sahota DS, Mol BW. The accuracy of endometrial sampling in patients with postmenopausal bleeding: a systematic review. Cancer Causes Control. 2016;27(4):571–85.*
16. *Dueholm M, Møller C, Rydbjerg S, Hansen ES, Ørtoft G. Reproducibility and clinical consequences of insufficient histology samples in women with suspected endometrial pathology. Ultrasound Obstet Gynecol. 2015;45(1):86–92.*
17. *Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: systematic review and meta-analysis. Lancet. 2008; 371:569–78.*
18. *Saed L, Varse F, Baradaran HR, Ayubi E, Moradi Y, Khateri S, et al. The global burden of endometrial cancer: A systematic review. Epidemiol Health. 2019; 41:e2019021.*
19. *Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II endometrial cancers: have they different risk factors? J Clin Oncol. 2013;31(20):2607–18.*
20. *Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 cancers: a population-based study. Lancet. 2014; 384:755–65.*
21. *Friberg E, Orsini N, Mantzoros CS, Wolk A. Diabetes mellitus and risk of endometrial cancer: A meta-analysis. Diabetologia. 2007; 50:1365–74.*
22. *Kucukmetin A, Naik R, Bryant A, Gupta JK. Management of women with insufficient endometrial biopsy: a clinical review. Obstet Gynecol Surv. 2010; 65(11):757–63.*
23. *Clark TJ, Barton PM, Coomarasamy A, Gupta JK, Khan KS. Investigating postmenopausal bleeding: cost effectiveness of initial diagnostic strategies. BJOG. 2006; 113(5):502–10.*

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ORIGINAL ARTICLE

Early Postoperative Outcome after Evacuation of Acute Subdural Haematoma – A Comparison of Craniotomy with Decompressive Craniectomy

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ABSTRACT

Background: *Acute subdural hematoma represents a major clinical entity in traumatic brain injury. The mortality of traumatic acute subdural haematoma is high. Craniotomy and decompressive craniectomy are two commonly used surgical techniques for treatment of traumatic acute subdural hematoma but which one is better surgical technique is still under debate.* ***Objective:*** *This study was done to evaluate the surgical outcome of traumatic acute subdural hematoma and to compare the surgical outcome between craniotomy and decompressive craniectomy with evacuation of hematoma.* ***Methods & Materials:*** *A hospital based randomized clinical trial was conducted from July 2016 to December 2017. Total 36 patients with traumatic acute subdural hematoma with pre-operative GCS 5-13, thickness of hematoma more than 10 mm, midline shift more than 5 mm and at least one pupil was reacting to light were included in this study. Data were collected by specially designed case record form and analysed usingStatisticalPackage for Social Sciences (SPSS) version 22.0).* ***Results:*** *Regardless of surgical technique used that is craniotomy (CR) or decompressive craniectomy (DC) with evacuation of hematoma, good recovery (GOS score-5) was 33.3%, moderate disability (GOS score= 4) 19.4%, severe disability (GOS score-3) 5.6%, persistent vegetative state (GOS score-2) 5.6%, and 36.1% patient died after surgery. In CR group according to Glasgow outcome scale (GOS) good recovery was 33.3%, moderate disability 11.1%, severe disability 11.1%, persistent vegetative state 5.6% and 38.9% patients died. In DC group, good recovery was 33.3%, moderate disability 27.8%, severe disability 0%, persistent vegetative state 5.6% and 33.3% patients died.* ***Conclusion:*** *Patients with traumatic acute subdural hematoma with GCS ≥ 9, bilateral reacting pupil and surgery within 24 hours craniotomy (CR) may be an alternative surgical option considering the possible complications of decompressive craniectomy as craniotomy and decompressive craniectomy showed no difference. But patients with poor clinical status and surgery after 24 hours primary decompressive craniectomoy (DC) may be more effective than craniotomy.*

Keywords: *Acute subdural haematoma; Traumatic brain injury; Craniotomy; Decompressive craniectomy; Surgical outcome; Glasgow Outcome Scale; Postoperative mortality; Randomized clinical trial.*

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INTRODUCTION

Acute subdural haematoma (ASDH) is one of the most life-threatening neurosurgical emergencies and a critical component of the global burden of traumatic brain injury (TBI). It occurs in approximately one-third of patients with severe TBI and is strongly associated with poor neurological outcomes and high mortality[1]. ASDH typically develops between the dura mater and the arachnoid membrane due to tearing of bridging veins or arterial injury following rapid acceleration–deceleration forces or direct head trauma [2]. The condition progresses rapidly, causing mass effect, midline shift, raised intracranial pressure (ICP), and impaired cerebral perfusion, all of which contribute to secondary brain injury [3]. Despite improvements in neuroimaging, neurocritical care, and surgical techniques, mortality in severe ASDH remains exceedingly high, frequently exceeding 50–60%, and is closely related to the initial Glasgow Coma Scale (GCS) score and the presence of concomitant parenchymal injuries [4,5]. The clinical outcome in ASDH depends not only on the size of the clot but also on the extent of the underlying primary brain damage, including cerebral contusions, diffuse axonal injury, and traumatic brain oedema [6]. These secondary brain insults play a decisive role in long-term functional recovery. Timely surgical intervention is essential when there is significant mass effect or neurological deterioration, as early evacuation reduces intracranial pressure, prevents herniation, and

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facilitates better cerebral perfusion [7]. Among the surgical interventions available, craniotomy (CR) and decompressive craniectomy (DC) are the two most widely practiced techniques for evacuating ASDH. Craniotomy allows clot evacuation followed by bone flap replacement, whereas decompressive craniectomy involves removal of the bone flap to accommodate brain swelling and reduce ICP. Although both procedures are well established, their relative benefits remain controversial. Some studies suggest craniotomy is adequate for most patients with minimal swelling, while others report improved ICP control with decompressive craniectomy, particularly in cases with significant brain oedema or refractory intracranial hypertension[8]. Despite extensive research, there is still no definite consensus regarding the optimal surgical approach for primary ASDH evacuation, and decisions often depend on surgeon preference and intraoperative findings [9,10]. Because of these uncertainties, further comparative evaluation of postoperative outcomes is essential. Therefore, the present study aims to compare the early postoperative outcomes of craniotomy versus decompressive craniectomy in the surgical management of acute subdural haematoma, with the objective of identifying the approach that offers better early recovery and clinical stability in patients with traumatic acute subdural haematoma (ASDH).

METHODS & MATERIALS

This randomized clinical trial was conducted in the Department of Neurosurgery, Dhaka Medical College Hospital, from July 2016 to December 2017. Written informed consent was obtained from the caregivers/legal guardians and initially 40 patients diagnosed with acute subdural haematoma requiring surgical evacuation were enrolled in this study. During surgery, six patients (four initially allocated to the craniotomy group and two to the decompressive craniectomy group) developed significant per-operative brain swelling, necessitating conversion to decompressive craniectomy. These patients were subsequently excluded from the study and to maintain group balance, two additional patients were further recruited into the craniotomy group and finally a total of 36 patients were included and categorized into two groups based on the surgical procedure performed: craniotomy (CR) group comprised 18 patients and decompressive craniectomy (DC) group comprised 18 patients. At admission Glasgow Coma Scale (GCS) was used to measure the depth and duration of impaired consciousness and coma of the cases. After 1 month follow up, the postoperative functional outcomes were measured by Glasgow Outcome Scale (GOS) and good outcome was determined by GOS score 5 and 4 and poor outcome was determined by GOS score 3,2 and 1. A pre-structured case record form was used to collect the data of this study. The collected data were methodically organized and analyzed using Statistical Package for Social Sciences (SPSS), version-22.0. Descriptive statistical analysis were performed and the results were presented as frequency and mean in the tables Chi-square test, Fisher's Exact test and unpaired t test were performed to compare the baseline, clinical and outcomes variables of the study, where, $p<0.05$ considered as the level of significance. The ethical clearance of this study was obtained from the Institutional Review Board (IRB) of Dhaka Medical College Hospital, Dhaka, Bangladesh.

RESULTS

A total of 36 patients were included in this study, with 18 in the craniotomy (CR) group and 18 in the decompressive craniectomy (DC) group. In the CR group, the most frequent 8 (44.4%) patients were aged 21–40 years and followed by 4 (22.2%) were 41–60 years, and 6 (33.3%) were 61–80 years. In the DC group, the most frequent 7 (38.9%) patients were aged 21–40 years and followed by 3 (16.7%) patients were aged 11–20 years and the same 3 (16.7%) were 41–60 years, and 5 (27.7%) were 61–80 years. The mean age of the patients of CR group was (50.36 ± 20.88 years) and the DC group was (41.77 ± 20.52 years) (p=0.164). In the CR group, 15 (83.3%) were male and 3 (16.7%) were female, whereas in the DC group, 12 (66.7%) were male and 6 (33.3%) were female. (p = 0.443) (Table-I). Road traffic accidents (RTA) were the most common cause, accounting for 22 (61.1%) of the cases. Among these, 9 (50.0%) occurred in the CR group and 13 (72.2%) in the DC group. Falls from height were responsible for 6 (16.7%) injuries, equally distributed between the groups: 3 (16.7%) in CR and 3 (16.7%) in DC. Fall of heavy weight accounted for 2 (5.6%) cases, with 1 (5.6%) from each group. Physical assault was observed in 6 (16.7%) cases, including 5 (27.8%) in the CR group and 1 (5.6%) in the DC group. (p = 0.295) (Table-II). In the CR group, 10 (55.6%) cases had right-sided haematoma and 8 (44.4%) had left-sided involvement. Likewise, in the DC group, 11 (61.1%) haematomas were right-sided and 7 (38.9%) were left-sided. (p = 0.502).. The mean midline shift was measured 8.38 ± 2.47 mm in the CR group and 8.41 ± 2.37 mm in the DC group (p = 0.782). Similarly, the mean thickness of the haematoma showed no meaningful difference, measuring 13.67 ± 3.16 mm in the CR group and 13.33 ± 2.65 mm in the DC group (p = 0.743) (Table-III). At admission in the CR group, 1 (5.6%) patient presented with a GCS score of 5–6, 5 (27.8%) with a score of 7–8, 9 (50.0%) with a score of 9–10, and 3 (16.7%) with a score of 11–13. In the DC group, 1 (5.6%) patient had a GCS of 5–6, 9 (50.0%) presented with a score of 7–8, 3 (16.7%) had a score of 9–10, and 5 (27.8%) had a score of 11–13 (p = 0.20) (Table-IV). The mean time interval between the incident and the operation was 24.27 ± 10.73 hours in the CR group and 21.72 ± 6.78 hours in the DC group (p= 0.399). Similarly, the time interval between hospital admission and the operation was comparable between groups, measuring 5.36 ± 3.20 hours in the CR group and 6.15 ± 2.68 hours in the DC group (p = 0.611). Patients undergoing craniotomy stayed in hospital 13.54 ± 4.48 days, whereas those in the DC group stayed 5.50 ± 6.64 days (p= 0.422) (Table-V). According to the Glasgow Outcome Score (GOS) at 1-month follow-up, in the CR group, 7 (38.9%) patients had died, 1 (5.6%) remained in a persistent vegetative state, 2 (11.1%) experienced severe disability, 2 (11.1%) showed moderate disability, and 6 (33.3%) achieved good recovery. In the DC group, 6 (33.3%) patients had died, 1 (5.6%) remained in a persistent vegetative state, none showed severe disability, 5 (27.7%) achieved moderate disability, and 6 (33.3%) achieved good recovery. Which was not statistically significant (p= 0.565) (Table-VI). In the craniotomy group, functional outcomes varied according to age and clinical characteristics. Among patients aged <40 years, 5 (71.4%) achieved a good outcome, while 2 (28.5%) experienced a poor outcome. In contrast, among those aged ≥40 years, only 3 (27.3%) had a good outcome whereas 8 (72.7%) had a poor outcome. (p = 0.145). GCS at admission also influenced outcomes, with 1 (16.7%) good and 5 (83.3%) poor outcomes among patients with GCS ≤8, compared to 7 (58.3%) good and 5 (41.7%) poor outcomes among those with GCS >8 (p= 0.152). Patients operated within 24 hours showed markedly better outcomes, with 8 (72.7%) achieving good outcome and 3 (27.3%) showing poor outcome. Conversely, all patients operated after 24 hours had poor outcomes (0% good vs. 7 (100%) poor), and this relationship was statistically significant (p = 0.004). Pupillary response did not show a significant association. Among those with normal or

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reactive pupils, 6 (50.0%) had good outcomes and 6 (50.0%) had poor outcomes. For those with unilateral fixed dilated pupils, 2 (33.3%) had good and 4 (66.7%) had poor outcomes (p=1.000). In the decompressive craniectomy group, 7 (70.0%) of patients aged <40 years had good outcomes compared to 3 (30.0%) with poor outcomes, whereas among those aged ≥40 years, 3 (37.5%) achieved good outcomes and 5 (62.5%) had poor outcomes which was not statistically significant (p = 0.342). For patients with GCS ≤8, 4 (40.0%) experienced good and 6 (60.0%) poor outcomes; among those with GCS >8, 6 (75.0%) had good and 2 (25.0%) had poor outcomes which was not significant (p = 0.188). Time to surgery showed that patients operated within 24 hours had better outcomes (9 (69.2%) good vs. 4 (30.8%) poor) compared to those operated after 24 hours (1 (20.0%) good vs. 4 (80.0%) poor) which was not statistical significance (p = 0.188). Pupillary response similarly did not show a significant association. Among patients with normal or reactive pupils, 8 (57.1%) achieved good outcomes and 6 (42.9%) had poor outcomes. In those with unilateral fixed dilated pupils, outcomes were evenly distributed, with 2 (50.0%) good and 2 (50.0%) poor (p=0.559) (Table-VII). The overall functional outcomes at 1 month demonstrated that 8 (44.4%) patients in the CR group achieved a good outcome, while 10 (55.6%) had a poor outcome. In comparison, 11 (61.1%) patients in the DC group experienced a good outcome, and 7 (38.9%) had a poor outcome. Although good outcomes were more frequent in the DC group, the difference between the two groups was not statistically significant (p = 0.317) (Table-VIII).

Table – I: Age and sex distribution of the study subjects (*n*=36)

	Group		p value
	CR(n=18) n (%)	DC(n=18) n (%)	
Age (years)			
11--20	0(0.0)	3 (16.7)	0.504
21 – 40	8 (44.4)	7 (38.9)	
41 – 60	4 (22.2)	3 (16.7)	
61 – 80	6 (33.3)	5 (27.7)	
Mean ±SD	50.36 ± 20.88	41.77 ± 20.52	0.164
Min - max	21 – 80.00	17 – 72.00	
Sex			
Male	15(83.3)	12(66.7)	0.443
Female	3(16.7)	6(33.3)	

Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

Table – II: Mode of injury of the study subjects (*n*=36)

Mode of injury	Group		Total	p value
	CR(n=18) n (%)	DC(n=18) n (%)		
RTA	9(50.0)	13 (72.2)	22(61.1)	0.295
Fall from height	3 (16.7)	3 (16.7)	6 (16.7)	
Fall of heavy weight	1 (5.6)	1 (5.6)	2 (5.6)	
Physical assault	5 (27.8)	1 (5.6)	6 (16.7)	

Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

Table – III: Location and thickness of haematoma and midline shifting of the study subject (*n*=36)

	CR(n=18) n (%)	DC(n=18) n (%)	p value
Acute sub dural haematoma			
Right	10 (55.6)	11 (61.1)	0.502
Left	8 (44.4)	7 (38.9)	
Midline shifting (mm)	8.38 ± 2.47	8.41 ± 2.37	0.782
Thickness of Hematoma (mm)	13.67 ± 3.16	13.33 ± 2.65	0.743

Unpaired t test and Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

Table – IV: At admission GCS score of the study subjects (*n*=36)

GCS score	Group		p value
	CR(n=18) n (%)	DC(n=18) n(%)	
5-6	1 (5.6)	1 (5.6)	0.212
7-8	5 (27.8)	9 (50.0)	
9-10	9 (50.0)	3 (16.7)	
11-13	3 (16.7)	5 (27.8)	

Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

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Table – V: Time interval between incidence & operation and length of hospital stay (*n*=36)

Time interval and length of hospital stay	Group		p value
	CR(n=18)	DC(n=18)	
Time interval between incidence and operation (hours)	24.27 ± 10.73	21.72 ± 6.78	0.399
Time interval between admission and operation	5.36± 3.20	6.15 ± 2.68	0.611
Length of hospital stay (days)	13.54± 4.48	15.5± 6.64	0.422

Unpaired t tests were performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

Table – VI: Distribution of functional outcome of the study patients according to GOS Score after 1 month follow up (*n*=36)

Functional Outcome	Group			p value
	CR(n=18) n (%)	DC(n=18) n (%)	Total	
Dead	7(38.9)	6(33.3)	13(36.1)	0.565
Persistent vegetative state	1(5.6)	1(5.6)	2(5.6)	
Severe disability (conscious but disabled)	2(11.1)	0(0.0)	2(5.6)	
Moderate disability (disabled but independent)	2(11.1)	5(27.7)	7(19.4)	
Good Recovery	6(33.3)	6(33.3)	12(33.3)	

Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI.

Table – VII: Distribution of functional outcome of the study patients by age and clinical determinants after 1 month follow up (*n*=36)

CR Group(n=18)		Outcome		p value
		Good outcome	Poor outcome	
Age(years)		n (%)	n (%)	0.399
	<40	5(71.4)	2(28.5)	0.145
	≥40	3(27.3)	8(72.7)	
GCS				
	≤ 8	1(16.7)	5(83.3)	0.152
	>8	7(58.3)	5(41.7)	
Time interval and operation (hours)				
	≤ 24	8(72.7)	3(27.3)	0.004
	>24	0(0.0)	7(100)	
Pupil				
Normal or dilated but reacting		6(50.0)	6(50.0)	1.000
Dilated and fixed (Unilateral)		2(33.3)	4(66.7)	
DC Group(n=18)				
Age(years)				
	<40	7(70.0)	3(30.0)	0.342
	≥40	3(37.5)	5(62.5)	
GCS				
	≤ 8	4(40.0)	6(60.0)	0.188
	>8	6(75.0)	2(25.0)	
Time interval and operation (hours)				
	≤ 24	9(69.2)	4(30.8)	0.188
	>24	1(20.0)	4(80.0)	
Pupil				
Normal or dilated but reacting		8(57.1)	6(42.9)	0.559
Dilated and fixed(Unilateral)		2(50.0)	2(50.0)	

Fisher's exact tests were performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI. Good outcome= Glasgow outcome scale score 5 and 4. Poor outcome= Glasgow outcome scale score 3, 2 and 1.

Table – VIII: Distribution of total good vs poor outcome of the study patients after 1 month follow up (*n*=36)

Outcome	Group		p value
	CR(n=18) n(%)	DC(n=18) n(%)	
Good outcome	8(44,4)	11(61.1)	0.317
Poor outcome	10(55.6)	7(38.9)	

Chi-square test was performed to measure the level of significance, p<0.05 considered as the level of significance with 95% CI. Good outcome= Glasgow outcome scale score 5 and 4. Poor outcome= Glasgow outcome scale score 3,2 and 1.

DISCUSSION

Traumatic acute subdural haematoma (ASDH) remains one of the most lethal types of head injury, in which primary brain injury appears to be a more decisive prognostic factor than the haematoma itself [11]. Despite major advances in emergency medical care, neuroimaging, surgical techniques and intensive care support, the morbidity and mortality associated with ASDH continue to be substantially high across treatment centres worldwide [12]. A recent study demonstrated that outcomes in severe head injury depend more on initial clinical condition, the extent of intracranial damage, associated injuries, patient age, and the timing of surgical intervention rather than the characteristics of the haematoma alone[13]. In contemporary neurosurgical practice, craniotomy (CR) and decompressive craniectomy(DC) remain the two principal operative techniques performed for ASDH

evacuation. The present study demonstrated that age, pre-operative GCS, pupillary response, and time interval between injury and surgery significantly influence postoperative outcomes. Moribund patients with GCS 3–4 and bilateral fixed pupils were excluded, along with six additional cases with peroperative severe brain swelling. The highest proportion of patients in this study belonged to the 21–40-year age group, which is consistent with prior study reporting a similar age distribution among ASDH patients [14], and the mean age values in this series closely resemble those reported in comparable cohorts [15]. Younger patients demonstrated better outcomes, while older age was strongly associated with poor prognosis, a trend well established in previous literature showing mortality exceeding 70% among patients older than 40 years [16]. Male predominance was observed in this cohort, a pattern that aligns with multiple reports of higher incidence of traumatic ASDH among young males due to greater exposure to high-risk activities [14]. However, the present study found no significant prognostic difference between the two sexes, which is consistent with findings from other research demonstrating no major outcome variation attributable to sex [17]. Road traffic accidents (RTAs) constituted the leading cause of ASDH in this study, followed by falls and physical assault, which mirrors the dominant injury patterns described in a similar study conducted in developing regions [18]. Preoperative neurological status emerged as a key determinant of outcome. Among patients with GCS ≤8, those treated with DC demonstrated better favourable outcomes than those undergoing craniotomy. This finding parallels observations from a study involving 91 patients, in which DC yielded superior results in severely impaired individuals [19]. Patients presenting with moderate GCS (9–13) showed improved outcomes with both procedures, though DC demonstrated a slightly higher proportion of favourable recovery. Timing of surgery also played a crucial role, as patients operated within 24 hours had substantially better recovery compared with those treated after 24 hours. This finding supports previous evidence suggesting that shorter intervals between injury and surgical intervention are associated with more favourable neurological outcomes [20]. Pupillary light reflex was another important prognostic factor. Patients with bilateral reacting pupils had markedly better outcomes compared with those with unilateral fixed dilated pupils. This relationship is consistent with earlier reports emphasizing the high mortality associated with absent or abnormal pupillary reflexes in ASDH patients [21]. The overall mortality in this study was 36.1%, slightly higher in the craniotomy group, which is within the range of previously reported mortality rates [22]. Overall, the favourable outcome rate in this study was 52.78%, with no statistically significant difference between craniotomy and decompressive craniectomy. However, subgroup analyses suggest that DC may be more beneficial in patients presenting with low GCS scores, unilateral fixed pupils, or delayed presentation, although these trends did not reach statistical significance [23]. Finally, the results of this study reaffirm that surgical outcomes in ASDH are primarily determined by three major factors, preoperative GCS, pupillary response and timing of surgery. Patients presenting with GCS above 8, bilateral reacting pupils, and early surgical intervention (within 24 hours) demonstrated favourable outcomes irrespective of surgical technique. While DC tended to offer better outcomes in patients with severe neurological deficits or late presentation, hence, a longitudinal study would be required to establish definitive conclusions regarding the superiority of one technique over the other.

LIMITATIONS OF THIE STUDY

This study is limited by its small sample size and single-center design, which may not represent a large population Postoperative long-term functional outcome follow up were not assessed due to the time constraint of the study. Finally, due to financial constraint radiological factors were also not evaluated in this study.

CONCLUSION

Patients with traumatic acute subdural hematoma with GCS ≥ 9, bilateral reacting pupil and surgery within 24 hours craniotomy (CR) may be an alternative surgical option considering the possible complications of decompressive craniectomy as craniotomy and decompressive craniectomy showed no difference. But patients with poor clinical status and surgery after 24 hours primary decompressive craniectomoy (DC) may be more effective than craniotomy.

RECOMMENDATIONS OF THE STUDY

Future studies with larger, multicentre samples are recommended to validate the comparative effectiveness of craniotomy and decompressive craniectomy in acute subdural hematoma. Long-term follow-up should be incorporated to assess functional recovery beyond the early postoperative period. Inclusion of detailed radiological parameters may also help refine surgical decision-making.

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REFERENCES

1. *Yanaka K, Kamezaki T, Yamada T, Takano S, Meguro K, Nose T. Acute subdural hematoma: prediction of outcome with a linear discriminant function. Neurol Med Chir (Tokyo). 1993; 33(8):552-8.*
2. *Bullock MR, Chesnut R, Ghajar J, et al. Surgical management of acute subdural hematomas. Neurosurgery. 2006; 58(3 Suppl):S16-24.*
3. *Williams JR, Randle J, Beuchel C, et al. Pathophysiology of traumatic subdural hematoma. J Clin Neurosci. 2018; 50:7-13.*
4. *Liege J, Mauritz W, Brazinova A, et al. Outcome after severe brain trauma due to acute subdural hematoma. J Neurosurg. 2012; 117(2):324-33.*
5. *Servadei F, Nasi MT, Giuliani G, et al. CT prognostic factors in acute subdural haematomas: the role of the "worst" CT scan. Br J Neurosurg. 2000; 14(2):110-6.*
6. *Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol. 2017; 16(12):987-1048.*
7. *Haselsberger K, Pucher R, Auer LM. Prognosis after acute subdural or epidural haemorrhage. Acta Neurochir (Wien). 1988; 90(3-4):111-6.*
8. *Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med. 2011; 364(16):1493-502.*
9. *Kolias AG, Kirkpatrick PJ, Hutchinson PJ. Decompressive craniectomy: past, present and future. Nat Rev Neurol. 2012; 9(7):405-15.*
10. *Adeleye AO, Olowookere KG. Primary decompressive craniectomy for acute subdural haematoma in severe traumatic brain injury: is it still relevant? Acta Neurochir (Wien). 2014; 156(11):2129-35.*
11. *Fell DA, Fitzgerald S, Moiel RH. Acute subdural hematoma: Review of 144 cases. J Neurosurg. 1975; 42(1):37–42.*
12. *Servadei F, Nasi MT, Compagnone C, et al. Evolving brain lesions in the first 12 hours after head injury. J Neurosurg. 1997; 87(4):558–568.*
13. *Cooper PR, Rovit RL, Ransohoff J. Influence of surgical timing on head injury outcome. Neurosurgery. 1976; 1(3):224–231.*
14. *Prahaladu P, et al. Clinical profile and outcome of acute subdural hematoma. Int Surg J. 2017;4(2):681–685.*

ISSN: 2663-9491 e-ISSN: 2789-6897

15. *Alagoz F, et al. Surgical outcomes in acute subdural hematoma. Ulus Travma Acil Cerrahi Derg. 2017; 23(4):301–306.*
16. *Marshall LF, Smith RW, Shapiro HM. The outcome of severe head injury with acute subdural hematoma. J Neurosurg. 1991; 75(2):175–182.*
17. *Woertgen C, et al. Sex as a prognostic factor in traumatic brain injury. Acta Neurochir. 2006;148(5):525–530.*
18. *Ayoub O, Elmallawany N. Acute subdural hematoma: Clinical characteristics. Egypt J Neurosurg. 2015; 30(2):123–128.*
19. *Li LM, et al. Decompressive craniectomy versus craniotomy in acute subdural hematoma. Acta Neurochir. 2012; 154(9):1551–1557.*
20. *Thabet AM, El Tayeb AA. Timing of surgery in acute subdural hematoma. Pan Arab J Neurosurg. 2015; 19(1):45–51.*
21. *Basim K, et al. Prognostic value of pupillary response in traumatic acute subdural hematoma. Neurosurg Rev. 2015; 38(1):119–125.*
22. *Stone JL, et al. Acute subdural hematoma outcome analysis: A review of 200 cases. J Trauma. 1983; 23(2):143–149.*
23. *Lietgeb L, et al. Early mortality in acute subdural hematoma following surgery. Acta Neurochir. 2012; 154(6):1063–1069.*

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ORIGINAL ARTICLE

Prostate Volume and PSA Trends – Clinical Predictors of Malignancy in Benign and Malignant Prostatic Diseases

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ABSTRACT

Background: *Prostate volume (PV) and prostate-specific antigen (PSA) are widely used clinical parameters in evaluating prostatic diseases. While PSA levels may increase in both benign and malignant conditions, smaller prostate volumes combined with elevated PSA improve malignancy prediction. Identifying reliable predictors is essential for timely diagnosis and appropriate management.* ***Aim of the study:*** *To evaluate the role of prostate volume and PSA trends as clinical predictors of malignancy in patients presenting with benign and malignant prostatic diseases.* ***Methods & Materials:*** *A prospective study was conducted at BIRDEM General Hospital, Dhaka, Bangladesh from July 2017 to June 2019. A total of 110 men aged ≥50 years with suspected prostatic disease underwent clinical assessment, transabdominal ultrasonography for prostate volume estimation, serum PSA measurement, and systematic prostate biopsy. Histopathology served as the diagnostic reference standard. Data were analyzed using SPSS version 26.0. Logistic regression identified independent predictors of malignancy. Diagnostic performance was evaluated through sensitivity, specificity, PPV, NPV, and accuracy.*

Result: *Malignancy was confirmed in 15.45% of participants. Malignant cases had significantly higher mean PSA levels (25.48±11.62 ng/mL) and larger PV (57.4±16.2 mL). PSA >10 ng/mL was the strongest predictor (OR 27.8; p<0.001), followed by PV Grade III/IV (OR 3.2; p=0.02). PSA >10 ng/mL demonstrated high specificity (94.6%) and accuracy (89.1%), while combining PSA >10 with PV Grade III/IV increased specificity to 97.8%.*

Conclusion: *PSA remains the strongest predictor of malignant prostatic disease, and incorporating prostate volume enhances diagnostic precision. Larger multicenter studies are encouraged.*

Keywords: *Prostate volume, PSA, Prostate cancer, Benign prostatic hyperplasia, Diagnostic predictors*

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INTRODUCTION

Prostate volume (PV) measures the size of the prostate, usually in cm^3 via imaging, while prostate-specific antigen (PSA) is a protein whose blood levels help screen for prostate conditions like benign prostatic hyperplasia (BPH) and prostate cancer. Globally, smaller prostate volumes, particularly those under 45 cm^3 and more so below 26 cm^3, are associated with a significantly higher likelihood up to about 69% of prostate cancer when PSA density exceeds 0.15 $ng/mL/cm^3$ [1]. In Bangladeshi, men evaluated for prostate disease, about 16% of prostate tissue specimens submitted for histopathology are found to be malignant, while roughly 82% are benign changes [2]. Prostate volume indicates the size of the prostate and can be measured via ultrasonography or MRI. Transrectal ultrasound (TRUS) estimates PV using the ellipsoid formula, while MRI employs semiautomatic or deep learning–based 3D segmentation for more precise measurements. Both methods slightly underestimate true pathological volume, though MRI generally shows higher accuracy and stronger correlation with surgical specimens [3,4]. In benign prostatic hyperplasia, PV typically increases due to enlargement of the transition zone, whereas in prostate cancer, changes in zonal volumes, such as altered ratios between the peripheral and transition zones, can help differentiate malignant from benign conditions. Although larger prostate volume is often associated with benign disease, cancer can also occur in larger prostates, so PV alone is not definitive for diagnosis; it serves as a useful factor to stratify risk when combined with other clinical parameters like PSA levels and imaging biomarkers [5]. PSA is a protein biomarker secreted by prostate tissue, widely used in clinical practice to screen for and monitor prostate diseases. PSA levels correlate with prostate pathology, generally increasing in both benign conditions like BPH and malignant prostate cancer, but the patterns and implications differ [6]. Trends in PSA, such as rising levels over time (PSA velocity) or the ratio

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of free to total PSA, help improve malignancy prediction beyond a single measurement, with PSA density providing additional risk stratification [7]. Combining prostate volume with PSA measurements, especially PSA density, improves the prediction of malignancy and helps guide biopsy decisions, as higher PSA density is associated with more aggressive cancer and advanced pathological stages [8]. However, challenges remain, including variability in PSA due to non-cancer factors and limitations in imaging accuracy for PV measurement, which can affect PSA density calculations [6]. While MRI offers more precise prostate volume measurements than ultrasound, limited availability makes ultrasound more common; combining PSA, PV, and other biomarkers improves early detection and risk stratification, but must be interpreted cautiously to prevent overdiagnosis [9]. Although national surveys report on NCDs, nutrition, and demographics in Bangladesh, detailed population-specific data across regions and subgroups remain limited, with urban-rural disparities often masked by aggregated national statistics [10]. This study aimed to evaluate the role of prostate volume and PSA trends as clinical predictors of malignancy in patients with benign and malignant prostatic diseases.

MATERIALS & METHODS

This study, conducted from July 2017 to June 2019 at BIRDEM General Hospital, Dhaka, Bangladesh. The study aimed to evaluate prostate volume and PSA trends as predictors of malignancy in patients presenting with suspected prostatic disease. A total of 110 consecutive male patients were enrolled. Patients were clinically evaluated and categorized into:

- Benign prostatic disease group (n=93)
- Malignant prostatic disease group (n=17)

Diagnosis was confirmed by histopathological examination following prostate biopsy.

Inclusion Criteria

- Men aged 50 years and above
- Patients with symptoms of elevated PSA
- Patients who underwent biopsy with available histopathology reports

Exclusion Criteria

- Prior history of prostate cancer
- Patients who received 5-alpha reductase inhibitors, androgen therapy, or previous prostate surgery
- Active urinary tract infection or prostatitis at the time of evaluation

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of BIRDEM General Hospital. Written informed consent was collected from all participants.

Biopsy and Histopathological Processing

All patients underwent systematic prostate biopsy following clinical and radiological evaluation. The biopsy specimens were immediately fixed in 10% formalin and submitted to the Department of Pathology for histopathological examination. Tissue samples were processed using the routine paraffin-embedding technique, which included overnight fixation, graded dehydration through ascending concentrations of alcohol, clearing in xylene, and embedding in paraffin wax. Paraffin blocks were sectioned at a thickness of 3–5 µm using a rotary microtome, and the sections were mounted on glass slides. The slides were subsequently deparaffinized in xylene, rehydrated through graded alcohol, and stained using Harris's hematoxylin followed by differentiation in acid alcohol and counterstaining with eosin. After staining, the sections were dehydrated, cleared, and mounted using DPX. Microscopically, nuclei stained blue, cytoplasm appeared pink to red, collagen and muscle fibers showed pink coloration, and red blood cells appeared bright red. Final histopathological diagnosis of benign or malignant prostatic disease was made based on evaluation of glandular architecture, cellular morphology, and nuclear atypia and was considered the reference standard for disease classification.

Data Collection

Data were collected prospectively. Demographic data included age at presentation. Clinical data were obtained through direct patient interviews and physical examination and included the presence of lower urinary tract symptoms such as burning sensation during micturition, increased urinary frequency, dribbling of urine, fever, hesitancy, urgency, and acute urinary retention. Laboratory data included serum prostate-specific antigen (PSA) levels, measured using a standardized immunoassay protocol in the hospital laboratory. PSA values were documented as continuous variables and further categorized into three groups (0–5 ng/mL, 5.1–10 ng/mL, and >10 ng/mL) for analysis. Radiological data consisted of prostate volume measurements obtained by transabdominal ultrasonography (USG). Prostate size values were recorded in milliliters and classified into four grades: Grade I (20–30 g), Grade II (31–50 g), Grade III (51–80 g), and Grade IV (>80 g). Histopathological data were obtained from prostate biopsy specimens processed in the Department of Pathology. Final diagnosis was categorized as either benign prostatic disease or malignant prostatic adenocarcinoma and used as the reference standard for statistical analysis. All collected data were cross-checked for completeness and accuracy before statistical entry.

Statistical Analysis

Data analysis was performed using SPSS version 26.0. Continuous variables were summarized as mean ± standard deviation and compared between benign and malignant groups using the independent samples t-test. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test when appropriate. Binary logistic regression was employed to identify independent predictors of malignant disease, and results were expressed as adjusted odds ratios (OR) with 95% confidence intervals (CI). The diagnostic accuracy of major predictors was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using standard 2×2 contingency tables. A p-value of <0.05 was considered statistically significant.

RESULT

Figure 1 shows that most patients had benign prostatic diseases 74.55%, while malignant prostatic disease accounted for 25.45%. Similarly benign cases had a mean age of 67.1±9.0 years, while malignant cases were slightly older at 70.5±7.8 years (p=0.12) (Table I). Increased frequency appeared in 100% of both groups. Burning sensation was reported by 50.54% of benign vs 64.71% of malignant cases (p=0.32). Fever was notably lower in malignant (5.88%) than benign (24.73%) (p=0.08). Other symptoms dribbling (86.02% vs 88.24%), hesitancy (80.65% vs 88.24%), urgency (93.55% vs

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88.24%) and urinary retention (79.57% vs 88.24%) were similar between groups.

Table II indicates that among the patients were more frequent in Grade I at 37.63% and Grade II at 41.94%, while malignant cases were higher in Grade III at 47.06% and Grade IV at 11.76%. Mean prostate volume was greater in malignant at 57.4 ± 16.2 mL compared to 44.8 ± 18.5 mL in benign. PSA trends showed 81.72% of benign in the 0–5 range, 12.90% in 5.1–10, and 5.38% above 10, whereas malignant patients had 23.53% in 0–5, 11.76% in 5.1–10, and 64.71% above 10, with a significantly higher mean PSA of 25.48±11.62 ng/mL.

PSA above 10 ng/ml showed the strongest association with malignancy, with an odds ratio of 27.8 and a confidence interval of 7.9–97.5 (Table III). Prostate Grade III or IV also increased risk, with an odds ratio of 3.2 and a confidence interval of 1.2–8.4. Age over 70 years (OR 1.7, 0.6–5.0), burning sensation (OR 1.8, 0.6–5.5), and urinary retention (OR 1.5, 0.4–5.1). Table IV demonstrates that PSA above 10 ng/ml showed good diagnostic performance, with a sensitivity of 64.7%, specificity of 94.6%, positive predictive value of 68.8%, negative predictive value of 93.3%, and overall accuracy of 89.1%. Prostate Volume Grade III/IV had moderate sensitivity of 58.8% and specificity of 79.6%, with PPV of 34.5%, NPV of 91.3%, and accuracy of 76.4%. Combining PSA above 10 ng/ml with Grade III/IV increased specificity to 97.8% and PPV to 80%, with overall accuracy of 89.1%.

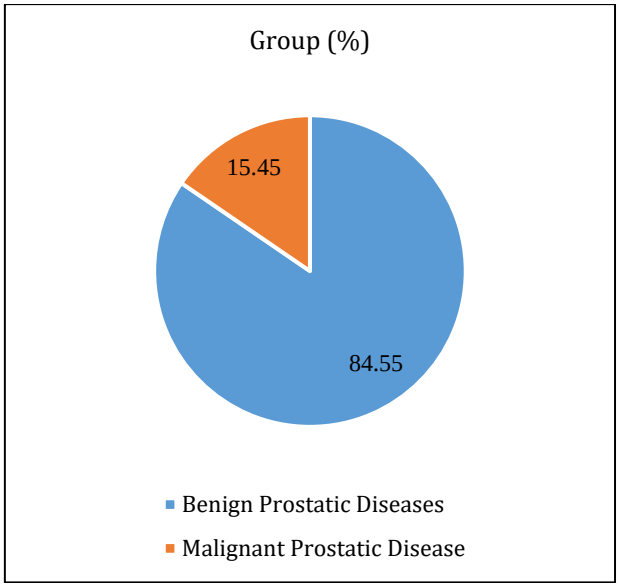

Figure – 1: Distribution of study participants by group (*n*=110)

Table – I: Baseline characteristics by disease group (*n*=110)

Variable	Benign (n=93)		Malignant (n=17)		P-value
	n	%	n	%	
Age (years), Mean ± SD	67.1 ± 9.0		70.5 ± 7.8		0.12
Complications					
Burning sensation	47	50.54	11	64.71	0.32
Increased frequency	93	100.00	17	100.00	1
Dribbling of urine	80	86.02	15	88.24	0.81
Fever	23	24.73	1	5.88	0.08
Hesitancy	75	80.65	15	88.24	0.5
Urgency	87	93.55	15	88.24	0.57
Urinary retention	74	79.57	15	88.24	0.48

Table – II: Prostate Volume (USG) and PSA Trends among patients (*n*=110)

Variable	Benign (n=93)		Malignant (n=17)		P-value
	n	%	n	%	
Prostate USG					
Grade I (20–30 g)	35	37.63	2	11.76	0.04
Grade II (31–50 g)	39	41.94	5	29.41	0.33
Grade III (51–80 g)	16	17.20	8	47.06	0.01
Grade IV (>80 g)	3	3.23	2	11.76	0.18
Prostate volume (mL), Mean ± SD	44.8 ± 18.5		57.4 ± 16.2		0.02
PSA Trends (ng/mL)					
0–5	76	81.72	4	23.53	<0.001
5.1–10	12	12.90	2	11.76	0.9
>10	5	5.38	11	64.71	<0.001
PSA level (ng/mL), Mean ± SD	6.42 ± 3.15		25.48 ± 11.62		<0.001

Table – III: Logistic regression for predictors of malignancy

Predictor	OR (95% CI)	P-value
PSA >10 ng/ml	27.8 (7.9–97.5)	<0.001
Prostate Grade III/IV	3.2 (1.2–8.4)	0.02
Age >70 years	1.7 (0.6–5.0)	0.32
Burning sensation	1.8 (0.6–5.5)	0.32
Urinary retention	1.5 (0.4–5.1)	0.48

Table – IV: Diagnostic accuracy of key predictors

Predictor	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PSA >10 ng/ml	64.7	94.6	68.8	93.3	89.1
Prostate Volume Grade III/IV	58.8	79.6	34.5	91.3	76.4
PSA >10 ng/ml + Prostate Volume Grade III/IV	47.1	97.8	80	91.3	89.1

DISCUSSION

Prostate disorders encompass a spectrum of conditions, ranging from benign hyperplasia and chronic prostatitis to malignant neoplasms, each exhibiting distinct clinical and biochemical profiles [11]. In the study, the majority of patients presented with benign prostatic diseases accounting for 84.55%, whereas malignant prostatic disease constituted 15.45% of cases, similar to findings by Tolani et al., who reported that benign prostatic hyperplasia and prostate cancer were diagnosed in 71.40% and 28.60% of patients, respectively [12]. Muhammad et al. reported 64.00% benign prostatic hyperplasia and 20.00% prostate cancer [13]. Mean age was 67.1 ± 9.0 years in benign and 70.5 ± 7.8 years in malignant cases (p = 0.12). Islam et al stated that patients with prostate cancer were notably older than those with benign prostatic hyperplasia, with mean ages of 72 ± 4.4 versus 64 ± 6.6 years, respectively (p = 0.00001) [14]. Xing et al. reported a mean age of 65.9 ± 8.7 years (range 37–86 years) [15]. Increased frequency occurred in 100% of both groups. Burning sensation was 50.5% vs 64.7% (p = 0.32), fever 24.7% vs 5.9% (p = 0.08), while dribbling, hesitancy, urgency, and retention were similar (86.0–93.5% vs 88.2–88.2%). Mobley et al. reported that 15–25% of men experience lower urinary tract symptoms (LUTS), such as nocturia, urgency, frequency, incomplete bladder emptying, stop-start urination, straining, post-void urgency, and weak urinary stream [16]. Tolani et al. reported that difficulty in urination (91.4%), low back pain (44.8%), urinary retention (38.1%), erectile dysfunction (31.4%), hematuria (22.9%), and chronic renal failure (4.8%) was observed among patients [12]. Benign cases were mainly Grade I–II (37.6%–41.9%) and malignant cases Grade III–IV (47.1%–11.8%). Mean prostate volume was 44.8 ± 18.5 mL (benign) vs 57.4 ± 16.2 mL (malignant). PSA >10 ng/mL was seen in 5.4% of benign vs 64.7% of malignant cases, with mean PSA 25.48 ± 11.62 ng/mL in malignancy. Yamashiro et al. stated an inverse relationship between prostate volume and the risk of prostate cancer [17]. Al-Azab et al. reported that prostate volume is a stronger predictor of cancer than PSA alone, especially when PSA is in the lower to intermediate range (2–9 ng/mL), indicating that in smaller glands, cancer contributes relatively more to PSA elevation than benign enlargement [18]. Wolff et al. reported that mean PSA density was significantly higher in prostate cancer than BPH (0.46 vs. 0.116, p < 0.005), indicating that absolute PSA alone has limited specificity [19]. Erdogan et al. demonstrated that free/total PSA ratio, prostate volume, and PSA density differed significantly between prostate cancer and non-cancer cases (p < 0.001) [20]. PSA >10 ng/mL was most strongly associated with malignancy (OR 27.8, 95% CI 7.9–97.5), followed by Grade III–IV prostate (OR 3.2, 95% CI 1.2–8.4); age >70 y, burning, and retention showed weaker associations (OR 1.5–1.8). Hwang et al. identified elevated PSA as a significant risk factor, with higher PSA levels associated with increased prostate cancer incidence (HR 1.77, 95% CI 1.67–1.88) [21]. Al-Azab et al. reported that smaller prostate volume was the strongest predictor of a positive biopsy (OR 0.26, p < 0.001), indicating that larger prostates, likely due to BPH, were more often associated with benign findings [18]. Tiger et al. reported that each 10 mL increase in prostate volume was associated with an approximately 30% lower risk of clinically significant prostate cancer [22]. PSA >10 ng/mL showed sensitivity 64.7%, specificity 94.6%, PPV 68.8%, NPV 93.3%, and accuracy 89.1%. Prostate volume Grade III/IV had sensitivity 58.8%, specificity 79.6%, PPV 34.5%, NPV 91.3%, and accuracy 76.4%. Combining PSA >10 ng/mL with Grade III/IV improved specificity to 97.8%, PPV to 80%, and overall accuracy remained 89.1%. Merriel et al. reported that PSA has high pooled sensitivity (~0.93) but low specificity (~0.20), indicating a substantial rate of false positives when used alone [23]. Saema et al. demonstrated that PSAD had superior discriminatory power over PSA, particularly in predicting cancer among patients with PSA in the 'grey zone' [24]. Khalid et al. demonstrated that MRI-derived PSAD with a cutoff of about 0.158 ng/mL/mL achieved 73.6% sensitivity and 92.7% specificity (AUC 0.83) for detecting prostate cancer [25].

Limitations of the study: This study has several limitations. The sample size was relatively small, particularly for malignant cases, which may limit generalizability. Prostate volume was measured using ultrasonography, which can underestimate true prostate size compared to MRI. Single-center design and lack of long-term follow-up restrict broader applicability and outcome assessment. PSA levels can be influenced by non-malignant factors such as inflammation or recent instrumentation, potentially confounding results. Additionally, other emerging biomarkers and imaging modalities were not evaluated, which may have enhanced diagnostic accuracy.

CONCLUSION

Prostate volume and PSA trends were shown to be significant clinical predictors of prostatic malignancy in this study. Patients with malignant disease had higher mean prostate volumes and markedly higher PSA levels compared to those with benign conditions. PSA above 10 ng/mL demonstrated the strongest association with malignancy, exhibiting high specificity and overall diagnostic accuracy. Prostate volume of Grade III/IV also contributed moderately to risk stratification, while combining elevated PSA with larger prostate grades further improved predictive specificity. These findings underscore the complementary value of integrating PSA trends and prostate volume assessment in clinical decision-making, enhancing early detection and guiding biopsy strategies in patients with suspected prostatic disease.

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Ethical approval: *The study was approved by the Institutional Ethics Committee.*

REFERENCES

1. *Liu Z, Yu Y, Hu R, Jian T, Yu K, Lu J. Effect of prostate volume on the predictive value of prostate-specific antigen density for prostate cancer. Translational Andrology and Urology. 2025 Jan 22;14(1):70.*
2. *Rahman MM, Alam MM, Khan MO, Karim MR, Hasan MS. Frequency of Prostate Cancer Among the Prostatic Tissue samples-Collected From Different Tertiary Level Hospital in Dhaka City. Bangladesh Journal of Urology. 2018;21(2):88-92.*

3. *Choe S, Patel HD, Lanzotti N, Okabe Y, Rac G, Shea SM, Gorbonos A, Quek ML, Flanigan RC, Goldberg A, Gupta GN. MRI vs transrectal ultrasound to estimate prostate volume and PSAD: impact on prostate cancer detection. Urology. 2023 Jan 1;171:172-8.*
4. *Zhang Z, Yang Q, Shiradkar R, Mirtti T, Azamat S, Xuan K, Xu J, Madabhushi A. A deep learning derived prostate zonal volume-based biomarker from T2-weighted MRI to distinguish between prostate cancer and benign prostatic hyperplasia. Medical Physics. 2025 Aug;52(8):e18053.*
5. *Lu Y, Yuan R, Su Y, Liang Z, Huang H, Leng Q, Yang A, Xiao X, Lai Z, Zhang Y. Biparametric MRI-based radiomics for noninvastive discrimination of benign prostatic hyperplasia nodules (BPH) and prostate cancer nodules: a bio-centric retrospective cohort study. Scientific Reports. 2025 Jan 3;15(1):654.*
6. *Bello ZM, Mohammed AZ, Kumurya AS, Abubakar SD, Ibrahim Y, Chiroma FA, Shema FB, Kabir IM. Discrepancy between PSA Levels and Gleason Score in Prostate Cancer from Northern Nigeria: A Histopathological Analysis. UMYU Scientifica. 2025 Jun 30;4(2):325-33.*
7. *Mo H, Hu C, Li P, Miao Z, Zhang H, Shen G, Sun J. PSA proportion of index lesion: a novel index for predicting prostate pathology outcomes in biopsy-naïve patients with PSA< 10 ng/ml and PI-RADS 3 lesions. World Journal of Urology. 2025 Jul 17;43(1):444.*
8. *Pattou M, Neuzillet Y, Ghoneim T, Bosset PO, Herve JM, Vanalderwerelt V, Bohin D, Lugagne PM, Soorojebally Y, Lebret T. PSA density correlates to pathology T stage and ISUP grade: insights from a cohort of 3568 radical prostatectomy cases. World journal of urology. 2025 Jul 17;43(1):445.*
9. *Preston MA, Batista JL, Wilson KM, Carlsson SV, Gerke T, Sjoberg DD, Dahl DM, Sesso HD, Feldman AS, Gann PH, Kibel AS. Baseline prostate-specific antigen levels in midlife predict lethal prostate cancer. Journal of Clinical Oncology. 2016 Aug 10;34(23):2705-11.*
10. *Garnett S, Biswas T, Pervin S, Rawal L. The prevalence of underweight, overweight and obesity in Bangladeshi adults: Data from a national survey.*
11. *Sultana SS, Hossain S, Rahman A. Histopathological Spectrum of Prostatic Lesions Evaluated in a Tertiary Hospital Histopathological Spectrum of Prostatic Lesions Evaluated in a Tertiary Hospital. Journal of Histopathology and Cytopathology. 2020 Jan;4(1):33-7.*
12. *Tolani MA, Khalifa AI, Afolayan AO. Clinicopathological characteristics of benign prostatic hyperplasia and prostate cancer in a University Teaching Hospital in Nigeria. Annals of Tropical Pathology. 2020;11(1):56-60.*
13. *Muhammad R, Bhatti MS, Khan MS, Ali S, Bokhari NM, Mehtab G, Ahmad I, Ali J. Prevalence of Benign Prostatic Hyperplasia and Prostate Cancer Among Adults in Pakistan. Indus Journal of Bioscience Research. 2025 Mar 15;3(3):164-8.*
14. *Islam MA, Haque MJ, Hossain MM, Islam SS. Prospective analysis of percent free prostate-specific antigen as a better predictor of early diagnosis of prostate cancer. Journal of Bio-Science. 2022;30(2):67-77.*
15. *Xing P, Chen L, Yang Q, Song T, Ma C, Grimm R, Fu C, Wang T, Peng W, Lu J. Differentiating prostate cancer from benign prostatic hyperplasia using whole-lesion histogram and texture analysis of diffusion-and T2-weighted imaging. Cancer Imaging. 2021 Sep 27;21(1):54.*
16. *Mobley D, Feibus A, Baum N. Benign prostatic hyperplasia and urinary symptoms: evaluation and treatment. Postgraduate medicine. 2015 May 4;127(3):301-7.*
17. *Yamashiro JR, de Riese WT. Any correlation between prostate volume and incidence of prostate cancer: a review of reported data for the last thirty years. Research and Reports in Urology. 2021 Oct 10:749-57.*
18. *Al-Azab R, Toi A, Lockwood G, Kulkarni GS, Fleshner N. Prostate volume is strongest predictor of cancer diagnosis at transrectal ultrasound-guided prostate biopsy with prostate-specific antigen values between 2.0 and 9.0 ng/mL. Urology. 2007 Jan 1;69(1):103-7.*
19. *Wolf JM, Scholz A, Boeckmann W, Jakse G. Differentiation of benign prostatic hyperplasia and prostate cancer employing prostatic-specific antigen density. European urology. 1994 Aug 11;25(4):295-8.*
20. *Erdogan A, Polat S, Keskin E, Turan A. Is prostate volume better than PSA density and free/total PSA ratio in predicting prostate cancer in patients with PSA 2.5–10 ng/mL and 10.1–30 ng/mL?. The Aging Male. 2020 Jan 2.*
21. *Hwang T, Oh H, Lee JA, Kim EJ. Prostate cancer risk prediction based on clinical factors and prostate-specific antigen. BMC urology. 2023 Jun 3;23(1):100.*
22. *Tiger S, Shpunt I, Beberashvili I, Avda Y, Smolyakov V, Lerman D, Goldshtein G, Shahabri W, Rubinshtein D, Jaber M, Croock R. Influence of Prostate Volume on Targeted Biopsy Outcomes and PI-RADS Predictive Value for Significant Prostate Cancer. Journal of Clinical Medicine. 2025 Jan;14(23):8476.*
23. *Merriel SW, Pocock L, Gilbert E, Creavin S, Walter FM, Spencer A, Hamilton W. Systematic review and meta-analysis of the diagnostic accuracy of prostate-specific antigen (PSA) for the detection of prostate cancer in symptomatic patients. BMC medicine. 2022 Feb 7;20(1):54.*
24. *Saema A, Kochakarn W, Lertsithichai P. PSA density and prostate cancer detection. Journal of the Medical Association of Thailand. 2012 Aug 5;95(5):661.*
25. *Khalid SY, Waraich TA, Elamin A. Evaluating the Diagnostic Accuracy of MRI-Derived Prostate-Specific Antigen (PSA) Density in Prostate Cancer Detection and its Association With Tumor Aggressiveness. Cureus. 2024 Nov 24;16(11).*

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ORIGINAL ARTICLE

Predictors of Functional Recovery after Arthroscopic Anterior Cruciate Ligament Reconstruction

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ABSTRACT

Background: *Arthroscopic anterior cruciate ligament reconstruction (ACLR) is a standard procedure to restore knee stability and function after ACL rupture. Functional recovery is influenced by multiple surgical, physiological, and psychosocial factors, yet predictors of optimal outcomes remain incompletely defined.* ***Aim of the study:*** *To identify clinical, surgical, and psychosocial predictors of excellent functional recovery following arthroscopic ACL reconstruction.* ***Methods & Materials:*** *A prospective observational study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, from September 2022 to March 2025. Forty-four patients with isolated ACL tears were enrolled and categorized into early (<3 weeks) and delayed (>3 weeks) surgery groups. All patients underwent standardized arthroscopic ACLR and rehabilitation. Functional outcomes were evaluated using Lysholm and Tegner scores and range of motion (ROM). Predictor variables included BMI, smoking, graft diameter, rehabilitation compliance, quadriceps strength, psychological readiness, prehabilitation, and time to return to sport. Data were analyzed using SPSS version 26, including descriptive statistics, chi-square tests, t-tests, univariate analysis, and multivariable logistic regression to identify independent predictors of excellent functional recovery.* ***Result:*** *The overall rate of excellent functional recovery was 56.8%. Multivariable analysis revealed that good rehabilitation compliance (OR 4.56, p<0.001), graft diameter ≥7.5 mm (OR 3.84, p=0.002), quadriceps strength ≥80% (OR 3.78, p=0.004), high psychological readiness (OR 4.01, p=0.001), non-smoking status (OR 3.42, p=0.003), and prehabilitation (OR 2.96, p=0.012) were significant independent predictors. Early surgery showed a positive trend but did not reach statistical significance (OR 2.14, p=0.069). Postoperative complications were minimal and comparable between groups.* ***Conclusion:*** *Functional recovery after ACLR is multifactorial, with rehabilitation adherence, graft size, quadriceps strength, psychological readiness, smoking status, and prehabilitation being key predictors of excellent outcomes. Integrating structured rehabilitation, preoperative conditioning, and psychological support is essential to optimize recovery, facilitate return to activity, and maintain long-term knee stability.*

Keywords: *ACLR, functional recovery, rehabilitation compliance, psychological readiness, quadriceps strength, SPSS, predictive factors, graft diameter*

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INTRODUCTION

Arthroscopic anterior cruciate ligament reconstruction is a minimally invasive surgical procedure that uses an arthroscope to repair a torn ACL by replacing it with a graft to restore knee stability and function [1]. Globally, the single-bundle technique is used in about 90% of anterior cruciate ligament reconstructions (ACLR), with hamstring tendon autografts preferred in approximately 53% of cases [2]. In Bangladesh, ACLR is predominantly performed in young males, with about 90% of patients being male and the majority aged between 20 and 35 years [3]. Risk factors for poorer functional recovery after ACLR include female gender and longer time from injury to surgery, both significantly increasing the risk of decreased knee function [4]. Older age, poor preoperative quadriceps strength, and residual postoperative pain are linked to worse quadriceps muscle strength recovery at one-year post-ACLR [5]. Higher body mass index, smoking, meniscal procedures, revision ACLR, and severe cartilage damage also predict inferior long-term outcomes and lower activity levels [6]. Poor functional performance at one year, especially failing to achieve ≥90% limb symmetry on hop tests, is associated with increased risk of early osteoarthritis progression [7]. Psychological factors such as fear of reinjury correlate with lower functional performance and a higher risk of second ACL injury after return to sport [8]. Early initiation of physical therapy (within

two weeks post-surgery) significantly improves functional recovery, proprioception, quadriceps strength, and knee range of motion after ACL reconstruction without increasing graft failure risk [9]. Complex decongestive therapy (CDT) effectively reduces limb swelling and pain in the early postoperative period and enhances joint functional recovery by a few days after surgery [10]. Accelerated rehabilitation protocols emphasizing early weight bearing, open kinetic chain exercises, neuromuscular electrical stimulation, and psychological readiness assessment have shown benefits in improving surgical outcomes and return-to-sport rates [11]. Stump-preserving arthroscopic ACL reconstruction combined with structured exercise rehabilitation not only reduces postoperative pain and swelling but also significantly enhances knee joint mobility, proprioception, and overall functional stability, leading to faster recovery, improved muscle strength, and a lower risk of long-term complications compared to stump-eliminating techniques [12]. Graft choice, whether hamstring or bone–patellar tendon–bone, does not appear to significantly influence early postoperative pain levels or knee range of motion; however, patients receiving hamstring grafts may experience a slightly faster recovery timeline, potentially allowing an earlier return to sports, work, and daily activities, likely due to reduced donor-site morbidity and quicker restoration of muscle strength. [13]. Overall, individualized, early, and closely supervised rehabilitation protocols that integrate physical conditioning, neuromuscular training, and psychological support are crucial for optimizing functional recovery after ACL reconstruction, as they enhance joint stability, improve muscle strength and coordination, reduce the risk of reinjury, and support a safe and timely return to sports, work, and daily activities[14]. The study aimed to identify the key predictors that influence functional recovery following arthroscopic anterior cruciate ligament reconstruction.

METHODS & MATERIALS

This was a hospital-based prospective observational analytical study conducted in the Department of Orthopedics Surgery, Bangabandhu Sheikh Mujib Medical University (BMU), Shahbagh, Dhaka, from September 2022 to March 2025. The study aimed to identify clinical, surgical, and psychosocial predictors of functional recovery after arthroscopic anterior cruciate ligament (ACL) reconstruction. A total of 44 patients with isolated ACL rupture presenting to the outpatient department during the study period were enrolled using a purposive sampling technique. Patients were allocated into two groups based on timing of surgery after injury:

- Group A (Early Surgery, n = 22): Operated within 3 weeks of injury
- Group B (Delayed Surgery, n = 22): Operated after 3 weeks of injury

This grouping enabled comparison of early versus delayed intervention in relation to postoperative recovery.

Inclusion Criteria:

- Age between 20 and 45 years
- Clinically and radiologically confirmed ACL tear (MRI)
- Underwent primary arthroscopic ACL reconstruction

Exclusion Criteria:

- Chronic ACL injury (>1 year)
- Multi-ligament knee injury
- Meniscal or chondral injury requiring intervention
- Fractures involving femoral condyle, tibial plateau, or patella
- Previous surgery on the affected knee
- Diagnosed knee osteoarthritis
- Knee infection, joint stiffness from acute injury, or sepsis
- Medically unfit for anesthesia or surgery

Ethical Considerations

Ethical clearance was obtained from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BMU). Written informed consent was obtained from all participants. Confidentiality and data security were maintained throughout the study period.

Surgical Technique

All patients underwent arthroscopic ACL reconstruction performed by experienced orthopedic surgeons under spinal or general anesthesia. Standard anterolateral and anteromedial portals were used. The grafts were prepared and inserted using routine anatomical tunnel placement techniques. Graft diameter was recorded intraoperatively. Postoperative fixation was done using standard fixation devices as per institutional protocol. All surgeries followed a uniform technique to minimize operator bias.

Postoperative Rehabilitation Protocol

A standardized rehabilitation protocol was followed by all patients. The protocol included early mobilization, quadriceps strengthening, progressive range-of-motion exercises, and later-stage return-to-activity training. Rehabilitation compliance was monitored and categorized as:

- Good: ≥80% adherence
- Poor: <80% adherence

Prehabilitation status (preoperative physiotherapy), psychological readiness, and compliance with exercises were explicitly recorded.

Data Collection

Data were systematically collected using a structured case record form. Sociodemographic characteristics, including age, gender, and body mass index (BMI), as well as clinical profiles such as mode of injury, duration of injury, and the side affected, were recorded for all participants. Operative details, particularly graft diameter, were documented intraoperatively. Preoperative and postoperative knee stability was assessed using the Anterior Drawer Test and Lachman Test. Functional outcomes were evaluated using the Lysholm knee scoring system, Tegner activity scale, and final knee range of motion (ROM) measured with a goniometer. Additionally, potential predictor variables for functional recovery were assessed, including BMI category, smoking habit, graft diameter (≥7.5 mm vs <7.5 mm), timing of surgery (early vs delayed), rehabilitation compliance, quadriceps muscle strength (≥80% vs <80%), psychological readiness, prehabilitation status, and time to return to sport (≤7 months vs >7 months). The primary outcome measure was functional recovery, classified based on the final Lysholm score as Excellent (≥91), Good (84–90), Fair (65–83), or Poor (<65). For the purposes of regression analysis, outcomes were dichotomized into Excellent recovery and others (Good, Fair, Poor combined).

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Statistical Analysis

All statistical analyses were performed using SPSS version 26. Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Group comparisons were conducted using the independent samples t-test for continuous variables and the chi-square test for categorical variables. To identify factors associated with excellent functional recovery, univariate analysis was first performed for each potential predictor variable. Variables showing a p-value <0.05 in univariate analysis were subsequently included in a multivariable logistic regression model to determine independent predictors. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and a p-value ≤0.05 was considered statistically significant.

RESULT

Table – I: Baseline characteristics of the study population (*n* = 44)

Variable	Group A (n = 22), n (%)	Group B (n = 22), n (%)	Total (N = 44), n (%)	P-value
Age Group (years)				
20 – 30	11 (50.00)	13 (59.09)	24 (54.55)	0.598
31 – 40	10 (45.45)	7 (31.82)	17 (38.64)	
41 – 45	1 (4.55)	2 (9.09)	3 (6.82)	
Mean ± SD	30.14 ± 5.89	29.41 ± 7.02	29.41 ± 6.41	0.549
Gender				
Male	18 (81.82)	20 (90.91)	38 (86.36)	0.38
Female	4 (18.18)	2 (9.09)	6 (13.64)	
Side Involved				
Right	15 (68.18)	12 (54.55)	27 (61.36)	0.353
Left	7 (31.82)	10 (45.45)	17 (38.64)	
BMI Category				
Normal (18.5–24.9)	17 (77.27)	18 (81.82)	35 (79.55)	0.466
Overweight (25–29.9)	5 (22.73)	3 (13.64)	8 (18.18)	
Obese (≥30)	0 (0.00)	1 (4.55)	1 (2.27)	
Mean ±SD	23.95 ±2.22	23.98 ±2.27	23.96 ±2.21	0.972
Mechanism of Injury				
Sports	10 (45.45)	11 (50.00)	21 (47.73)	0.679
Road traffic accident	8 (36.36)	9 (40.91)	17 (38.64)	
Domestic accident	4 (18.18)	2 (9.09)	6 (13.64)	

Table – II: Operative and clinical variables (*n* = 44)

Variable	Group A (n = 22), n (%)	Group B (n = 22), n (%)	P-value
Duration of injury (days)	13.32 ± 3.37	106.00 ± 56.20	0.001
Graft diameter (mm)	7.4 ± 0.5	7.5 ± 0.4	0.468
Anterior Drawer Test (Pre-op)			
Grade II	7 (31.82)	5 (22.73)	0.498
Grade III	15 (68.18)	17 (77.27)	
Anterior Drawer Test (Post-op)			
Grade 0	20 (90.91)	19 (86.36)	0.635
Grade I	2 (9.09)	3 (13.64)	
Lachman Test (Pre-op)			
Grade II	5 (22.73)	3 (13.64)	0.434
Grade III	17 (77.27)	19 (86.36)	
Lachman Test (Post-op)			
Grade 0	19 (86.36)	18 (81.82)	0.68
Grade I	3 (13.64)	4 (18.18)	

Table – III: Functional outcome scores among respondents

Parameter	Group A (n = 22), Mean ±SD	Group B (n = 22), Mean ±SD	P-value
Lysholm (Pre-op)	54.32 ± 6.76	56.59 ± 5.11	0.148
Lysholm (Final)	90.14 ± 3.82	88.59 ± 4.19	0.241
Tegner (Pre-op)	6.41 ± 1.20	6.86 ± 1.21	0.192
Tegner (Final)	5.91 ± 1.02	5.86 ± 0.71	0.841
Final ROM (degree)	134.77 ± 3.27	134.09 ± 2.94	0.481

Table – IV: Final postoperative outcome of the study (*n* = 44)

Variable	Group A (n = 22), n (%)	Group B (n = 22), n (%)	Total (N = 44), n (%)	P-value
Functional Category				
Excellent (≥91)	14 (63.64)	11 (50.00)	25 (56.82)	0.624
Good (84–90)	7 (31.82)	9 (40.91)	16 (36.36)	
Fair (65–83)	1 (4.55)	2 (9.09)	3 (6.82)	
Poor (<65)	0	0	0	

Complication				
Paresthesia	3 (13.64)	4 (18.18)	7 (15.91)	0.982
Superficial infection	1 (4.55)	1 (4.55)	2 (4.55)	
Knee stiffness	1 (4.55)	1 (4.55)	2 (4.55)	
None	17 (77.27)	16 (72.73)	33 (75.00)	

Table – V: Distribution of predictor variables (*n* = 44)

Predictor	Frequency (n)	Percentage (%)
Rehabilitation compliance		
Good	29	65.91
Poor	15	34.09
Smoking habit		
Smoker	12	27.27
Non-smoker	32	72.73
Quadriceps strength		
≥80%	27	61.36
<80%	17	38.64
Psychological readiness		
High	31	70.45
Low	13	29.55
Prehabilitation		
Yes	26	59.09
No	18	40.91
Return to sport		
≤7 months	24	54.55
>7 months	20	45.45

Table – VI: Univariate analysis of predictors of excellent functional recovery

Variable	Excellent	Others	P-value
Normal BMI	23	12	0.004
Early surgery	15	10	0.018
Graft ≥7.5 mm	18	6	0.002
Non-smoker	23	9	<0.001
Good rehabilitation	21	8	<0.001
Quadriceps ≥80%	20	7	0.002
Psychological readiness	22	9	<0.001
Prehabilitation	19	7	0.003
Return ≤7 months	18	6	0.001

Table – VII: Multivariable logistic regression analysis

Predictor	Adjusted OR	95% CI	P-value
Graft ≥7.5 mm	3.84	1.62–9.12	0.002
Good rehabilitation	4.56	2.01–10.36	<0.001
Psychological readiness	4.01	1.71–9.43	0.001
Non-smoker	3.42	1.38–8.47	0.003
Quadriceps strength ≥80%	3.78	1.50–9.51	0.004
Prehabilitation	2.96	1.22–7.21	0.012
Early surgery	2.14	0.94–4.88	0.069

DISCUSSION

This study highlights key clinical, surgical, and rehabilitation-related predictors that shape functional recovery following arthroscopic anterior cruciate ligament reconstruction [15]. Most patients were males aged 20–30 years (54.6%; mean age comparable, p=0.549), with right-sided injuries (61.4%), normal BMI (79.6%), and injuries primarily from sports (47.7%) or road traffic accidents (38.6%). Mlv et al. reported a mean age of 27.97 years in their study. Males predominated (91.1%), whereas females accounted for 8.9%. Road traffic accidents (RTA) were the leading cause of injury (47.6%), followed by sports-related injuries (39.5%) [16]. Prentice et al. stated that the majority of participants had a BMI <25 kg/m^2 (58.7%, 56.4%, and 62.5% in Luxembourg, Norway, and Sweden, respectively), with overweight (25–29 kg/m^2) accounting for 31.4–33.7% and obesity (≥30 kg/m^2) ranging from 6.2% to 10.1%. Right-sided injuries were slightly more frequent than left (50.9–55.3% vs 44.7–49.1%). Winter sports were the leading mechanism of injury (14.0–17.4%), while motorsport/motor vehicle (1.0–4.4%) and work-related injuries (1.7–3.1%) were less common; other causes accounted for 4.8–9.2% [17]. Group A underwent significantly earlier surgery (13.32 ± 3.37 vs 106.00 ± 56.20 days; p = 0.001), with preoperative Grade II–III anterior drawer and Lachman instability improving postoperatively to Grade 0 in over 85% of patients in both groups. Reijman et al. reported a mean score of 88.8 for the early group and 84.5 for the delayed group at 9 months follow-up [18]. In another study, Rahman et al. reported that 90% and 96.67% of patients undergoing ACL reconstruction with autologous hamstring grafts had negative Lachman and anterior drawer tests, respectively [19]. Final outcomes were comparable between groups, with high Lysholm scores (90.14 ± 3.82 vs. 88.59 ± 4.19; p = 0.241), similar Tegner scores (p = 0.841), and

a nearly identical mean range of motion of 134°. Hur et al. reported mean Tegner scores of 6.0 ± 1.6 in the early group and 5.6 ± 1.5 in the delayed group, with mean range of motion of 138.6 ± 4.1° and 138.8 ± 5.6°, respectively [20]. Most patients had excellent (56.8%) or good (36.4%) outcomes, with fair (6.8%) and no poor recoveries; complications were minimal, mainly paresthesia (15.9%) and occasional infection or stiffness (4.6% each). A systematic review and meta-analysis by Ferguson et al. and Shen et al. concluded that there is currently no definitive evidence favoring early versus delayed anterior cruciate ligament reconstruction in terms of knee stability, range of motion, complications, or functional outcomes [21-22]. Good rehabilitation compliance (65.9%) and prehabilitation (59.1%) were independent predictors of excellent functional outcomes. Giesche et al. stated that preoperative neuromuscular training (prehabilitation) was associated with improved self-reported knee function and higher postoperative return-to-sport rates [23]. Jiang et al. stated that restoration of quadriceps strength after ACL reconstruction is often associated with enhanced functional performance and improved graft and patient outcomes [24]. In this study, 70.45% of patients demonstrated high psychological readiness, where Everhart et al. highlighted self-efficacy, motivation, and expectations as key determinants of ACLR success, rehabilitation compliance, and return to sport [25]. Normal BMI, early surgery, larger grafts, non-smoking, good rehab compliance, strong quadriceps, high psychological readiness, prehab, and return to sport ≤7 months were all linked to excellent outcomes. Galea et al. reported non-smokers were more likely than smokers to achieve superior functional outcomes after ACL reconstruction and limited or inconsistent advantages of early versus delayed ACL reconstruction regarding long-term functional outcomes and graft failure [26]. Hsu et al. stated that higher BMI was associated with reduced quadriceps symmetry index after ACL reconstruction [27]. Good rehab (AOR 4.56), psychological readiness (AOR 4.01), graft ≥7.5 mm (AOR 3.84), non-smoking (AOR 3.42), quadriceps ≥80% (AOR 3.78), and prehab (AOR 2.96) were significant predictors ($p < 0.05$), with early surgery showing a non-significant positive trend (AOR 2.14). Carter et al. stated that preoperative exercises (prehab) may enhance quadriceps strength and early postoperative function (hop tests, knee scores), though evidence remains limited and heterogeneous [28].

Limitations of the study: The present study has several limitations. The sample size was relatively small (n = 44), limiting the statistical power and generalizability of the findings. Being a single-center study, results may not reflect outcomes in other institutions with different surgical expertise or rehabilitation protocols. The follow-up period was limited, restricting assessment of long-term functional outcomes and risk of reinjury or osteoarthritis. Additionally, some variables, such as psychological readiness and rehabilitation compliance, relied on self-reporting, introducing potential bias.

CONCLUSION

This study highlights that functional recovery after arthroscopic anterior cruciate ligament reconstruction is influenced by a combination of surgical, physiological, and psychosocial factors. Multivariable analysis identified good rehabilitation compliance, adequate graft diameter (≥7.5 mm), strong preoperative quadriceps strength (≥80%), high psychological readiness, non-smoking status, and prehabilitation participation as independent predictors of excellent postoperative outcomes. Early surgery demonstrated a favorable trend but did not reach statistical significance. These findings underscore the importance of a comprehensive, patient-centered approach that integrates optimal surgical technique, structured and supervised rehabilitation, preoperative conditioning, and psychological support. Implementing such strategies can maximize functional recovery, facilitate timely return to sport or daily activities, and improve long-term knee joint stability.

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REFERENCES

1. *Gurucharan S, Sonth S, Sekar S, Vyasa K, Parameshwar A, Rajaneesh B. Impact of surgery timing on functional outcomes in arthroscopic anterior cruciate ligament reconstruction. Res J Med Sci. 2025;:1–6. doi:10.36478/makrjms.2025.1.551.556.*
2. *Sherman SL, Calcei J, Ray T, Magnussen RA, Musahl V, Kaeding CC, Clatworthy M, Bergfeld JA, Arnold MP. ACL Study Group presents the global trends in ACL reconstruction: biennial survey of the ACL Study Group. Journal of ISAKOS. 2021 Nov 1;6(6):322-8.*
3. *Hossain MS, Chowdhury AZ, Mahmud CI, Hossain S, Alam MS. Analysis of Surgical Complications and Functional Recovery Following Arthroscopic ACL Reconstruction with Quadriceps Tendon. Sch J App Med Sci. 2024 Nov;11:1544-9.*
4. *Kurniawati I, Witari NP, Dewi AA, Kerans FF, Sumadewi KT, Astini DA, Evayanti LG. Female gender and time from injury to surgery as risk factors for decreased knee functions in ACL injury survivors. Physical Therapy Journal of Indonesia. 2025 Jun 5;6(1):88-91.*
5. *Hasegawa, S., Nakagawa, Y., Yoshihara, A., Nakamura, T., Katagiri, H., Hayashi, M., Yoshimura, H., Nagase, T., Sekiya, I. and Koga, H., 2023. Older age, poor preoperative quadriceps muscle strength, and residual pain as risk factors for poor quadriceps muscle strength recovery at 1 Year after ACL reconstruction: a TMDU MAKS study of 402 patients. Orthopaedic Journal of Sports Medicine, 11(9), p.23259671231194593.*
6. *MOON Knee Group. 10 year outcomes and risk factors after ACL reconstruction: a MOON longitudinal prospective cohort study. The American journal of sports medicine. 2018 Mar;46(4):815.*
7. *Patterson B, Culvenor AG, Barton CJ, Guermazi A, Stefanik J, Morris HG, Whitehead TS, Crossley KM. Poor functional performance 1 year after ACL reconstruction increases the risk of early osteoarthritis progression. British Journal of Sports Medicine. 2020 May 1;54(9):546-55.*
8. *Paterno MV, Flynn K, Thomas S, Schmitt LC. Self-reported fear predicts functional performance and second ACL injury after ACL reconstruction and return to sport: a pilot study. Sports health. 2018 May;10(3):228-33.*
9. *Alqahtani TA, Kardm SM, Alnakhli HH, Alyazedi FM, Kandakurti PK, Reddy RS. Impact of early vs. delayed physical therapy on functional recovery, proprioception, and return to sport after anterior cruciate ligament (ACL) reconstruction: a cross-sectional study. Journal of Orthopaedic Surgery and Research. 2025 Jul 12;20(1):644.*
10. *Ren Y, Ge R, Yang C, Tan Y, Song H, Liu R, Huang M, Niu Z, Yang L, Liu W. Efficacy of complex decongestive therapy in managing limb swelling, pain, and enhancing functional recovery after arthroscopic reconstruction of anterior cruciate ligament. Applied Nursing Research. 2025 Apr 1;82:151915.*
11. *Jenkins SM, Guzman A, Gardner BB, Bryant SA, Del Sol SR, McGahan P, Chen J. Rehabilitation after anterior cruciate ligament injury: review of current literature and recommendations. Current reviews in musculoskeletal medicine. 2022 Jun;15(3):170-9.*
12. *Li S, Tang S, Zhu B, Zhong Y, Ren X. Effect of stump-preserving arthroscopic reconstruction or stump-eliminating arthroscopic reconstruction combined with exercise rehabilitation therapy on knee functional recovery in patients with anterior cruciate ligament injuries. The Annals of The Royal College of Surgeons of England. 2025 Jul 30.*
13. *AbuMahara S, Rujbani H, Elmahdi K, Elhammal N, Abdulwaret M, Shagloub N. Early Functional Recovery and Range of Motion After*

ACL Reconstruction: A Prospective Study Comparing Bone-Patellar Tendon-Bone vs. Hamstring Autografts. AlQalam Journal of Medical and Applied Sciences. 2025 Aug 3:1592-5.

14. *Glattke KE, Tummala SV, Chhabra A. Anterior cruciate ligament reconstruction recovery and rehabilitation: a systematic review. JBJS. 2022 Apr 20;104(8):739-54.*
15. *Della Villa F, Ricci M, Perdisa F, Filardo G, Gamberini J, Caminati D, Della Villa S. Anterior cruciate ligament reconstruction and rehabilitation: predictors of functional outcome. Joints. 2015 Oct;3(04):179-85.*
16. *Mlv SK, Mahmood A, Vatsya P, Garika SS, Mittal R, Nagar M. Demographic characteristics of patients who underwent anterior cruciate ligament reconstruction at a tertiary care hospital in India. World Journal of Clinical Cases. 2023 May 26;11(15):3464.*
17. *Prentice HA, Lind M, Mouton C, Persson A, Magnusson H, Gabr A, Seil R, Engebretsen L, Samuelsson K, Karlsson J, Forssblad M. Patient demographic and surgical characteristics in anterior cruciate ligament reconstruction: a description of registries from six countries. British journal of sports medicine. 2018 Jun 1;52(11):716-22.*
18. *Reijman, M., Eggerding, V., van Es, E., van Arkel, E., van den Brand, I., van Linge, J., Zijl, J., Waarsing, E., Bierma-Zeinstra, S. and Meuffels, D., 2021. Early surgical reconstruction versus rehabilitation with elective delayed reconstruction for patients with anterior cruciate ligament rupture: COMPARE randomised controlled trial. Bmj, 372.*
19. *Rahman, M.M., Hossen, M., Iqbal, C., Mahmud, A.T.M., Ahmed, A.F.U. and Rahman, T., 2021. Evaluation of the results of arthroscopic anterior cruciate ligament reconstruction with quadruple strand hamstring autograft fixed by biodegradable screws. International Journal of Orthopaedics, 7(1), pp.746-750.*
20. *Hur, C.I., Song, E.K., Kim, S.K., Lee, S.H. and Seon, J.K., 2017. Early anterior cruciate ligament reconstruction can save meniscus without any complications. Indian Journal of Orthopaedics, 51, pp.168-173.*
21. *Ferguson, D., Palmer, A., Khan, S., Oduoza, U. and Atkinson, H., 2019. Early or delayed anterior cruciate ligament reconstruction: Is one superior? A systematic review and meta-analysis. European Journal of Orthopaedic Surgery & Traumatology, 29, pp.1277-1289.*
22. *Shen, X., Liu, T., Xu, S., Chen, B., Tang, X., Xiao, J. and Qin, Y., 2022. Optimal timing of anterior cruciate ligament reconstruction in patients with anterior cruciate ligament tear: a systematic review and meta-analysis. JAMA Network Open, 5(11), pp.e2242742-e2242742.*
23. *Giesche F, Niederer D, Banzer W, Vogt L. Evidence for the effects of prehabilitation before ACL-reconstruction on return to sport-related and self-reported knee function: A systematic review. PloS one. 2020 Oct 28;15(10):e0240192.*
24. *Jiang H, Zhang L, Zhang RY, Zheng QJ, Li MY. Comparison of hamstring and quadriceps strength after anatomical versus non-anatomical anterior cruciate ligament reconstruction: a retrospective cohort study. BMC musculoskeletal disorders. 2021 May 18;22(1):452.*
25. *Everhart JS, Best TM, Flanigan DC. Psychological predictors of anterior cruciate ligament reconstruction outcomes: a systematic review. Knee Surgery, Sports Traumatology, Arthroscopy. 2015 Mar;23(3):752-62.*
26. *Galea-O'Neill RJ, Bruder AM, Goulis J, Shields N. Modifiable factors and their association with self-reported knee function and activity after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Physiotherapy Theory and Practice. 2021 Aug 3;37(8):881-94.*
27. *Hsu WH, Fan CH, Yu PA, Chen CL, Kuo LT, Hsu RW. Effect of high body mass index on knee muscle strength and function after anterior cruciate ligament reconstruction using hamstring tendon autografts. BMC Musculoskeletal Disorders. 2018 Oct 10;19(1):363.*
28. *Carter HM, Littlewood C, Webster KE, Smith BE. The effectiveness of preoperative rehabilitation programmes on postoperative outcomes following anterior cruciate ligament (ACL) reconstruction: a systematic review. BMC musculoskeletal disorders. 2020 Oct 3;21(1):647.*

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ORIGINAL ARTICLE

Radiological Outcomes of Mini-Plate versus K-Wire Fixation in Metacarpal Shaft Fractures

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ABSTRACT

Background: *Metacarpal shaft fractures are common hand injuries, and optimal fixation remains controversial. Mini-plate and Kirschner wire (K-wire) fixation are widely employed, yet comparative radiological outcomes are sparsely reported.* ***Aim of the study:*** *To prospectively compare radiological healing, alignment, and complication rates between mini-plate and K-wire fixation in patients with metacarpal shaft fractures.* ***Methods:*** *This prospective comparative study was conducted at the Department of Orthopaedic Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, from January 2023 to March 2025. A total of 28 adult patients (age 18–50 years) with closed metacarpal shaft fractures were enrolled and assigned to either mini-plate (n = 14) or K-wire fixation (n = 14). Standardized surgical techniques and postoperative protocols were applied. Radiological assessments included time to union, angular and rotational alignment, malunion, and implant-related complications. Data were analyzed using appropriate statistical tests, with $p < 0.05$ considered significant.* ***Result:*** *The mini-plate group demonstrated a significantly shorter mean time to union (7.86 ± 1.03 weeks) compared to the K-wire group (8.14 ± 1.66 weeks, p = 0.044). Early union (≤8 weeks) was achieved in 100% of mini-plate cases versus 78.6% in K-wire cases (p = 0.048). Angular deformity was lower in the mini-plate group (1.9° ± 1.2° vs. 3.8° ± 2.1°, p = 0.032). Malunion, loss of reduction, and non-union occurred exclusively in the K-wire group, although the overall complication rate difference (14.3% vs. 42.9%) did not reach statistical significance (p = 0.094).* ***Conclusion:*** *Mini-plate fixation offers superior radiological outcomes, including faster union and better angular alignment, with fewer complications compared to K-wire fixation in metacarpal shaft fractures. These findings support the use of rigid internal fixation with mini-plates for enhanced mechanical stability and predictable radiological healing.*

Keywords: *Metacarpal shaft fracture, Mini-plate fixation, K-wire fixation, Radiological outcomes, Malunion, Bony union*

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INTRODUCTION

Metacarpal shaft fractures are breaks occurring along the long, central part (shaft) of the metacarpal bones, which are the five bones in the hand connecting the wrist to the fingers [1]. Worldwide, metacarpal fractures make up roughly 18–44% of all hand fractures, and among those treated surgically, a substantial majority are fixed using plates (like mini-plates) [2]. In Bangladesh, roughly 65.5% of surgically treated metacarpal fractures are fixed with mini-plates (versus ~31% with K-wires) [3]. Proper fixation is essential for metacarpal shaft fractures to correct displacement, angulation, or rotational deformities and restore hand function [4]. Surgical fixation options commonly used include Kirschner wires (K-wires), plates and screws (locking or nonlocking), intramedullary headless compression screws, and absorbable implants [5]. Mini-plate fixation theoretically offers superior biomechanical stability, providing rigid fixation that supports early mobilization without prolonged splinting and reduces the risk of rotational deformity compared to K-wires. Plates, especially locking plates, have higher tensile strength and stiffness than K-wires, resulting in better grip strength, range of motion, and lower rates of rotational deformity and reoperation [6]. Unicortical plate fixation minimizes soft tissue damage by avoiding excessive drilling into the volar cortex, potentially reducing complications related to screw placement [7]. K-wire fixation offers advantages such as shorter operative time and fewer hardware-related complications compared to other fixation methods, making it a viable option in certain cases. However, it has limitations, including a higher rate of malunion and potential for fixation failure due to lower biomechanical stability compared to plates or screws [8]. The biomechanical strength of K-wire fixation can be improved by

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techniques such as adding a figure-of-eight cerclage wire, which significantly increases fixation stiffness and maximum fracture force [9]. Radiological assessment is crucial in evaluating treatment success as it allows for monitoring fracture alignment, detecting malunion or nonunion, and assessing implant position and stability, which are essential for guiding postoperative management and ensuring optimal functional outcomes. Regular imaging helps identify complications early and confirms that the fracture is healing appropriately, supporting timely intervention if needed [10]. Uncertainties in comparing K-wire and plate fixation mainly arise from inconsistent findings and limited high-quality comparative studies, especially regarding long-term radiological outcomes and specific patient subgroups [11]. Some meta-analyses show slight functional advantages for volar locking plates, but without clinically significant differences in DASH scores or wrist motion, and no clear superiority in radiographic parameters like volar tilt or radial inclination [12]. However, plate fixation tends to yield better radiological alignment and lower malunion rates, particularly in complex or osteoporotic fractures, while K-wires remain suitable for simpler fractures. There is a notable gap in standardized, long-term radiological assessments comparing how well each method restores and maintains bone anatomy, which is critical for predicting functional outcomes. Direct comparison of radiological outcomes is necessary to determine which fixation method better preserves anatomical alignment, reduces malunion, and supports optimal wrist biomechanics, thereby guiding treatment choice [13]. This study aimed to compare radiological outcomes of mini-plate fixation versus K-wire fixation in metacarpal shaft fractures, to determine which method provides superior bone healing and alignment.

METHODS & MATERIALS

This prospective comparative study was conducted in the Department of Orthopaedic Surgery at Bangabandhu Sheikh Mujib Medical University (BMU), Shahbag, Dhaka, over a 27-month period from January 2023 to March 2025. A total of 28 patients with metacarpal shaft fractures were enrolled after applying predefined inclusion and exclusion criteria. Eligible participants were allocated into two groups based on the fixation technique used: Mini-Plate fixation (n = 14) and K-Wire fixation (n = 14).

Inclusion & Exclusion Criteria

Inclusion Criteria

- Adults aged 18–50 years
- Closed, radiologically confirmed metacarpal shaft fracture
- Duration of injury < 7 days
- Fit for anaesthesia and surgical intervention

Exclusion Criteria

- Pathological fractures
- Associated fractures of the hand (multiple phalangeal or carpal injuries)
- Open fractures
- Concomitant head injury or polytrauma
- Patients unwilling to participate or follow up

Surgical Techniques

All operative procedures were performed by fellowship-trained orthopaedic hand surgeons under standard aseptic conditions.

In the **Mini-Plate group**, open reduction and internal fixation were achieved through a dorsal longitudinal incision over the involved metacarpal. The extensor apparatus was gently retracted, ensuring minimal soft-tissue disruption to preserve vascular supply. Anatomical reduction was obtained under direct visualization and stabilized using a 1.5–2.0 mm titanium mini-plate fixed with cortical screws. Optimal plate position, screw length, and fracture alignment were confirmed using intraoperative fluoroscopy. Stability was re-assessed through controlled passive motion of the involved digit before closure.

In the **K-Wire group**, fractures were managed with closed or mini-open reduction followed by percutaneous fixation using 1.6–2.0 mm Kirschner wires. Antegrade or retrograde techniques were selected based on fracture configuration and surgeon preference. Wires were cut and bent externally to facilitate removal. Fluoroscopy was used to verify fracture alignment, rotational control, wire trajectory, and stability.

All patients were immobilized in a forearm-based dorsal splint for 2–3 weeks, after which graded active mobilization was initiated. K-wires were removed at 4–6 weeks, depending on radiographic evidence of callus formation.

Data Collection

Data were collected prospectively using a standardized case record form. Baseline information included demographic characteristics, mechanism of injury, fracture pattern, number of involved metacarpals, and preoperative radiographs. Operative details such as type of fixation, duration of surgery, intraoperative reduction quality, and postoperative immobilization were documented for every patient. Radiographs (posteroanterior, oblique, and lateral views) were obtained immediately after surgery and during follow-up visits at 2 weeks, 6 weeks, and 12 weeks, and subsequently until union was achieved. Radiological assessments included time to union, cortical bridging, angular deformity, rotational malalignment, and any loss of reduction. Complications such as malunion, non-union, implant failure, and pin-tract infection (for the K-wire group) were also recorded. All radiographic measurements were independently evaluated by two blinded orthopaedic surgeons to reduce observer bias. Clinical and radiological data were compiled and verified before statistical analysis.

Statistical Analysis

Data were analyzed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the Independent Samples t-test or Mann–Whitney U test based on normality assumptions. Categorical data were presented as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test where appropriate. Relative risk (RR) with 95% confidence intervals (CI) was calculated for radiological complications and malalignment outcomes. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study adhered to the ethical principles outlined in the Declaration of Helsinki (1964) and its subsequent amendments. Written informed consent was obtained from each patient prior to enrollment. Confidentiality of patient data was ensured throughout the study, with secure storage and restricted access. The study protocol received approval from the Academic Committee of the Department of Orthopaedic Surgery and subsequently obtained Institutional Review Board (IRB) clearance from BMU, Dhaka.

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RESULT

In the K-wire group, 42.86% were aged 20–30 years, 50.00% were 31–40 years, and 7.14% were 41–50 years. In comparison, the Mini-plate group showed 35.71%, 50.00%, and 14.29% across these age categories, respectively, with no significant difference (p=0.809). Male predominance was observed in both groups (78.57% in K-wire vs. 85.71% in Mini-plate, p=0.622). The involved limb was right-sided in 78.57% of K-wire cases and 64.29% of Mini-plate cases. Single metacarpal fractures were slightly more common in the K-wire group (78.57%) than the Mini-plate group (71.43%). Fracture patterns also showed no major differences, with transverse fractures accounting for 42.86% vs. 57.14%, oblique fractures 35.71% vs. 14.29%, and spiral fractures 14.29% vs. 28.57% in the K-wire and Mini-plate groups, respectively (Table 1). Mean union time was 7.86±1.03 weeks in the Mini-plate group versus 8.14±1.66 weeks in the K-wire group (p=0.044). Early union (≤6 weeks) occurred in 57.14% (8/14) of Mini-plate cases compared to only 21.43% (3/14) of K-wire cases (p=0.035). All Mini-plate cases (14/14; 100%) achieved union within 8 weeks, whereas only 78.57% (11/14) of K-wire cases did so (p=0.048). Notably, 21.43% (3/14) of K-wire patients required 10–12 weeks for union (Table 2). Malalignment >5° was absent in the Mini-plate group but present in 14.29% (2/14) of K-wire cases. Angular deformity was significantly lower with Mini-plates (1.9°±1.2°) compared to K-wires (3.8°±2.1°, p=0.032). Rotational malalignment and loss of reduction were each seen in 7.14% (1/14) of K-wire cases, but none in the Mini-plate group (Table 3). Across fracture patterns, Mini-plates consistently achieved higher early union rates 100% in transverse, 80% in oblique, and 100% in spiral fractures, compared to 87.5%, 50%, and 75%, respectively, in K-wire cases (Table 4). Table 5 demonstrates that Mini-plate fixation showed no cases of loss of reduction, non-union, or malunion (all 0%), whereas the K-wire group demonstrated 7.1% loss of reduction, 7.1% non-union, and 14.3% malunion. Although these differences favored mini-plates, the relative risks 7.1 for loss of reduction and non-union and 3.5 for malunion were not statistically significant (p-values 0.32 and 0.21). Implant failure was absent in both groups (0%). Therefore, mini-plates had 2 cases (14.3%), while K-wires had 6 cases (42.9%), giving a relative risk of 3.0. However, this trend did not reach statistical significance (p = 0.094)

Table – I: Baseline demographics and fracture characteristics of the study population (*n* = 28)

Parameter	K-Wire (n=14)		Mini-Plate (n=14)		p- value
	n	%	n	%	
Age (Years)					
20-30	6	42.86	5	35.71	0.809*
31-40	7	50.00	7	50.00	
41-50	1	7.14	2	14.29	
Mean± SD	31.57± 6.05		32.57± 6.43		0.769**
Gender					
Male	11	78.57	12	85.71	0.622*
Female	3	21.43	2	14.29	
Hand Dominancy					
Right	14	100.00	14	100.00	1.00*
Left	0	0.00	0	0.00	
Involved limb					
Right	11	78.57	9	64.29	0.403*
Left	3	21.43	5	35.71	
Fractured MC bones					
Single	11	78.57	10	71.43	0.592*
Two	3	21.43	3	21.43	
Three	0	0.00	1	7.14	
Fracture pattern					
Transverse	6	42.86	8	57.14	0.356*
Oblique	5	35.71	2	14.29	
Spiral	2	14.29	4	28.57	
Comminuted	1	7.14	0	0.00	

Table – II: Time to bony union and radiological healing outcomes of the study population

Outcome	Mini-Plate (n=14)		K-Wire (n=14)		p-value
	n	%	n	%	
Time to union (weeks)					
Mean± SD	7.86 ± 1.03		8.14 ± 1.66		0.044†
Union ≤ 6 weeks	8	57.14	3	21.43	0.035*
Union ≤ 8 weeks	14	100.00	11	78.57	0.048*
Union 10–12 weeks	0	0.00	3	21.43	0.12*

Table – III: Radiographic alignment and malunion parameters of the study population

Parameter	Mini-Plate (n=14)	K-Wire (n=14)	Relative Risk (95% CI)	p-value
Malalignment >5°	0 (0.00)	2 (14.29)	3.5 (0.33–37.3)	0.21*
Angular deformity (°)	1.9 ± 1.2	3.8 ± 2.1	1.9 ± 1.8	0.032†
Rotational malalignment, n (%)	0 (0.00)	1 (7.14)	7.1 (0.33–151)	0.32*
Loss of reduction, n (%)	0 (0.00)	1 (7.14)	7.1 (0.33–151)	0.32*

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Table – IV: Association between fracture pattern and early radiological union (≤ 8 weeks) of the study population

Fracture Pattern	Mini-Plate (n)	Mean Time to Union (weeks ± SD)	Union ≤ 8 Weeks, n (%)	K-Wire (n)	Mean Time to Union (weeks ± SD)	Union ≤ 8 Weeks, n (%)	% Achieving Union	p-value
Transverse	6	7.0 ± 1.0	6 (100.00)	8	8.0 ± 1.41	7 (87.50)	92.90	0.29*
Oblique	5	7.8 ± 1.2	4 (80.00)	2	8.5 ± 1.29	1 (50.00)	66.70	0.32*
Spiral	2	7.5 ± 0.7	2 (100.00)	4	7.75 ± 1.26	3 (75.00)	83.30	0.41*
Comminuted	1	7	1 (100.00)	0	-	-	50.00	-

Table – V: Radiological complications and implant-related outcomes of the study population

Complication	Mini-Plate (n=14)	K-Wire (n=14)	Relative Risk (95% CI)	p-value
Loss of reduction	0 (0.00)	1 (7.1)	7.1 (0.33–151)	0.32*
Non-union (>12 weeks)	0 (0.00)	1 (7.1)	7.1 (0.33–151)	0.32*
Malunion	0 (0.00)	2 (14.3)	3.5 (0.33–37.3)	0.21*
Implant failure	0 (0.00)	0 (0.00)	-	-
Any complication	2 (14.3)	6 (42.9)	3.0 (0.67–13.4)	0.094*

DISCUSSION

Metacarpal shaft fractures remain a common hand injury, with management strategies evolving to optimize both fracture healing and functional recovery. The choice between K-wire and mini-plate fixation continues to be debated, particularly regarding radiological outcomes, stability, and complication profiles. In the present study, the mean age of patients was 32.57 ± 6.43 years in the mini-plate group and 31.57 ± 6.05 years in the K-wire group, consistent with previous reports by Kumar et al. (2021) and Barua et al. (2024), who reported mean ages of 31.2, 32.4, and 33.14 years, respectively [14-15]. A predominance of male patients was observed in both groups (85.7% vs. 78.6%), which aligns with the literature indicating a higher incidence of metacarpal fractures in men, with prevalence ranging from 60% to 93% [16-17]. Moreover, fractures occurred predominantly in the dominant right hand, a pattern reported in previous studies by Kumar et al. (2021) and Lv et al. (2021), where 76.7% and 70% of cases involved the dominant hand, respectively [14,18]. Regarding fracture patterns, transverse, oblique, spiral, and comminuted fractures were evenly distributed between groups without significant differences. This is consistent with findings from Barua et al. (2024) and Lv et al. (2021), who reported that single metacarpal fractures accounted for approximately 76–80% of cases, two fractures for 15–17%, and three fractures for 5–7% of patients [15,18]. Literature review further indicates that transverse fractures are the most prevalent pattern, representing 50–70% of cases [17]. Time to bony union emerged as a key differentiator between the two fixation methods. The mini-plate group achieved a mean union time of 7.86 ± 1.03 weeks, significantly shorter than the 8.14 ± 1.66 weeks observed in the K-wire group (p = 0.044). Early union within 6 weeks was observed in 57.1% of patients treated with mini-plates versus 21.4% in the K-wire group (p = 0.035), and complete union within 8 weeks occurred in 100% of mini-plate cases compared to 78.6% of K-wire cases (p = 0.048). These findings suggest that rigid internal fixation with mini-plates confers enhanced mechanical stability, allowing for accelerated radiographic healing [19]. Similar outcomes have been reported in prior studies demonstrating that plate fixation facilitates earlier bone union and promotes early rehabilitation compared to percutaneous K-wire fixation [20]. When analyzing fracture pattern-specific outcomes, transverse and spiral fractures demonstrated consistently favorable healing in both groups. Nevertheless, mini-plate fixation achieved complete union within 8 weeks across all fracture patterns, whereas K-wire fixation showed lower union rates in oblique fractures (50%) and comminuted fractures (50%). Comparable findings were reported by Omer et al. (2020), with union rates of 80% and 28% for mini-plate and K-wire groups, respectively [21], while Mahmoud et al. (2020) observed 90% union at eight weeks in both fixation modalities [20]. Radiographic alignment and malunion were also superior in the mini-plate group. Angular deformity averaged 1.9° ± 1.2° in the mini-plate group compared to 3.8° ± 2.1° in the K-wire group (p = 0.032). No cases of malalignment greater than 5° or rotational deformity were noted in the mini-plate group, whereas the K-wire group had two cases of malalignment and one rotational malalignment. Loss of reduction occurred in one K-wire case but was absent in the mini-plate group. These findings are consistent with previous studies demonstrating superior radiological stability with rigid internal fixation. A large retrospective analysis by Lv et al. reported lower rotational deformity in the mini-plate group compared to K-wire fixation (1° vs 6°, p < 0.05), with fewer postoperative complications and better maintenance of alignment [18]. Similarly, prospective studies have emphasized that mini-plate fixation provides stable internal fixation, facilitating early mobilization and reducing the risk of malalignment, whereas K-wire fixation may be associated with higher rates of angular and rotational deformities [18,22]. Regarding radiological complications and implant-related outcomes, the mini-plate group exhibited a lower overall complication rate (14.3%) compared to the K-wire group (42.9%), though statistical significance was not reached (p = 0.094). Specifically, malunion, loss of reduction, and non-union were observed exclusively in the K-wire group, while no implant failures were noted in either group. These findings reinforce previous meta-analyses indicating that mini-plate fixation not only provides superior radiological outcomes but also reduces the risk of secondary complications associated with K-wire fixation, such as malalignment or delayed union [23].

Limitations of the study: This study is limited by its relatively small sample size and single-center design, which may affect generalizability. Short-term follow-up precluded assessment of long-term functional outcomes, hardware irritation, and late complications. Additionally, although radiographic evaluations were blinded, subtle interobserver variability cannot be excluded. Finally, the study did not assess patient-reported outcomes or cost-effectiveness, which may influence clinical decision-making between mini-plate and K-wire fixation.

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CONCLUSION AND RECOMMENDATIONS

In the present study, mini-plate fixation demonstrated superior radiological outcomes compared to K-wire fixation in metacarpal shaft fractures. Patients treated with mini-plates achieved faster time to union, higher rates of early radiological healing, and significantly lower angular deformity, with no cases of malunion, loss of reduction, or non-union. Although overall complication rates were not statistically significant, K-wire fixation was associated with higher incidences of radiographic misalignment and delayed union. These findings support the preferential use of mini-plate fixation for enhanced stability, predictable healing, and improved functional outcomes.

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REFERENCES

1. *Taha R, Davis T, Montgomery A, Karantana A. Management of metacarpal shaft fractures: a multicentre cross-sectional study. Bone & Joint Open. 2024 Aug 8;5(8):652-61.*
2. *Nemirov D, Kasper AA, Sherman M, Siddiqui H, Ilyas AM, Hozack B. Metacarpal Fracture Trends in Treatment: A Matched Cohort Analysis of 1022 Patients. Archives of Bone and Joint Surgery. 2025;13(8):489.*
3. *Barua S, Chowdhury MM, Mustafa M, Islam SA, Nag R, Mahmud MT. Study on Fixation Methods for Metacarpal Bone Fracture. Medicine Today. 2024 Jul 31;36(2):87-9.*
4. *Chiu YC, Hsu CE, Ho TY, Ting YN, Tsai MT, Hsu JT. Bone plate fixation ability on the dorsal and lateral sides of a metacarpal shaft transverse fracture. Journal of orthopaedic surgery and research. 2021 Jul 7;16(1):441.*
5. *Dreyfuss D, Allon R, Izacson N, Hutt D. A comparison of locking plates and intramedullary pinning for fixation of metacarpal shaft fractures. Hand. 2019 Jan;14(1):27-33.*
6. *Kubota Y, Kaku N, Tabata T, Tagomori H, Tsumura H, Choi DJ, Kim JE, Oh JR, Kim DS, Yeom JS, Kang SK. A comparative study of tensile strength of three operative fixation techniques for metacarpal shaft fractures in adults: a cadaver study. Clinics in orthopedic surgery. 2019 Mar;11(1):120-5.*
7. *Hifny MA, Abdelrasheed AA, Ahmed AM, Hafez MM, Park TH. Reliability of unicortical plate fixation for metacarpal shaft fractures: A preliminary clinical report with short-term follow-up. InAnnales de Chirurgie Plastique Esthétique 2025 May 1 (Vol. 70, No. 3, pp. 153-159). Elsevier Masson.*
8. *Adachi A, Takegami Y, Nakashima H, Mishima K, Kobayashi K, Imagama S. Comparative clinical outcomes of K-wire fixation versus screw fixation in Lisfranc joint injuries: A multicenter (TRON group) retrospective study. The Journal of Foot and Ankle Surgery. 2025 Jun 24.*
9. *Chiu YC, Hsu CE, Ho TY, Ting YN, Tsai MT, Hsu JT. Effect of a figure-of-eight cerclage wire with two Kirschner wires on fixation strength for transverse metacarpal shaft fractures: an in vitro study with artificial bone. BMC Musculoskeletal Disorders. 2021 May 10;22(1):431.*
10. *Alotaibi MN, Aldaraani LG, Altala AS, Alqurashi AA, Alateeq IS, Alkhamisi AA, Allehaimeed IS, Jad AY, Alosaimi H, Alharbi BH, Alenezi A. Comparing the Outcomes of Cast Immobilization with and Without K-Wire Fixation for Displaced Distal Radius Fractures in the Pediatric Population: A Systematic Review and Meta-Analysis. Medicina. 2025 May 6;61(5):852.*
11. *Chaudhry H, Kleinlugtenbelt YV, Mundi R, Ristevski B, Goslings JC, Bhandari M. Are volar locking plates superior to percutaneous K-wires for distal radius fractures? A meta-analysis. Clinical Orthopaedics and Related Research®. 2015 Sep;473(9):3017-27.*
12. *Franceschi F, Franceschetti E, Paciotti M, Cancilleri F, Maffulli N, Denaro V. Volar locking plates versus K-wire/pin fixation for the treatment of distal radial fractures: a systematic review and quantitative synthesis. British medical bulletin. 2015 Sep 1;115(1):91-110.*
13. *Brennan SA, Kiernan C, Beecher S, O'Reilly RT, Devitt BM, Kearns SR, O'Sullivan ME. Volar plate versus k-wire fixation of distal radius fractures. Injury. 2016 Feb 1;47(2):372-6.*
14. *Kumar A, Kumar R, Batra A, Biswas S, Pathak A, Ranjan R. A Comparative Study Between Miniplate Fixations Versus K-wire Fixation in Closed Metacarpal Fractures. International Journal of Health Sciences.;5(S2):720-39.*
15. *Barua S, Chowdhury MM, Mustafa M, Islam SA, Nag R, Mahmud MT. Study on Fixation Methods for Metacarpal Bone Fracture. Medicine Today. 2024 Jul 31;36(2):87-9.*
16. *Wutphiriya-angkul S. Comparison of miniplate and K-wire in treatment of metacarpal and phalangeal fractures. The THAI Journal of Surgery. 2009 Jun 30;30(1-2).*
17. *Abulsoud MI. Comparative study between intramedullary K wires versus mini-plates and screws in fixation of metacarpal shaft fractures in adults. Al-Azhar International Medical Journal. 2020 Dec 1;1(12):299-305.*
18. *Lv F, Nie Q, Guo J, Tang M. Comparative analysis of the effects of AO mini-plate and Kirschner wire pinning in the metacarpal fractures: A retrospective study. Medicine. 2021 Jul 2;100(26):e26566.*
19. *Kurakar M, Joshi U. Comparative study of miniplate vs reconstruction plate in the management of bilateral parasymphysis mandible fracture: FEM analysis. Journal of Maxillofacial and Oral Surgery. 2023 Mar;22(1):9-17.*
20. *Mahmoud W, Abd El Omar M, Elbandrawy A. Management of unstable metacarpal shaft fractures by k-wires versus mini-plate fixation. The Scientific Journal of Al-Azhar Medical Faculty, Girls. 2020 Jul 1;4(3):415-.*
21. *OMER M. Kirschner Wire versus Miniplate Internal Fixation Effectiveness for Metacarpal Fractures in Pakistani Population.*
22. *Agarwal BK, Ravikumar AS, Sridhar DK. A prospective study of functional outcome between Mini-plates and percutaneous K-wire fixation following metacarpal shaft fractures. Int J Orthop Sci. 2019;5(4):328-1.*
23. *Xu J, Zhang C. RETRACTED ARTICLE: Mini-plate versus Kirschner wire internal fixation for treatment of metacarpal and phalangeal fractures in Chinese Han population: a meta-analysis. Journal of Orthopaedic Surgery and Research. 2014 Apr 11;9(1):24.*

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CASE REPORT

Ocular Cystinosis-Bilateral Corneal Crystals and Macular Atrophy in a Child

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ABSTRACT

Introduction: *Cystinosis is a rare autosomal-recessive lysosomal storage disorder caused by CTNS gene mutations, leading to cystine accumulation in multiple organs. Ocular involvement often precedes systemic disease and provides critical diagnostic clues.* ***Case Presentation:*** *We describe a 7-year-old child presenting with photophobia, bilateral corneal crystals, and visual decline. Slit-lamp examination revealed dense, refractile stromal deposits, while fundus evaluation showed macular atrophy and mild optic disc pallor. Systemic evaluation identified growth retardation and rickets-like deformities, consistent with nephropathic cystinosis. Laboratory and genetic testing confirmed the diagnosis.* ***Discussion:*** *This case emphasizes the correlation between ocular and systemic manifestations in cystinosis. Corneal and retinal findings serve as accessible biomarkers for disease burden and treatment adherence. Early ophthalmic recognition enables timely initiation of cysteamine therapy and systemic management, mitigating renal and skeletal complications.* ***Conclusion:*** *Ocular cystinosis, though rare, offers a unique diagnostic window for systemic disease. Routine slit-lamp screening in children with photophobia or growth failure and interdisciplinary management can significantly improve visual and systemic prognosis.*

Keywords: *Cystinosis, Corneal crystals, Macular atrophy, Pediatric ophthalmology, Lysosomal storage disorder*

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INTRODUCTION

Cystinosis is a rare, autosomal-recessive lysosomal storage disorder caused by mutations in the *CTNS* gene, which encodes cystinosin—a transmembrane lysosomal transporter responsible for cystine efflux [1]. Defects in this protein result in intralysosomal accumulation of cystine crystals within multiple organs and tissues, ultimately leading to progressive multisystem damage [2]. The estimated global incidence ranges from 1 in 100,000 to 1 in 200,000 live births, though under-diagnosis and late recognition remain common due to variable phenotypic expression [3]. Three main clinical variants are recognized: infantile nephropathic (≈95 % of cases), juvenile or late-onset nephropathic, and ocular or non-nephropathic cystinosis [4]. The infantile form is the most severe, typically presenting within the first year of life with renal Fanconi syndrome, metabolic acidosis, and growth retardation. The ocular form, by contrast, may remain isolated to the eyes for years before systemic abnormalities become apparent.

The pathophysiology of ocular cystinosis reflects widespread lysosomal deposition of cystine crystals in the cornea, conjunctiva, iris, ciliary body, and retina [2]. In the cornea, crystal accumulation begins at the anterior peripheral stroma and progresses centrally and posteriorly with age [5]. Progressive deposition produces increased light scatter, glare sensitivity, and ocular surface irregularities. Patients frequently present with photophobia, blepharospasm, and recurrent erosions due to epithelial disruption [6]. These symptoms typically develop by 12 to 18 months in infantile nephropathic cases, often serving as the first clinically recognizable sign of the disease [7]. The severity of corneal involvement usually correlates with systemic cystine load, making ophthalmic findings a useful biomarker for disease progression and treatment response [2].

Posterior segment changes, although less common, have important implications for visual prognosis. Studies using fundus photography and in vivo confocal microscopy have documented pigment epithelial mottling, chorioretinal atrophy, and macular involvement resulting in reduced visual acuity and field constriction [7]. Histopathologic analyses show cystine crystals in the retinal pigment epithelium (RPE) and choroid, confirming that cystinosis affects both anterior and posterior ocular structures [8]. Persistent photophobia and visual decline are often exacerbated by these posterior changes. Recent advances in imaging, such as optical coherence tomography (OCT), have enhanced the ability to monitor posterior involvement and quantify crystal burden non-invasively, aiding early therapeutic intervention [2].

Although ocular changes may dominate the early clinical course, cystinosis is fundamentally a systemic disease. In its nephropathic form, patients develop generalized proximal tubular dysfunction leading to renal Fanconi syndrome, with polyuria, aminoaciduria, and phosphate wasting. These abnormalities cause rickets, growth failure, and skeletal deformities [9]. The accumulation of cystine crystals in bone,

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muscle, and endocrine tissues further contributes to stunted growth and metabolic imbalance [10]. Importantly, ocular findings such as bilateral corneal crystals often appear before overt renal manifestations, sometimes preceding systemic diagnosis by several years [11]. This temporal relationship underscores the ophthalmologist's pivotal role in early detection. A slit-lamp examination revealing the characteristic refractile, needle-shaped crystals can guide clinicians toward confirmatory testing, including leukocyte cystine quantification and genetic analysis.

Early ophthalmic identification of cystinosis is particularly vital because timely systemic therapy with cysteamine can substantially delay progression of renal and extra-renal complications [3]. Delay in diagnosis often results in irreversible systemic damage, including chronic kidney disease and growth impairment. Hence, interdisciplinary collaboration between ophthalmologists, pediatricians, and nephrologists is critical to improving outcomes [12]. Recent reviews emphasize that ocular monitoring should be integrated into long-term management, as corneal and retinal findings not only indicate local disease but also reflect systemic therapeutic efficacy [2,10].

The relationship between ocular and systemic disease in cystinosis also exemplifies shared embryologic and molecular pathways between the eye and kidney. Both organs rely on lysosomal and tubular transport systems, making them vulnerable to metabolic derangements [13]. Studies of ocular–renal syndromes reveal common mechanisms involving oxidative stress and the renin–angiotensin–aldosterone system, which may amplify tissue injury [14]. Consequently, detailed ophthalmic examination serves not only diagnostic but also prognostic functions, providing insight into systemic disease status.

In summary, cystinosis represents a rare but instructive metabolic disorder linking ocular and systemic pathology through a unifying lysosomal mechanism. Corneal and retinal changes, often detected long before systemic manifestations, make the eye a natural window to diagnosis. Awareness of these characteristic findings allows ophthalmologists to play a central role in early recognition, multidisciplinary coordination, and preservation of both visual and systemic function. This case adds to the expanding literature emphasizing that ocular cystinosis, though visually disabling, is diagnostically invaluable for identifying a life-threatening systemic disease in its earliest and most treatable stages.

CASE HISTORY

A 7-year-old boy named Raj Dev, the second child of non-consanguineous, healthy parents from Sylhet, presented to the ophthalmology outpatient department with complaints of poor growth since age two, bowing of both legs since birth, inability to run properly, and loss of appetite. He was fully immunized according to the national schedule, and there was no family history of similar illness or inherited disorders.

Systemic History

The child's caregivers denied any urinary abnormalities, such as polyuria, polydipsia, or nocturnal enuresis. There was no history of diarrhea, constipation, vomiting, convulsions, or respiratory distress. There was no record of prolonged drug intake, including vitamin D or anticonvulsant therapy.

General Examination

The child appeared short and stunted for his age, with an overall thin habitus. His vital signs were within normal limits: temperature 98.5 °F, pulse 82 bpm, respiratory rate 22 breaths/min, and blood pressure 90/60 mm Hg. Physical examination revealed frontal bossing and a box-shaped head. Skeletal changes were evident, including widened wrists and ankles, enlarged costochondral junctions (rachitic rosary), and bowing of both lower limbs with knee deformity, consistent with features of rickets. The abdomen was soft with mild hepatomegaly. Cardiovascular and respiratory system examinations were unremarkable. Cognitive evaluation indicated mild mental retardation.

Ocular Examination

On ocular inspection, both eyes were orthophoric with no evidence of strabismus or ptosis. The anterior segment of each eye showed bilateral hazy corneas containing multiple fine, refractile crystalline deposits throughout the entire stromal thickness. The density of crystals was greater in the peripheral cornea and relatively sparse centrally. The iris details appeared indistinct, but the anterior chamber depth was normal, pupillary light reflexes were brisk and equal, and the lenses were clear bilaterally.

Best-corrected visual acuity (BCVA) was 6/36 in both eyes.

Fundus Findings

Due to anterior corneal haze, the media were mildly hazy, limiting fine visualization. The optic discs showed mild pallor with normal retinal vasculature. The maculae exhibited chorioretinal atrophy with absent foveal reflex, suggestive of early macular degeneration secondary to cystine deposition. No active retinal hemorrhage or exudate was observed.

Clinical Impression

Based on the combination of growth retardation, skeletal deformities suggestive of rickets, and ocular crystalline keratopathy with macular atrophy, the child was provisionally diagnosed with ocular cystinosis associated with systemic features of infantile nephropathic cystinosis. The presence of corneal crystal deposition and posterior segment involvement indicated advanced ocular disease, while the skeletal abnormalities implied systemic metabolic dysfunction, possibly due to renal Fanconi-type pathology.

Initial Management and Counseling

The child and caregivers were counseled on the probable diagnosis and the need for multidisciplinary evaluation. Baseline investigations including urinary amino acid analysis, serum electrolytes, and renal function tests were recommended to assess systemic involvement. Cystine crystal deposition was explained as a hallmark of cystinosis, and referral to pediatric nephrology was advised for confirmation through leukocyte cystine quantification and genetic testing for *CTNS* mutation.

Ophthalmic management was planned to include topical cysteamine hydrochloride drops (0.44 %) to reduce corneal crystal density and regular follow-up for visual acuity, photophobia, and ocular surface integrity. The parents were educated on protective measures against light exposure and the importance of systemic therapy initiation to prevent further ocular and systemic deterioration.

Figure – 1: Ocular cystinosis

The findings in this child illustrate the classical ocular phenotype of cystinosis-related crystalline keratopathy, together with systemic stigmata of a generalized lysosomal storage disorder. Early ophthalmologic recognition is crucial, as the ocular signs often precede severe renal and skeletal manifestations, allowing timely initiation of multidisciplinary management.

DISCUSSION

The present case highlights the diagnostic and clinical relevance of ocular cystinosis in a pediatric patient presenting with bilateral corneal crystals, macular atrophy, and systemic features including growth retardation and rickets-like skeletal deformities. Cystinosis is an autosomal-recessive lysosomal storage disorder caused by mutations in the CTNS gene, which encodes the lysosomal cystine transporter cystinosin. The resultant cystine accumulation leads to progressive cellular dysfunction and multisystem involvement encompassing renal, skeletal, endocrine, neurological, and ocular systems [1,3]. While nephropathic cystinosis typically presents in infancy with renal Fanconi syndrome, ocular manifestations can precede systemic symptoms by several years, serving as a critical window for early detection [10].

Ocular findings in this child, particularly bilateral corneal crystal deposition, mirror classical descriptions of cystinosis-related keratopathy where crystals initially appear in the peripheral anterior stroma and progressively extend centrally and posteriorly [5,7]. This deposition disrupts stromal architecture, increases light scatter, and contributes to photophobia and reduced visual acuity [2]. The presence of macular atrophy and mild optic disc pallor further indicates posterior segment involvement, a feature less frequently reported in pediatric ocular cystinosis but associated with disease progression and chronic oxidative stress in the retinal pigment epithelium [7]. Similar retinal degeneration and chorioretinal atrophy have been noted in advanced cases, reinforcing the link between cystine accumulation and photoreceptor damage [15].

From a pathophysiologic standpoint, oxidative stress and lysosomal dysfunction play pivotal roles in tissue damage. Excess cystine promotes apoptosis and collagen disorganization within the corneal stroma, compromising transparency and structural integrity [2]. The degenerative macular changes in the present case are consistent with cumulative oxidative damage and cystine deposition in the RPE [16]. These mechanisms illustrate how local ocular findings may mirror the systemic burden of cystine, underscoring their utility as biomarkers of overall disease activity.

The coexistence of ocular and skeletal abnormalities in this patient further exemplifies the systemic reach of cystinosis. Growth failure and rickets-like deformities observed here are compatible with renal Fanconi syndrome, a hallmark of nephropathic cystinosis [3]. Comparable pediatric reports describe ocular signs preceding or paralleling systemic metabolic bone disease, highlighting the diagnostic value of early ophthalmic evaluation [9]. Consequently, routine slit-lamp screening in children presenting with photophobia or unexplained growth retardation should be prioritized to facilitate timely referral and systemic evaluation [11].

Management in this case followed established recommendations involving topical cysteamine hydrochloride (0.44%) for reducing corneal crystal density and systemic cysteamine therapy to lower intracellular cystine levels. While systemic therapy effectively mitigates renal and endocrine complications, its limited corneal penetration necessitates concurrent topical administration [2,5]. Regular monitoring using slit-lamp biomicroscopy and optical coherence tomography (OCT) remains essential to assess both anterior and posterior segment response [17].

This case underscores the multidisciplinary dimension of cystinosis management, integrating ophthalmology, nephrology, and pediatrics. It demonstrates how characteristic ocular findings—corneal crystals and macular changes—can provide critical diagnostic cues for a systemic lysosomal disorder. Furthermore, it reinforces that ophthalmic surveillance not only detects disease early but also reflects systemic treatment adherence and efficacy [10,13]. Therefore, enhancing clinical awareness of ocular cystinosis among pediatric and ophthalmic practitioners is vital for preventing irreversible visual and systemic sequelae.

CONCLUSION

This case reinforces the diagnostic and prognostic value of ocular findings in pediatric cystinosis. The coexistence of bilateral corneal crystals, macular atrophy, and systemic features such as growth retardation and skeletal deformities highlights the systemic nature of this lysosomal storage disorder. Recognizing the characteristic refractile corneal crystals on slit-lamp examination remains essential for early diagnosis, particularly when renal or systemic manifestations are subtle or delayed. Timely initiation of combined systemic and topical cysteamine therapy, along with regular ophthalmic monitoring using slit-lamp and OCT, can slow progression and improve quality of life. This report underscores the critical role of ophthalmologists as front-line detectors of systemic metabolic disease and advocates for multidisciplinary collaboration among pediatricians, nephrologists, and ophthalmologists to optimize outcomes. Increased awareness and early screening in children with photophobia or unexplained growth failure may prevent irreversible ocular and systemic sequelae.

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REFERENCES

1. *Elmonem MA, Veys KR, Soliman NA, van Dyck M, van den Heuvel LP, Levtchenko E. Cystinosis: a review. Orphanet Journal of Rare Diseases [Internet]. 2016 Apr 22 [cited 2025 Oct 22];11(1):47. Available from: https://doi.org/10.1186/s13023-016-0426-y*
2. *Devitt L. Ocular cystinosis – A review of disease, diagnosis, and future treatment options. Arch Clin Exp Ophthalmol [Internet]. 2024 Oct 31 [cited 2025 Oct 22];Volume 6(Issue 1):6–12. Available from: https://www.probiologists.com/article/ocular-cystinosis-a-review-of-disease-diagnosis-and-future-treatment-options*
3. *Topaloglu R. Extrarenal complications of cystinosis. Pediatr Nephrol. 2024 Aug;39(8):2283–92.*
4. *Chkioua L, Amri Y, Saheli C, Mili W, Mabrouk S, Chabchoub I, et al. Molecular characterization of CTNS mutations in Tunisian patients with ocular cystinosis. Diagn Pathol. 2022 May 6;17(1):44.*
5. *Shams F, Livingstone I, Oladiwura D, Ramaesh K. Treatment of corneal cystine crystal accumulation in patients with cystinosis. Clin Ophthalmol [Internet]. 2014 Oct 10 [cited 2025 Oct 22];8:2077–84. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4199850/*
6. *Klintworth GK. Corneal dystrophies. Orphanet J Rare Dis. 2009 Feb 23;4:7.*
7. *Rozitis E, Petsoglou C, Devasahayam R, Hau S, Lacorzana J. Typical Manifestations of the Different Corneal Deposits by In Vivo Confocal Microscopy (IVCM): A Review. Clin Exp Ophthalmol. 2025;53(7):834–57.*
8. *Vinals AF, Kenyon KR. Corneal Manifestations of Metabolic Diseases. International Ophthalmology Clinics [Internet]. 1998 Winter [cited 2025 Oct 22];38(1):141. Available from: https://journals.lww.com/internat-*

ophthalmology/citation/1998/03810/Corneal_Manifestations_of_Metabolic_Diseases.12.aspx

9. *Heroor A, Verma A, Achanta DS, Edward DP, Ramappa M. Unveiling cystinosis in India. J Rare Dis [Internet]. 2024 Jun 25 [cited 2025 Oct 22];3(1):25. Available from: https://doi.org/10.1007/s44162-024-00046-x*
10. *Biswas S, Gaviria M, Malheiro L, Marques JP, Giordano V, Liang H. Latest Clinical Approaches in the Ocular Management of Cystinosis: A Review of Current Practice and Opinion from the Ophthalmology Cystinosis Forum. Ophthalmol Ther. 2018 Dec;7(2):307–22.*
11. *Kumar MJ, Kotak PS, Acharya S, Nelakuditi M, Parepalli A. A Comprehensive Review of Ocular Manifestations in Systemic Diseases. Cureus. 2024 Jul;16(7):e65693.*
12. *Yang G, Mack H, Harraka P, Colville D, Savige J. Ocular manifestations of the genetic renal tubulopathies. Ophthalmic Genet. 2023 Dec;44(6):515–29.*
13. *Lai S, Perrotta AM, Bagordo D, Mazzaferro S, Menè P, Errigo F, et al. Literature review on the cross-link between ocular and renal disease: renin angiotensin aldosterone system is a main actor. Eur Rev Med Pharmacol Sci. 2022 Jul;26(13):4774–88.*
14. *Salehi O, Mack H, Colville D, Lewis D, Savige J. Ocular manifestations of renal ciliopathies. Pediatr Nephrol. 2024 May;39(5):1327–46.*
15. *Pastores GM. Lysosomal Storage Disorders: Principles and Practice. World Scientific; 2010. 179 p.*
16. *Zhang M, Zhang R, Zhao X, Ma Z, Xin J, Xu S, et al. The role of oxidative stress in the pathogenesis of ocular diseases: an overview. Mol Biol Rep. 2024 Mar 27;51(1):454.*
17. *Veys K. Innovation in monitoring and treatment of nephropathic cystinosis. 2019 [cited 2025 Oct 22]; Available from: https://lirias.kuleuven.be/retrieve/546970*