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EDITORIAL

ORIGINAL ARTICLES

Litigation in Medical Practice

Medical litigation occurs when a patient claims harm due to healthcare provider's negligence to meet the accepted standard of care. These cases often involve allegations of misdiagnosis, surgical errors, medication mistakes, child birth injuries etc. Every patient and their family should be considered as a potential litigant, especially when the health care has been declared as a service industry, which is the foundation of breaking the bond, respect and trust between the doctor and patient.

In Nepal Medical sector is growing rapidly and the incidence of Medical malpractice are also common. The legal framework in Nepal governing Medical malpractice is based on Nepal Medical Council Act, 1964 (amended in 2020), the National penal code 2074 (2017) and the consumer protection act 2075 (2018). The legal framework of Medical malpractice in Nepal has evolved significantly over the years. The Nepal Medical Council plays a critical role in regulating Medical practice and addressing the issue of professional misconduct. The National penal code recognizes gross negligence as a criminal offense and provides for punishment of fine and imprisonment based on the gravity of offense. Consumer protection act, of Nepal recognizes patients as consumers and health care service as a type of service. If the Medical services are deemed deficient, the victims are given the right to seek the remedy before the court.

In our Country certain elements of Medical malpractice must be proven to establish Medical negligence.

- Duty of care: Healthcare providers must have owed a duty of care to the patients.
- Breach of duty: Evidence that the healthcare provider failed to meet standard of care.
- Causation: Breach of duty must be directly linked to the harm suffered by patient.
- Damage: Patient must have suffered quantifiable harm as a result of negligence.

Of late consumer court has given its verdict on some of the cases of Medical negligence in Nepal, which has been praised as a victory for patient's right by majority. But on the other side this decision has created an ambiguity and fear among the Medical fraternity. This as a result will push the healthcare providers towards the defensive Medical practice which includes ordering a lot of tests, avoiding risky treatments. These things will increase the treatment cost, workload of healthcare providers and will harm the patients the consumer court is trying to protect.

To overcome the problem both healthcare providers and law makers should be careful and keep the balance. There should be no injustice to the healthcare providers, healthcare providing institutions and patients. Healthcare provider should be highly responsible, accountable and dutiful to mitigate the avoidable medical errors. Medical students should be taught about the Medical ethics, Medical negligence and its consequences at the graduation level itself. Similarly, Institutional improvements such as compulsory monitoring protocols, standardizing Medical records and malpractice insurance should be established. Furthermore initiatives should be taken to educate the people about the realistic outcomes and complexity of the healthcare procedures.

Prof. Dr. Anup Sharma

MS (General Surgery), Fellowship (GI Onco-Surgery)

Editor- In-Chief

Post-Operative Resumption of Clear Liquids Orally at 2 Hours And 6 Hours, In Patients Undergoing Elective Surgeries Under General Anesthesia: A Comparative Study

Regmi NK[1], Sharma A[2], Kharel S[3]

ABSTRACT

Introduction: Early oral nutrition initiation is an essential component of multimodal perioperative care. It is associated with early intestinal function recovery, better immunity, improved wound healing, early ambulation, and decreased morbidity. However, a gap exists between postoperative feeding evidence and its practical application. **Aims:** To compare patient's satisfaction regarding thirst and the occurrence of post-operative nausea, vomiting, and aspiration of gastric contents after resumption of clear liquid orally at 2 hours and 6 hours postoperatively**. Methods:** Ninety-six patients, aged 18 to 70 years, of either sex and ASA I to II, who underwent elective surgeries under general anesthesia, were randomly divided into two equal groups: group 1 and group 2. Patients in group 1 were given clear liquid orally at 2 hours, and group 2 at 6 hours postoperatively. Patient satisfaction regarding thirst, occurrence of postoperative nausea, vomiting, aspiration of gastric contents, and flatus time were compared between the two groups. SPSS 20 was used for data analysis. Student T-test, Chi-square test, Fisher's test, and Man-Whitney test were applied. **Results:** Gender distribution and mean age in both groups had no statistical difference, with P values of 0.358 and 0.331, respectively. The thirst distress scale and post-operative flatus time were significantly lower, whereas Likert's satisfaction level regarding thirst was higher in group 1 compared to group 2, with P-values of 0.00, 0.038, and 0.001, respectively. APFEL grading and postoperative nausea and vomiting grading were statistically similar, with p-values of 0.26 and 0.116, respectively. No aspiration occurred in both groups. **Conclusion:** Compared to 6 hours, resumption of clear liquid 2 hours postoperatively after general anesthesia decreases thirst distress and post-operative flatus time, with the additional benefit of increasing patient satisfaction levels, without any difference in post-operative aspiration rate.

***Keywords**:* Aspiration, clear fluid, double blinded study, postoperative resumption, two and six hours

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INTRODUCTION

Early release of thirst has both physiological and psychological benefits, along with better patient satisfaction, without added complications, even in surgeries like gastrointestinal, obstetrics and laryngeal surgeries done under general anesthesia.[1] The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend that oral intake can be initiated within the first hour of surgery in most patients.[2] Despite clear evidence and guidelines, many anesthesiologists still fear that early initiation of clear liquids after general anesthesia may lead to post-operative nausea and vomiting (PONV) and clinically significant pulmonary aspiration of gastric contents.[3,4] Hence, they force their patients to iatrogenic thirst.[1,5] This deep-rooted fear among anesthesiologists may be because there are still not many studies that compare the early initiation of clear liquids with the regularly practiced 6-hour protocol. Hence, we have chosen this study to compare the resumption of clear liquid at 2 hours with 6 hours postoperatively after general anesthesia. We compared PONV, pulmonary aspiration of gastric contents, patients' satisfaction regarding quenching of thirst, extent of thirst and flatus time between the two groups.

METHODS

This comparative study is a prospective, double-blinded study

conducted from November 2024 to April 2025 at Nepalgunj Medical College Teaching Hospital in 96 patients, following IRC approval.

Sample Size:

Computation of Cohen's d (standardized mean difference) was done with a formula[6], d = μ1−μ2/sp

Where, d= Cohen's d, μ1 = mean in group 1, μ2 = mean in group 2 and sp = pooled standard deviation. Taking the reference of Yin X et al[7], d = 46.27−61.09/ 20.07 = 0.74.

This was followed by calculating conversion of Cohen's d into Mann- Whitney effect size (Area under the curve) with the formula AUC = Φ (d/√ 2) = 0.70, where Φ is the standard normal cumulative distribution function[6]

After taking 95% confidence interval and 99% power, finally, the sample size calculation for Mann-Whitney U test was done with the formula[6]

$n=(Z1-\alpha/2+Z1-\beta)^2 / 6 \times(AUC-0.5)^2$

where, Z1−α/2 = 1.96, Z1−β = 2.33, AUC = 0.70 (from the above calculation)

With a 15% drop-out rate, the final total sample size calculated was 92, i.e., 46 for each group. However, due to availability of cases that could be logistically managed and would be more beneficial with respect to increased power and better precision, it was decided to study a total of 96 subjects, i.e., 48 for each group.

Patients of the 18-70 years age group, with ASA I-II, who underwent elective surgeries under general anesthesia were included in the study. Patients with severe obesity, gastroesophageal reflux disease, diabetes, and a history of alcohol and drug abuse, along with patients with surgeries for intestinal obstruction, craniotomies, and lower segment cesarean section (LSCS), were excluded.

After obtaining written consent, all the patients included in the study went through routine pre-anesthetic checkups and routine premedication. On arrival at the operation room, their vitals were monitored, and general anesthesia was given. In the operation room, single or combination of antiemetics like ondansetron, promethazine hydrochloride, and dexamethasone were administered, according to the APFEL simplified risk score.[8] Once the surgery was over, the patients were shifted to the post-operative ward. In the post-operative ward, patients were divided into two groups randomly: group 1 and group 2, with a 1:1 ratio, after concealment with a sequential numbered opaque sealed envelope technique.

Patients in group 1 were given water to drink after 2 hours of operation and in group 2 after 6 hours. Patients' body positions while drinking were kept supine, with their heads elevated at 30°. The degree of thirst distress (Table I), PONV (Table III), postoperative pulmonary aspiration, and patients' satisfaction regarding quenching thirst (Table II) were recorded. Postoperative pulmonary aspiration was graded as 0- None, 1- cough, 2-pneumonitis, 3-pulmonary edema, 4-ARDS. Time for the first passage of flatus and the presence or the absence of abdominal bloating was also recorded. The record-keeping was done by anesthesiologists unaware of the group the patients belonged to.

Statistical analysis

Data were analyzed with SPSS 20. The T-test was applied to compare continuous data, the Mann-Whitney test for ordinal data, and either the Chi-square test or the Fisher's exact test

	Not Uncomfortable	A little Uncomfortable	Very Uncomfortable
Dry Mouth	0	1	2
Dry Lips	0	1	2
Thick Tongue	0	1	2
Thick Saliva	0	1	2
Dry Throat	0	1	2
Bad taste	0	1	2
Want to drink	0	1	2
Final Score			

Table I: Peri-operative thirst distress scale[9]

Grade	Level of satisfaction
1	Extremely Not Satisfied
2	Not Satisfied
3	Moderately Satisfied
4	Very Satisfied
5	Extremely satisfied

Table II: Five-point Likert's scale[10]

Grade	Quantification of PONV
1	No PONV
2	Nausea only
3	Vomiting< 3 times a day
4	Vomiting > 3times a day

Table III: Quantification of PONV[11]

The presence or absence of post-operative aspiration was recorded.

RESULTS

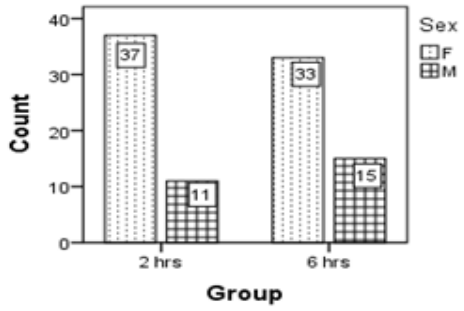

Figure 1: Gender Distribution among the groups

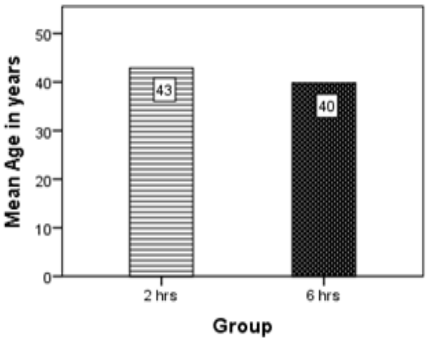

Figure 2: Mean Age between the groups

Both study groups had the majority of female patients, and the gender distribution in both groups was similar, with a P value of 0.358 when the Chi-square test was applied (Figure 1).

The mean age in group 1 and group 2 were 43 years and 40 years respectively (Figure 2). When a student T-test was applied, there was no statistical difference in the mean age between the two groups. The p-value was 0.331.

Types of Surgeries					
Group 1 (2 hrs)			Group 2 (6 hrs)		
Surgeries	Frequency	Percentage	Surgeries	Frequency	Percentage
Discectomy	3	6.3%	Excision of lipoma	1	2.1%
Excision of Goiter	1	2.1%	Excision of LN	1	2.1%
Lap Chole	33	68.8%	Lap Chole	37	77.1%
Hysteroscopy	1	2.1%	RT URSL	1	2.1%
FESS	2	4.2%	Rt PCNL	1	2.1%
ORIF	2	4.2%	ORIF	6	12.5%
Polypectomy	1	2.1%	Polypectomy	1	2.1%
Pyeloplasty	1	2.1%			
Septoplasty	2	4.2%			
Sistrunk Operation	1	2.1%	Total	48	100.0%
Tonsillectomy	1	2.1%			
Total	48	100.0%			

Table IV: Types of Surgeries

Laparoscopic Cholecystectomy was the most common surgery with 69% and 77% in group 1 and group 2 respectively (Table IV).

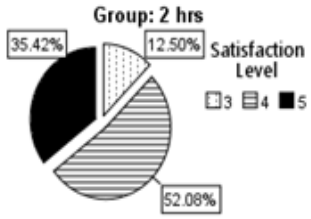

Figure 3: Likert's Level of satisfaction group 1

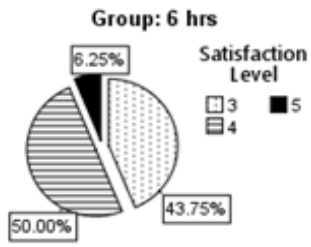

Figure 4: Likert's Level of satisfaction group 2

Approximately half of the patients in both groups had level 4 satisfaction, but level 5 satisfaction (Figure 3 and 4) and overall satisfaction level were statistically higher (Table V) in group 1 than in group 2.

	Group	N	Mean Rank	Sum of Ranks	P Value
Apfel Simplified Risk Score	1	48	51.63	2478.00	0.246
	2	48	45.38	2178.00	
Grade of PONV	1	48	45.33	2176.00	0.116
	2	48	51.67	2480.00	
Thirst distress scale	1	48	34.70	1665.50	0.001
	2	48	62.30	2990.50	
Satisfaction Level	1	48	59.47	2854.50	0.001
	2	48	37.53	1801.50	
Post op Aspiration	1	48	48.50	2328.00	1.000
	2	48	48.50	2328.00	

Table V: Comparison of Apfel score, Grade of PONV, thirst distress scale, Likert's satisfaction level, and post-op aspiration between the two groups (Man Whitney Test)

The thirst distress scale was significantly lower in group 1, compared to group 2, whereas Apfel score and PONV were statistically similar (Table V). None of the patients in both groups had post-operative aspiration of gastric contents.

	Group	N	Mean	Std. Deviation	Levene's test for Equity Sig.	Sig. (2 tailed)
Flatus Time in hours	1	48	15.44	5.831	0.701	0.038
	2	48	18.35	7.648		

Table VI: Comparison of first post-operative flatus time between the groups (Independent T-test)

Post-operative flatus time was significantly reduced in group 1 (Table VI).

2 cases in group 2 had abdominal bloating, and none in group 1. When compared using Fisher's exact test, the p-value was 0.495.

DISCUSSION

Delaying postoperative feeding gives no added advantages.[2] Prolonged thirst can lead to negative emotions such as anxiety, irritability, and postoperative delirium, as well as various metabolic, neurohumoral, and immunological complications.[12] Aspiration of gastric contents, the most feared post-operative complication related to feeding and general anesthesia, occurs due to the relaxation of the cardiac sphincter and the suppression of the gag reflex as a physiological effect of general anesthesia. However, newer studies suggest that early, but multiple small amounts of gradual fluid consumption lead to early physiological adaptation and recovery of gastrointestinal and laryngeal function after general anesthesia, without increasing the incidence of postoperative complications.[12] Various observational studies, meta-analyses, and multicentric trials support early oral intake after surgery.[2] Even "ultra-early" postoperative feeding has been practiced in some hospitals since 2015, where the patients are allowed to drink clear liquid immediately after stabilization in the post-anesthesia recovery room.[13]

In our study, the demographic profile regarding gender distribution and the mean age between the two groups was statistically similar, with p-values of 0.358 and 0.331, respectively. Laparoscopic cholecystectomy was the most common surgery in both groups, 69% and 77% in group 1 and group 2, respectively. The difference in the Apfel score between the two groups was also statistically insignificant with a P value of 0.26.

In our study, the Man Whitney test showed a significantly lower thirst distress scale in patients receiving oral clear liquid in group 1 than in group 2 with a p-value of 0.001. Sun Zj, Sun X, Huo Y, et al conducted a study on 306 patients receiving both general and regional anesthesia, among which 286 (93.5%) patients regained oral fluids within 2 h after surgery, where the thirst scale was significantly reduced in patients regaining oral fluids within 2 hours.[14]

In our study, when the patients' satisfaction level regarding thirst was compared, group 1 had a significantly higher level of satisfaction than group 2, with a p-value of 0.001. Similarly, in the study by Yin X, Ye L, Zhao L, Li L, and Song J on 983 patients, there was a significantly higher level of satisfaction in patients who received early oral hydration after general anesthesia, rather than in the 4-hour group, with a P- value of 0.001.[15]

In our study, the post-operative flatus time was significantly reduced in group 1 than in group 2 with a p-value of 0.038. Zou Y, Zhang X, Li Y, and Liu C compared post-operative feeding at 2 hours as an experimental group and 6 hours as a control group in 70 patients who underwent lumbar discectomy under general anesthesia. Similar to our study, their study showed that the flatus time was significantly reduced in the 2-hour group compared to the 6-hour group, with a p-value of 0.001.[16] The same study showed that bloating was significantly lower in the experimental group16 unlike ours where there was no significant difference in abdominal bloating between the groups with a p-value of 0.495. In our study, there were no cases of post-operative aspiration. The above mentioned study conducted by Sun Zj. Sun X, Huo Y, et al observed that no adverse events, such as aspiration pneumonia or gastroesophageal reflux, occurred.[14] This observation is consistent with our study.

In our study, there was no significant difference in PONV grading with a p-value of 0.26. Similarly, in the study by Zou Y, Zhang X, Li Y, and Liu C, there was no significant difference in the incidence of PONV between the two groups with a p-value of 0.205.[16]

The randomized trial done by Yin X, Ye L, Zhao L, Li L, and Song J on 983 patients, showed no major differences in nausea (7.6% vs 6.5%) and vomiting (4.5% vs 4.1%) postoperatively with P values 0.53 and 0.75 respectively.[15] This study also supports our study findings regarding PONV.

LIMITATIONS

Although diversification of cases was there, most cases in the study were laparoscopic cholecystectomy.

CONCLUSION

Postoperative clear liquid can be resumed within 2 hours of general anesthesia. It decreases thirst distress and post-operative flatus time with an additional benefit of increasing patient satisfaction levels, without any difference in post-operative aspiration rate when compared to the resumption of clear liquid in 6 hours.

REFERENCES

1. Lai L, Zeng L, Yang Z, et al. Current practice of postoperative fasting: results from a multicenter survey in China. BMJ Open. 2022;12(7):e060716. doi:10.1136/ bmjopen-2021-060716

2. Toms A. S, Rai E. Operative fasting guidelines and postoperative feeding in pediatric anesthesia - current concepts. Indian J anesth. 2019; 63(9):707–12. https:// doi.org/10.4103/ija.

3. Thomas M, Engelhardt T. Think drink! Current fasting guidelines are outdated. BJA. 2017; 118(3):291-93. https://doi.org/10.1093/bja/aew450

4. Schenk J, de Klerk, ES, Bouman D, Geerts BF, Hollmann MW, Hermanides J et al. Reducing postoperative fasting times by implementing a food service in the Post Anaesthesia Care Unit (PACU). Clin Nutr ESPEN. 2022;51:280–87. https://doi.org/10.1016/j.clnesp.2022.08.015

5. Rattray M, Roberts S, Marshall A, Desbrow B. A systematic review of feeding practices among postoperative patients: is practice in line with evidence-based guidelines? J Hum Nutr diet. 2018;31(2):151–67. https://doi.org/10.1111/jhn.12486

6. Julious SA. Sample sizes for clinical trials with Normal data. Stat Med. 2004;23(12):1921-86. doi: 10.1002/sim.1783.

7. Yin X, Ye L, Zhao L, Li L, Song J. Early versus delayed postoperative oral hydration after general anesthesia: a prospective randomized trial. Int J Clin Exp Med. 2014;7(10):3491-6. PMID: 25419388; PMCID: 4238515

8. Alejo, Leni; de Guia, Cherry; Rodriguez, Cynthia; and Luck-Bird, Cassandra, "Effectiveness of Apfel Simplified Risk Score in Predicting Postoperative Nausea and Vomiting in Day Surgery Unit" (2021). 2021 Providence Nurse Research Conference. 10. https://digitalcommons.providence.org/prov_rn_conf_all/10

9. Martins PR, Fonseca LF, Rossetto EG, Mai LD. Developing and validating the Perioperative Thirst Discomfort Scale. Rev Esc Enferm USP. 2017;51:e03240. doi: http://dx.doi.org/10.1590/S1980-220X2016029003240

10. Vagias, Wade M. Likert-type scale response anchors. Clemson International Institute for Tourism & Research Development, Department of Parks, Recreation and Tourism Management. Clemson University.2006

11. Xie F, Sun DF, Yang L, Sun ZL. Effect of anesthesia induction with butorphanol on postoperative nausea and vomiting: A randomized controlled trial. World J Clin Cases 2023; 11(32): 7806-13

12. Dai S, Chen L, Wu M. et al. Timing of early water intake post-general anesthesia: a systematic review and meta-analysis. BMC Anesthesiol. 2024;24:135 https://doi.org/10.1186/s12871-024-02520-x

13. Franco A. C., Bicudo-Salomão A, Aguilar-Nascimento J. E., Santos T. B and Sohn, R. V. Ultra-early postoperative feeding and its impact on reducing endovenous fluids. Rev Col Bras Cir. 2020; 47:e20202356. doi: 10.1590/0100-6991e-20202356

14. Sun Zj, Sun X, Huo Y. et al. Abbreviated perioperative fasting management for elective fresh fracture surgery: guideline adherence analysis. BMC Musculoskelet Disord. 2022;23:688. https://doi.org/10.1186/s12891-022-05574-5

15. Yin X, Ye L, Zhao L, Li L, Song J. Early versus delayed postoperative oral hydration after general anesthesia: a prospective randomized trial. Int J Clin Exp Med. 2014;7(10):3491-6. PMID: 25419388; PMCID: PMC4238515.

16. Zou Y, Zhang X, Li Y, Liu C. Preliminary Study on the Feasibility of Early Feeding After General Anesthesia and Lumbar Spine Surgery in Middle-aged and Elderly Patients. Am J Nurs Sci. 2019;8(6):346-50. doi: 10.11648/j.ajns.20190806.19.

ORIGINAL ARTICLE

Subgaleal Drain Placement Following Intracranial Surgeries: A Prospective Observational Study on Outcomes and Complications

Ghimire N[1], Kolakshyapati M[2], Tiwari GP[3], Ghimire N[4]

ABSTRACT

Introduction: Subgaleal drains are commonly used following intracranial surgeries to prevent hematoma accumulation and enhance wound healing. However, there is limited evidence regarding the outcomes and complications associated with drain placement. There is also a lack of standardized protocols regarding the use of drain following craniotomies. **Aims:** To evaluate the postoperative outcomes, including complication rates, duration of ICU and hospital stay following subgaleal drain placement in patients undergoing intracranial surgeries. Additionally, the aim was to correlate the patient characteristics with the duration of drain placement. **Methods:** A prospective observational study was conducted among 40 patients at Nepalgunj Medical College. Demographic, clinical and postoperative data were collected, including drain duration, ICU and hospital stay and complications such as cerebrospinal fluid leak, wound infection, and periorbital swelling. All data were analyzed using SPSS version 26. **Results:** Among 40 patients with subgaleal drains, the mean duration of drain placement was 4.55 days, with 55% of drains removed within 5 days with the threshold being <30ml/24 hrs. The most frequent complication was periorbital swelling (72%), followed by surgical site infection (30%) and wound dehiscence (27.5%). CSF leaks occurred in 10% of cases, while meningitis and pneumocephalus were rare (<5%). There was no statistically significant correlation between the patient characteristics (Age, sex, diagnosis and type of surgery) to the duration of drain placement. **Conclusion:** Subgaleal drain placement following intracranial surgery appears to be generally safe and effective owing to the removal of drain in less than 5 days without clinical untoward effects. There is no correlation of duration of drain placement to patient demographics and surgical parameters including postoperative complications. suggesting the need of standardized early drain removal protocols. The self-limiting and minor, manageable complications like periorbital swelling, surgical site infection and wound dehiscence are most frequent complications and are independent of the drain duration placement.

Keywords: Craniotomy, Complications, Hypertension, Intracranial surgery, Neurosurgery, Skin closure, Subgaleal Drain

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INTRODUCTION

Numerous surgical nuances have been highlighted in literature to reduce complications and accelerate recovery following intracranial surgeries. These include meticulous surgical techniques, proper dura and skin closure, and the strategic placement of surgical drains.[1] The use of drains has been shown to lower both recurrence and mortality rates.[2] However, postoperative complications such as intracranial bleeding, cerebrospinal fluid (CSF) leakage, surgical site infections and meningitis can still arise. These complications may lead to prolonged hospital stays, increased morbidity and mortality, and higher healthcare costs.[3–6] Surgical evacuation followed by placement of postoperative drain remain standard in many intracranial procedures. Subgaleal drain placement, specifically used to reduce fluid accumulation under the scalp (subgaleal collections), has its own advantages and risks.[6] While it can potentially facilitate surgical site infections, secondary wound break

down, and even meningitis in the presence of a CSF leak,[1 7] it is also associated with shorter hospital stays, a higher likelihood of being discharged home and improved functional outcomes. It is important to note that negative suction drainage may lead to severe complications such as brain swelling and even death, particularly after procedures like cranioplasty.[8,9] The recent TOSCAN trial, in a post hoc analysis, suggested that subgaleal drains may offer a safer risk profile and comparable efficacy to subdural drains.[10] Understanding the implications of subgaleal drain placement on patient outcomes including the incidence of complications, duration of hospitalization, morbidity, mortality, and overall treatment costs is vital for optimizing neurosurgical practices and improving patient care.

METHODS

A prospective observational study was conducted at Nepalgunj Medical College over a six-months period (May 2024 - October 2024) to evaluate the outcomes and potential complications of subgaleal drain placement following intracranial surgeries. The ethical approval for the study was obtained from the Institutional Review Committee of Nepalgunj Medical College.

Inclusion criteria:

1. Patients from the Department of Neurosurgery who underwent procedures for brain tumors, hemorrhages, traumatic injuries, aneurysms, or ischemic stroke and add Brain abscess also.

2. Willing to give consent for the study.

Exclusion criteria:

1. Patients with chronic liver or kidney disease,

2. Patients with coagulation disorders, prior radiation therapy, or those receiving immunosuppressive treatment.

Collected data included demographic and clinical information such as age, sex, diagnosis, and comorbidities, along with detailed surgical records covering craniotomy type, presence of dural defects, incision length, and closure methods. Postoperative metrics included drain duration, length of ICU and hospital stay, and complications such as CSF leaks, wound infections, meningitis, pneumocephalus and periorbital swelling. The subgaleal drain output was measured 24 hourly. Drain was intermittently clamped and was removed if the output dropped below 30 ml.

Statistical analysis

All data were analyzed using SPSS version 26. The continuous variables (age, incision size duration of hospital and ICU stay, duration of drain) were mentioned as means. Similarly, categorical variables (complications, comorbidities) were analyzed using chi-square test to determine the association with drain duration, hospital and ICU stay.

RESULTS

Variables	Frequency (F)	Percentage (%)
Age (in years)		
<=20	4	10
21-39	8	20
40-60	15	37.5
>60	13	32.5
Mean age (years) 47.6		
Sex		
Male	28	70
Female	12	30
Comorbidities		
Diabetes Mellitus	6	15
Hypertesion	12	30
Diagnosis		
Ischemic stroke	8	20
Intracerebral hematoma	11	27.5
Ruptured aneurysm	4	10
Brain tumor	2	5
Extradural Hematoma(EDH)	4	10
Subdural Hematoma(SDH)	10	25
Cerebral contusion	1	2.5
Surgery		
Decompressive craniectomy with lax duroplasty	8	20
Craniotomy with clipping of aneurysm	4	10
Craniotomy with tumor decompression	2	5
Craniotomy and evacuation of hematoma	18	45
Decompressive craniectomy with evacuation of Hematoma	7	17.5
Craniotomy with excision of brain tuberculoma	1	2.5

Table I (a): Demographic and clinical data of Patients: (n=40)

Among the 40 patients enrolled in the study, the mean age was 47.6 years. A male predominance was observed, with 70% of the participants being male and 30% female. Regarding comorbidities, 15% patients were diabetic, and 30% had history of hypertension. The common diagnosis were intracerebral hematoma and subdural hematoma, each comprising 27.5% and 25% of cases respectively. This was followed by ischemic stroke (20%) and extradural hematoma (10%). Less frequently observed conditions included brain tumors, ruptured aneurysms and cerebral contusion. Craniotomy and evacuation of hematoma was the most commonly performed surgery, undertaken in 45% of the patients.

Parameters	Frequency (F)	Percentage (%)
Incision length (cm)		
Mean	9.775 cm	
Incision breadth(cm)		
Mean	9.3 cm	
Size of craniotomy		
<=25 cm^2	16	40
>25 cm^2	24	60
Glasgow coma scale		
Mild (13-15)	10	25
Moderate (9-12)	22	55
Severe(<=8)	8	20
Type of skin closure		
Mattress	14	35
Continuous interlocking	26	65
Dural defect length		
None	26	65
1cm	7	17.5
2cm	7	17.5
Duration of drain (days)		
<5 days	22	55
>=5 days	18	45
Days of ICU stay		
<5 days	10	25
>=5 days	30	75
Complications		
None	7	17.5
Periorbital swelling	29	72
CSF leak	4	10
Surgical site infection	12	30
Wound dehiscence	11	27.5
Meningitis	2	5
Pneumocephalus	1	2.5

Table I (b): Clinical parameters, Perioperative data and surgical outcome of patients (n=40)

The mean incision length and breadth were 9.775 cm and 9.3 cm, respectively. Craniotomies measuring more than 25 cm^2 were more frequently observed, accounting for 60% of cases. A majority of patients (55%) presented with a moderate Glasgow Coma Scale (GCS) score at the time of admission. Regarding skin closure techniques, continuous interlocking suturing was the most commonly applied method (65%) while mattress suture was used in 35% of cases. The mean ICU stay was 8.6 days, and the average total hospital stay was 17.8 days. In terms of dural closure, 65% of patients had no dural defect. Sub-galeal drains were typically maintained for less than 5 days in the majority of patients (55%), with the mean drain duration being 4.55 days. The prevalence of complications (at least one complication) following drain placement in intracranial surgeries was 82.5%. Periorbital swelling was the most frequently reported complication (72%), followed by surgical site infection (30%) and wound dehiscence (27.5%). Less frequently observed complications included CSF leaks, meningitis, and pneumocephalus.

Parameters	Duration of drain less than 5 days	Duration of drain more than 5 days	P value (0.05)
Age			
<=20	4	0	0.23
21-39	3	5	
40-60	8	7	
>60	7	6	
Sex			
Male	17	11	0.26
Female	5	7	
Diabetes Mellitus (+)	33	3	0.534
Diabetes Mellitus (-)	189	15	
Hypertension (+)	74	8	0.122
Hypertension (-)	18	10	
Diagnosis			
Ischemic stroke	4	4	0.313
Intracerebral hematoma	4	7	
Ruptured aneurysm	2	2	
Brain tumor	1	1	
Extradural Hematoma(EDH)	4	0	
Subdural Hematoma(SDH)	7	3	
Cerebral contusion	0	1	
Type of Surgery			
Decompressive craniectomy with lax	4	4	
Duroplasty	3	1	
Craniotomy with clipping of aneurysm	2	0	
Craniotomy with tumor decompression	7	11	
Craniotomy and evacuation of hematoma	6	1	
Decompressive craniectomy with evacuation of Hematoma	0	1	
Glasgow coma scale			
Mild	7	3	

Moderate	12	10	0.159
Severe	3	5	
Dural defect			
None	14	12	0.514
1cm	3	4	
2cm	5	2	
Type of skin closure			
Mattress	8	6	0.87
Continuous interlocking	14	12	
Complications			
No complications	5	2	0.97
Complications+	17	16	

Table II: Association of patient characteristics and surgical factors with duration of drain: (n=40)

Drain duration was independent of patient characteristics like age, sex, diagnosis, type of surgery, comorbidities, neurological status, or surgical factors (dural defect and type of skin closure) in this cohort. There is also no significant association of complications with the duration of drain placement. Sub group descriptive frequency analysis showed that drain duration was independent of the individual complications like periorbital swelling and wound dehiscence, implying no added benefit of reducing wound dehiscence and periorbital swelling by keeping the drain for longer period of time.

DISCUSSION

The average drain time in this study is 4.55 days, supports current recommendations that early drain removal decreases the risk of an infected hematoma with little compromise to hematoma formation. The common complications observed were periorbital swelling (72%), surgical site infections (30%), and wound dehiscence (27.5%). The commonest complication being periorbital swelling may be due to tracking of fluid along the subcutaneous planes, exacerbated by subgaleal drainage dynamics as also mentioned by Gazzeri et al.[6] These complications are consistent with previously reported postoperative complications following craniotomies, including intracranial or extracranial hemorrhage, cerebrospinal fluid (CSF) leakage, delayed wound healing, and wound infections.[11, 12] While subgaleal drains are routinely employed to prevent subgaleal fluid collections and minimize wound tension, inappropriate management of these drains may contribute to postoperative complication. Our findings align with the study by Hani et al., which demonstrated that subgaleal drain placement is generally safe and effective, with no reported parenchymal injuries.[13] However there are some mentions in research studies done by Roth et al[7] and Van Roost et al[9] of very rare but serious complications such as intracranial hypotension, hematoma formation, and pseudo hypoxic brain swelling associated with suction drainage. The result of this research states that there is a change in opinion for subgaleal drains in comparison with subdural drains due to the fact that with the former the placement is quick and clean and the possibility of direct cortical injury is less.[2,8,13] Moreover, the infection rates post-surgery in our study were very low which is suggestive of a good sterile technique and a careful attempt at prophylactic antibiotics.[3,4] After all, proper adjustment of suction strength and continuous patient monitoring is to be ensured. The lack of correlation between drain duration and patient factors contrasts with Roth et al[7] who associated prolonged drainage with comorbidities like diabetes. This discrepancy may stem from our smaller sample size or stricter adherence to the 30 mL/24-hour output threshold for removal. Our findings align more closely with the TOSCAN trial's post hoc analysis by Hani et al[13] which favored subgaleal over subdural drains for safety and comparable efficacy. The is no significant association between the duration of drain and the presence of complications. This suggests that complication rates were similar whether drains were removed earlier (<5 days) or later (≥5 days).This supports the fact that we have removed drain not considering the presence of complications but only keeping up the criteria of 30ml/day. In contrast to the study done by Roth et al[7], which stated the higher infection rates with prolonged drain placement, our study does not state any association. This may indicate strict aseptic protocols in our institute as well as exclusion of immunocompromised patients. This unassociated assertion is in alignment to the study done by Gazzeri et al[6], where drain duration was independent of outcomes.

Further studies involving larger sample sizes and comparative analyses are warranted to validate these findings and optimize best practices in neurosurgical care.

LIMITATIONS

This study has limitations inherent to its single-center design and small sample size (n=40), which may limit generalizability. Larger, multi-center studies could validate our findings and explore subgroup analyses (e.g., tumor vs. trauma patients). Additionally, the lack of a control group (e.g., no-drain patients) precludes definitive conclusions about drain efficacy.

CONCLUSION

Subgaleal drain placement following intracranial surgery appears to be generally safe and effective, with the majority of patients undergoing drain removal within five days. There is no significant association observed between drain duration and other demographic and surgical parameters including complications. The complications after drain placement are minor and usually self-limiting. Early removal of subgaleal drain appears feasible across diverse populations.

REFERENCES

1. Hamou HA, Kotliar K, Tan SK, Weiß C, Christian B, Clusmann H, et al. Surgical nuances and placement of subgaleal drains for supratentorial procedures—a prospective analysis of efficacy and outcome in 150 craniotomies. Acta Neurochir (Wien). 2020;162(4):729–36.

2. Ishfaq A. Outcome in chronic subdural hematoma after subdural vs. subgaleal drain. J Coll Physicians Surg Pak. 2017; 27(7):419–22.

3. Abu Hamdeh S, Lytsy B, Ronne-Engstrom E. Surgical site infections in standard neurosurgery procedures: a study of incidence, impact and potential risk factors. Br J Neurosurg. 2014; 28(2):270–5.

4. Barker FG 2nd. Efficacy of prophylactic antibiotics against meningitis after craniotomy: a meta-analysis. Neurosurgery. 2007; 60(5):887–94.

5. Kumar A, Maartens NF, Kaye AH. Evaluation of the use of BioGlue in neurosurgical procedures. J Clin Neurosci. 2003; 10(6):661–4.

6. Gazzeri R, Galarza M, Neroni M, Canova A, Refice GM, Esposito S. Continuous subgaleal suction drainage for the treatment of chronic subdural hematoma. Acta Neurochir (Wien). 2007; 149(5):487–93.

7. Roth J, Galeano E, Milla S, Hartmannsgruber MW, Weiner HL. Multiple epidural hematomas and hemodynamic collapse caused by a subgaleal drain and suction-induced intracranial hypotension: case report. Neurosurgery. 2011; 68(6):E271–5.

8. Li S, Farsakh A, Toomey F, Tan D, Tran V, Castle-Kirszbaum M, et al. Subdural versus subgaleal drain placement after minicraniotomy for chronic subdural hematoma. Oper Neurosurg (Hagerstown). 2025; 28(1):69–75.

9. Van Roost D, Thees C, Brenke C, Oppel F, Winkler PA, Schramm J. Pseudohypoxic brain swelling: a newly defined complication after uneventful brain surgery, probably related to suction drainage. Neurosurgery. 2003; 53(6):1315–26.

10. Schmidt FA, Schön V, Petr O, Freyschlag CF, Thomé C. Subgaleal drainage with one burr-hole for chronic subdural hematomas: Our two-years' experience. Brain Spine. 2024; 4(6):101738.

11. Mantur M, Lukaszewicz-Zajac M, Mroczko B, Kulakowska A, Ganslandt O, Kemona H, et al. Cerebrospinal fluid leakage—reliable diagnostic methods. Clin Chim Acta. 2011; 412(11–12):837–40.

12. Rotenberg BW, Marchie A, Cusimano MD. Skin sealants: an effective option for closing cerebrospinal fluid leakage. Can J Surg. 2004; 47(6):466–8.

13. Hani L, Vulcu S, Branca M, Fung C, Z'Graggen WJ, Murek M, et al. Subdural versus subgaleal drainage for chronic subdural hematomas: a post hoc analysis of the TOSCAN trial. J Neurosurg. 2019:1–9 Aug 30; 133(4):1147-1155.

Utility of Enterocheck as a Rapid Diagnostic Tool for Typhoid Fever in Children

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ABSTRACT

Introduction: Typhoid is a major cause of morbidity and mortality worldwide. The annual incidence in the Indian subcontinent including Nepal has approximately 6 million cases each year. Blood culture is the gold standard for diagnosis but it requires well-equipped laboratory and trained staffs. Enterocheck is a rapid immunoassay which detects IgM antibodies to lipopolysaccharide specific to S. typhi in human blood. It is an alternative test which detects early infection. **Aims:** To study the sensitivity and specificity of Enterocheck for diagnosing typhoid. **Methods:** The cross-sectional study was carried out in the department of Pediatrics and Microbiology at Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke, from August 2023 to February 2024, on 145 children, above 6 months- 15 years of age, who presented with fever for more than 72 hours and other features (e.g. headache, abdominal pain, vomiting, diarrhea or constipation, hepatomegaly, splenomegaly) suggestive of typhoid fever. Blood culture was done by aseptic standard method and Enterocheck was done according to the manufacturer's instructions. **Results:** Of the 145 cases, 17 (11.7%) had blood cultures positive for S. typhi and 29 (20%) were positive using Enterocheck. Male: female ratio was 2.15:1 and was most common in the age group 5 to 10 years (51.03%). The sensitivity and specificity of Enterocheck was 88.23% and 89.06% respectively (p-value<0.01). **Conclusion:** Enterocheck test was easy to perform and did not require special equipment or trained staffs. It had high sensitivity and specificity. Thus, it can be used as an alternative to blood culture for diagnosis of typhoid fever.

Keywords: Blood culture, Enterocheck, Sensitivity, Specificity, Typhoid fever

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INTRODUCTION

Typhoid fever (TF) is a systemic febrile illness caused by Salmonella serotypes S. typhi, S. paratyphi A, B and C.[1] It is a major cause of morbidity and mortality worldwide, causing about 21 million cases with >600,000 deaths each year, according to World Health Organization.[2,3] The disease occurs in all age group with highest incidence among children aged 5 to <15 years.[4] The annual incidence in South Asia is 976 per 100,000 people and the Indian subcontinent including Nepal has approximately 6 million cases each year.[5,6] It is transmitted faeco-orally and more cases are seen in areas with increased urbanization, limited safe water and health systems.[3] Signs and symptoms of TF are non-specific. Therefore, laboratory tests are essential for accurate diagnosis.[7,8] Blood culture is the gold standard for diagnosis with sensitivity of approximately 40%-60%.[9] However, it requires well-equipped laboratory and trained staffs, that are significantly deficient in rural areas of developing world.[8,9] Widal test has been traditionally used as a rapid serologic test but it shows moderate sensitivity and specificity. Therefore, a rapid diagnostic method, which is reliable, easy to perform, with good sensitivity and specificity, without need for sophisticated equipment, is needed. Enterocheck is a rapid immunoassay which works on the principle of immunochromatography for detection of IgM antibodies to lipopolysaccharide specific to S. typhi in human blood.[9,10] Detection of IgM antibodies serve as a good early marker of recent infection of disease. This study was undertaken to evaluate the role of Enterocheck test in diagnosis of typhoid fever.

METHODS

The cross-sectional study was carried out in the department of Pediatrics and Microbiology at Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke from August 2023 to February 2024. Ethical clearance was obtained from the Insti

tutional Review Committee, Nepalgunj Medical College and Teaching Hospital. The study included 145 children, above 6 months to 15 years of age, who presented with fever for more than 72 hours and other features (e.g. headache, abdominal pain, vomiting, diarrhea or constipation, hepatomegaly, splenomegaly) suggestive of typhoid fever. Selection of cases was done by the convenient sampling method. After obtaining written informed consent, detailed relevant history and clinical examination, a blood sample by vein puncture was collected using aseptic techniques for blood culture and the Enterocheck test.

Blood culture: About 2 ml of blood was collected from the peripheral vein, inoculated into brain heart infusion (BHI) broth with 0.5 % SPS (sodium polyanethol sulphonate) bottles in 1:10 dilution and incubated at 37°C for 1 week. The formation of turbidity and hemolysis indicated the growth of bacteria. Once growth was seen on liquid medium, it was then sub-cultured after 1, 3, 7 days on blood agar and MacConkey agar. The isolated bacteria were identified to the species level by standard microbiological tests (Colony characteristics on different culture media, Gram stain findings and results of different biochemical tests (indole, triple sugar iron agar, citrate, urease and oxidase). Inoculation and sub-culturing was done by on-duty lab technician and reporting was done by microbiologist as per standard protocol.

Enterocheck test: was conducted on serum samples according to the manufacturer's instructions. The kit components of the device were brought to room temperature before testing. 5µl of serum was dispensed into the specimen port 'A' using a micropipette, and five drops of sample running buffer were dispensed into the buffer port 'B'. At the end of 15 minutes, results were interpreted according to leaflet, by on-duty technician.

The results were tabulated and statistically analyzed using SPSS version 25. Using blood culture as the gold standard, the sensitivity, specificity, positive and negative predictive values of the Enterocheck test were calculated and Chi square test was applied to calculate p-value.

RESULTS

A total of 145 patients, clinically suspected of typhoid fever, were investigated by both blood culture and Enterocheck. Among them, 17 (11.7%) patients had blood cultures positive for S. typhi and 29 (20%) were positive using Enterocheck. In the study, 99 (68.27%) were males with a male: female ratio of 2.15:1, as shown in the Figure 1. Most of the cases were, aged between 5 to 10 years, 74 (51.03%), with the median age of 10 years. 39 (26.89%) cases were of 6 months to 5 years, and 32 (22.06%) were aged 10-15 years (Figure 2).

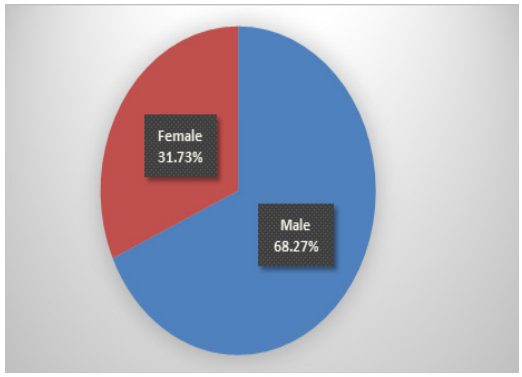

Figure 1: Sex distribution of the study population

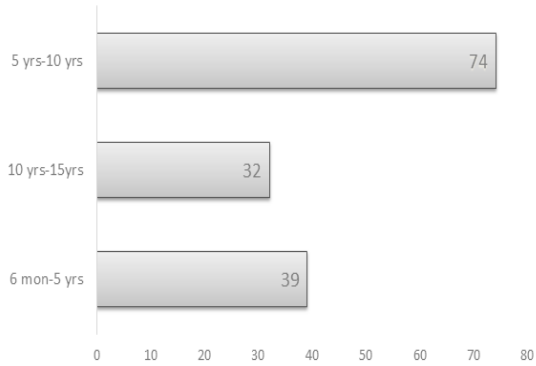

Figure 2: Age distribution of the study population

Of the 145 patients studied, 31 were positive for S. typhi by Enterocheck or blood culture or both. Both tests were positive in 15 of the 31 cases. In 14 patients, Enterocheck was positive but blood culture was negative and in 2 Enterocheck negative but blood culture was positive, as shown in Table I. Using blood culture as the gold standard, the sensitivity of Enterocheck was 88.23%, specificity 89.06%, negative predictive value 98.27%, positive predictive value 51.72% and there was statistically significant association ($p<0.01$).

Enterocheck	Blood Culture		
	Positive	Negative	Total
Positive	15	14	29
Negative	2	114	116
Total	17	128	145

Table I: Comparison of results of Enterocheck with blood culture

Sensitivity- 88.23%, negative predictive value- 98.27%, specificity- 89.06%, positive predictive value- 51.72%, p-value <0.01.

DISCUSSION

Typhoid fever is a systemic illness with a significant morbidity and mortality in developing countries.[11] Any delay in diagnosis and inappropriate therapy increases the risk of outcome.[12] Blood culture has remained the gold standard for diagnosis of typhoid fever. However, a study from Delhi found it of limited

value when undertaken during the early phase of illness when isolation of the organism is difficult.[11] The sensitivity of blood culture in typhoid fever is also limited by the low bacterial count in blood and prior antimicrobial therapy.[12]

In the present study blood culture positivity among clinically suspected typhoid cases was in 17 cases (11.70%). Similar to the study by Sreenivasa B et al in India has positivity of 14%.[13] In a study by Devaranavadagi RA et al blood culture was positive in 20% of cases[14] which is contrast to our study. The relative low rate of positivity in the present study might be due to widespread and irrational use of antibiotics and low volume of blood obtained for cultures among children. Enterocheck test was positive in 20.48% in a study by Anagha K et al[15] which is similar to the present study where positivity of Enterocheck test was 20%. The result is also consistent with the study by Sreenivasa B et al where test was positive in 27.5% cases.[13]

In present study, male predominance was seen 68.27%. Similar results were reported in studies by Jog S et al[16] and Ganesh R et al.[17] Commonest age group of typhoid fever in the present study was 5 to 10 years (51.03%) similar to the study by Devaranavadagi RA et al.[14] A study done by R Modi et al also reported maximum incidence of typhoid in the age group 6 to 10 year.[18] These results were in concordance with the concept that typhoid fever is common in school age children. They are at high risk of consuming contaminated drinking water and street foods which make them more vulnerable to exposure to typhoid bacilli.

The sensitivity of Enterocheck in the present study was 88.23% and specificity was 89.06%. Similar to the study by Anusha R et al where the sensitivity and specificity of Enterocheck was 85.5% and 88.6% respectively.[19] Whereas in a study by Narayanappa D et al sensitivity and specificity of Typhidot-M was 92.6% and 37.5% respectively.[20] This difference might be due to genomic diversity among S.typhi isolates and differences in antigenic epitopes, various stages of the illness and the rate of increase of IgG antibodies, which might interfere with IgM antibodies. The present study showed statistically significant association between Enterocheck and blood culture (p-value <0.01), similar to the study by Maheshwari V et al[21] and Udayakumar S et al.[22] Two patients in the present study were positive by blood culture but negative by Enterocheck. The false negative results by latter might be due to test's failure to detect low levels of antibodies.[2] False positive results might be because of prior treatment with antibiotics or low bacterial counts in blood.[23]

LIMITATIONS

The sample size was small with convenient sampling method. Blood culture, used as the gold standard, itself has limited sensitivity, which might have affected the result. Cross-reactivity of Enterocheck with non-typhoidal Salmonella or other febrile illnesses, prior antibiotics use and variable timing of illness during sample collection in different patients might also have altered the specificity.

CONCLUSION

Enterocheck is a practical alternative to other tests for rapid diagnosis of typhoid fever, where traditional culture facilities are not available. It has high sensitivity and specificity, can detect cases early, and is easy to perform with minimal infrastructure and availability of results within about 15 minutes.

REFERENCES

1. Willke A, Ergonul O, Bayar B. Widal test in diagnosis of typhoid fever in Turkey. Clin Diagn Lab Immunol. 2002; 9(4):938–41.
2. Olsen SJ, Pruckler J, Bibb W, Thanh NT, Trinh TM, Minh NT, et al. Evaluation of rapid diagnostic tests for typhoid fever. J Clin Microbiol. 2004; 42(5):1885-9.
3. Crump JA, Luby SP, Mintz ED: The global burden of typhoid fever. Bull World Health Organ. 2004; 82(5):346-53.
4. World Health Organization. Typhoid vaccines: WHO position paper. 2018. Available at https://www.who.int/immunization/policy/position_papers/typhoid/en/
5. Buckle GC, Walker CLF, Black RE. Typhoid fever and paratyphoid fever: Systematic review to estimate global morbidity and mortality for 2010. J Global Health.2012;2(1):1-9.
6. Divyashree S, Nabarro L, Veeraraghavan B, Rupali P. Enteric fever in India: Current scenario and future directions. Tropl Med Internat Health. 2016; 21(10):1255–62.
7. Dutta S, Sur D, Manna B, Sen B, Deb AK, Deen JL, et al. Evaluation of new-generation serologic tests for the diagnosis of typhoid fever: data from a community-based surveillance in Calcutta, India. Diag Microbiol Infect Dis. 2006; 56(4):359-65.
8. Krishna S, Desai S, Anjana VK, Paranthaaman RG. Typhidot (IgM) as a reliable and rapid diagnostic test for typhoid fever. Ann Trop Med Public Health. 2011; 4:42-4.
9. Wijedoru L, Mallett S, Parry CM. Rapid diagnostic tests for typhoid and paratyphoid (enteric) fever. Cochr Database Systematic Rev. 2017; 26(5).
10. Ghimire JP, Upadhyay RR. Prevalance of typhoid fever in Kathmandu valley and its rapid diagnosis by detection of IgM antibodies. J Nepal Assoc Med Lab Sciences. 2008; 9:7–10.
11. Sherwal BL, Dhamija RK, Randhawa VS, Jais M, Kaintura A, Kumar M. A comparative study of Typhidot and Widal test in patients of Typhoid fever. J Indian Acad Clin Med. 2004; 5:244-6.
12. Begum Z, Hossain MA, Shamsuzzaman AK, Ahsan MM, Musa AK, Mahmud MC, et al. Evalutaion of Typhidot (IgM) for early diagnosis of typhoid fever. Bangladesh J Med Microbiol. 2009; 3:10-13.
13. Sreenivasa B, Kumar GV. Comparative Study of Widal and Typhidot Test in the Diagnosis of Typhoid Fever in Children. J Nepal Paediatr Soc. 2016; 36(2):131-5.
14. Devaranavadagi RA, Srinivasa S. A study on clinical profile of typhoid fever in children. Int J Contemp Pediatr. 2017:4(3):1067-73.
15. Anagha K, Deepika B, Shahriar R, Sanjeev K. The easy and early diagnosis of typhoid fever. J Clin Diagn Res. 2012; 6(2):198-9.

16. Jog S, Soman R, Singhal T, Rodrigues C, Mehta A, Dastur FD. Enteric fever in Mumbai–clinical profile, sensitivity patterns and response to antimicrobials. JAPI. 2008;56:237-40.

17. Ganesh R, Janakiraman L, Vasanthi T, Sathiyasekeran M. Profile of typhoid fever in children from a tertiary care hospital in Chennai-South India. Indian J Pediatr. 2010; 77(10):1089-92.

18. Modi R. Clinical profile and treatment outcome of typhoid fever in children at a teaching hospital, Ahmedabad, Gujarat, India. Int J Med Sci Public Health. 2016; 5:212-6.

19. Anusha R, Ganesh R, Lalitha J. Comparison of a rapid commercial test, Enterocheck WB®, with automated blood culture for diagnosis of typhoid fever. Ann Trop Pediatr. 2011; 31(3):231-4.

20. Narayanappa D, Sripathi R, Jagdishkumar K, Rajani HS. Comparative study of dot enzyme immunoassay (Typhidot-M) and Widal test in the diagnosis of typhoid fever. Indian Pediatr. 2010; 47:331-3.

21. Maheshwari V, Kaore NM, Ramnani VK, Sarda S. A comparative evaluation of different diagnostic modalities in the diagnosis of typhoid fever using a composite reference standard: A tertiary hospital based study in Central India. JCDR. 2016;10(10):1-4.

22. Udayakumar S, Pushpalatha K, Sagar HN, Swathi M, Yoganand R, Sushma C. Comparative study of Typhidot-M with Widal and blood culture in diagnosis of enteric fever. Indian Journal of Child Health. 2017;4(1):64-7.

23. Mohanty SK, Ramana KV. Single and unpaired sera tube Widal agglutination test in enteric fever. Saudi J Gastroenterol. 2007; 13(4):213.

Assessment of Serum Calcium and Phosphorus in Patients with Hypothyroidism: A Hospital-Based Cross-Sectional Study

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ABSTRACT

Introduction: Hypothyroidism is a clinical status resulting from a deficiency of thyroid hormones or, more rarely, from their impaired activity at the tissue level. Divalent ions, such as calcium and phosphorus are required as cofactors for many enzymes in various metabolic pathways that are directly or indirectly regulated by thyroid hormones. So, a decrease in thyroid hormone can result in mineral disturbances, which lead to an increased incidence of osteoporosis, metabolic syndrome, and cardiovascular diseases. **Aims:** To assess the alteration of serum calcium and phosphorus in patients with hypothyroidism. **Methods:** A Hospital-based comparative cross-sectional study was conducted at Nepalgunj Medical College Teaching Hospital, Kohalpur, Nepal. A total of 130 participants, aged 18–60 years, were selected for the study. Out of these, 65 participants diagnosed with hypothyroidism were recruited into the hypothyroid group, and 65 euthyroid, healthy individuals visiting the hospital for routine check-ups were recruited into the euthyroid group. Blood samples were collected over a six-months period, starting from September 27, 2024, and analyzed for free triiodothyronine, free thyroxine, thyroid-stimulating hormone, calcium, and phosphorus to assess the alterations in calcium and phosphorus levels in hypothyroidism. **Results:** Our study showed that serum calcium levels were significantly decreased, while serum phosphorus levels were significantly increased, in both subclinical hypothyroidism and overt hypothyroidism ($p < 0.05$) compared to euthyroid individuals. Among the hypothyroid group, serum thyroid-stimulating hormone manifested a significant negative correlation with calcium ($r = -0.275$, $p = 0.02$) and a positive correlation with phosphorus ($r = 0.166$, $p = 0.186$). **Conclusion:** The present study concludes that hypothyroid participants exhibited serum electrolyte disturbances, such as decreased calcium and increased phosphorus in comparison to euthyroid participants.

***Keywords*:** Hypothyroidism, Serum Calcium, Phosphorus, Thyroid hormones

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INTRODUCTION

Approximately 300 million people worldwide suffer from thyroid dysfunction.[1] In Nepal prevalence of thyroid dysfunction varies between 22.42% to 29.0%[2-4] whereas prevalence of hypothyroidism ranges between 12.41% to 25%.[2-4] Hypothyroidism is a medical condition characterized by increased thyroid stimulating hormone (TSH) with normal or decreased thyroid hormones.[5] The divalent ions like calcium and phosphate are required for many enzymes as a cofactor in various metabolic pathways, which are directly or indirectly regulated by thyroid hormones.[6] Hypocalcemia and hyperphosphatemia are common mineral disturbances in hypothyroidism.[7,8] According to some literature, hypothyroidism causes a drop in serum calcium and phosphorus[6, 9] however other studies reported an increase in serum phosphorous and a decrease in serum calcium.[10] Even in another study, normal levels of serum calcium and phosphorus were observed.[11] Metabolism of cal-

cium and phosphorus are often altered in thyroid disorders[12] and some studies indicates that abnormalities in the metabolism of these divalent cations are linked to metabolic disorders, hypertension, and cardiovascular diseases.[13,14] Since the impact of thyroid hormones on serum calcium and phosphorus is yet unclear and there is a paucity of data about the impact of thyroid hormones on serum calcium and phosphorus from western region of Nepal. So, the current study was undertaken with an aim to assess serum calcium and phosphorus levels in patients with hypothyroidism and compare them with euthyroids in a tertiary care hospital at Kohalpur and the data generated through the present study will help to formulate standard treatment guidelines for better patient care as needed.

METHODS

A hospital-based comparative cross-sectional study was conducted at the Department of Biochemistry of Nepalgunj Medical College Teaching Hospital (NGMCTH), Kohalpur, from September 2024 to March 2025. Ethical clearance for the study was obtained from the Institutional Review Committee of NGMCTH (Ref: 19/081-082 dated September 27, 2024), and oral and written consents were obtained from all participants before enrollment in the study. The participants were of both sexes, with an age range between 18 and 60 years. On the basis of participants self-reporting as well as on the basis of recent clinical and laboratory examination, participants having hepatic disorders, diabetes mellitus, cardiovascular disorders, pregnant women, bone diseases and taking mineral supplements were excluded from the study. Using the following formula, a convenient sampling technique was employed to determine the sample size.[2]

Prevalence of hypothyroidism (P): 12.41%[2]

Error (d)= 8 %

Z= 1.96

q =1-p = 0.875

Sample size (n) = Z^2pq/d^2

$= (1.96)^2(0.1241)\ (0.875)/\ (0.08)^2$

=65

A total of 130 participants were enrolled in the study. Out of which 65 participants attending the medicine outpatient department of NGMCTH diagnosed with hypothyroidism were enrolled in the hypothyroid group which were further stratified into subclinical hypothyroidism (SCH) and overt hypothyroidism (OHY) and an equal number of age and sex matched healthy individual having normal thyroid function test who attended the hospital for routine health checkup were enrolled in the euthyroid group. Three milliliters of fasting venous blood were collected in a gel tube under aseptic conditions. They were subjected to centrifugation for 5 minutes at 3500 revolutions per minute (RPM) to separate serum for biochemical analysis. Serum thyroid-stimulating hormone (TSH) was estimated by sandwich immunoluminometric assay, while serum free triiodothyronine (FT3) and free thyroxine (FT4) were assessed by competitive immunoluminometric assay using Maglumi 800. Serum calcium and phosphorus was estimated by Arsenazo III and phosphomolybdate method respectively using Mindray BS 430 wet chemistry analyzer. Thyroid function test, included FT3, FT4 and TSH. Data was entered in a Microsoft Excel spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. The data was not normally distributed so all the biochemical parameters were expressed as median with inter quartile range (IQR). The Mann- Whitney test was applied to compare the biochemical parameters of hypothyroid and euthyroid group. Spearman's correlation was employed to see the correlation of TSH with calcium and phosphorus among the hypothyroid group. A p-value <0.05 was considered statistically significant.

RESULTS

Out of 130 participants in the current study, the majority of participants were female in both the hypothyroid group (43) and the euthyroid group (45) and the majority of participants belonged to the age group 51 – 60 years in both the hypothyroid and euthyroid group.

Parameters		Median (Interquartile range)		
		Total participants	Hypothyroid group	Euthyroid group
Age (years)		44.91 ± 10.36 (23 – 60)	45.92 ± 10.43 (23 – 60)	43.89 ± 10.26 (25 – 59)
Age group (years)	≤ 30	17 (13.0%)	9 (13.8%)	8 (12.3%)
	31 - 40	37 (28.4%)	17 (26.1%)	20 (30.8%)
	41 - 50	21 (16.1%)	11 (16.9%)	10 (15.4%)
	>50	55 (42.3%)	28 (43.0%)	27 (41.5%)
Sex	Male	42 (32.3)	22 (33.8 %)	20 (30.8%)
	Female	88 (67.7)	43 (66.2 %)	45 (69.2%)
TSH (µIU/ml)		4.21 (2.57 – 12.1)	12.1 (8.3 – 24.5)	2.57 (1.73 – 3.11)
FT4 (ng/dl)		1.23 (1.1 – 1.43)	1.15 (0.74 – 1.34)	1.3 (1.2 – 1.49)
FT3 (pg/ml)		2.89 (2.13 – 3.21)	2.49 (1.23 – 2.90)	3.1 (2.56 – 3.35)
Calcium (mg/dl)		9.14 (2.57 – 12.1)	8.6 (7.91 – 9.41)	9.7 (9.01 – 10.12)
Phosphorus (mg/dl)		3.25 (2.93 – 3.75)	3.66 (2.93 – 3.92)	3.12 (2.91 – 3.37)

TSH: Thyroid stimulating hormone, FT4: Thyroxine, FT3: Free triiodothyronine

Table I: Baseline characteristics of the hypothyroid group and euthyroid group

Table I shows that the majority of the participants in both the hypothyroid group and the euthyroid group belonged to the age group ≥50 years, which was about 43.0% and 41.5%, respectively. Serum TSH and phosphorus levels increased, while serum FT3, FT4 and Calcium Levels decreased in the hypothyroid group compared to the euthyroid group. Age was expressed in mean ± SD (minimum - maximum age).

Parameters	Median (Interquartile range)			p value a vs c	p value b vs c
	Hypothyroid group		Euthyroid group [c]		
	SCH[a](n = 33)	OHY[b](n = 32)			
Age (years)	44 (34 – 56)	47 (31 – 55)	45 (35 – 54)	0.719	0.957
TSH (µIU/ml)	9.76 (6.40 – 16.6)	22.5 (11.5 – 49.4)	2.57 (1.73 – 3.11)	0.001	0.001
FT4 (ng/dl)	1.23 (1.14 – 1.39)	0.59 (0.18 – 0.71)	1.3 (1.2 – 1.49)	0.034	0.001
FT3 (pg/ml)	2.65 (2.21 – 3.12)	1.16 (1.05 – 1.69)	3.1 (2.56 – 3.35)	0.023	0.001
Calcium (mg/dl)	8.7 (8.17 – 9.66)	8.51 (7.91 – 9.17)	9.7 (9.01 – 10.12)	0.001	0.001
Phosphorus (mg/dl)	3.50 (3.05 – 3.89)	3.73 (2.91 – 3.98)	3.12 (2.91 – 3.37)	0.02	0.003

TSH: Thyroid stimulating hormone, FT4: Thyroxine, FT3: Free triiodothyronine, SCH: Subclinical hypothyroidism, OHY: Overt hypothyroidism, n: Number of participants, a vs cMann-Whitney U test between SCH and euthyroid group, b vs c Mann-Whitney U test, between OHY and euthyroid group. P < 0.05 was considered statistically significant and was indicated in bold type.

Table II: Comparison of biochemical profile of participants between the hypothyroid group and the euthyroid group

Table II represents that serum calcium, FT3 and FT4 were significantly decreased in the SCH and OHY compared to euthyroid group while serum TSH and phosphorus were significantly increased in the SCH and OHY compared to euthyroid group. Mann-Whitney U test was used to generate p value.

Group	Parameter	Calcium	Phosphorus
Hypothyroid group	TSH	r: -0.275* p value: 0.027	r: 0.166 p value: 0.186

r denotes Spearman's correlation coefficient; a p-value < 0.05 was considered statistically significant and was indicated in bold type

Table III: Spearman's correlation of TSH with calcium and phosphorus in the hypothyroid group

Table III shows that serum calcium was negatively correlated with TSH, and this correlation was statistically significant (r = -0.275, p = 0.02). In contrast, there was no correlation between serum phosphorus and TSH.

DISCUSSION

The current study enrolled 65 participants diagnosed with hypothyroidism into the hypothyroid group and an equal number of euthyroid healthy participants into the euthyroid group to assess the alteration of serum calcium and phosphorus in hypothyroidism. Our study manifested female predominance with majority and minority of the participants belonged to the age group >50 years and ≤30 years respectively as well as the median age of the participants in SCH, OHY and euthyroid was 44 years, 47 years and 45 years respectively, which shows that the age differences between the comparison group were not statistically significant. However, serum calcium was significantly decreased while serum phosphorus was significantly increased in both SCH and OHY compared to the euthyroid group, respectively.

In the current study, approximately 66.2% of the participants in the hypothyroid group were female, suggesting that hypothyroidism was more prevalent in women than in men, which is consistent with the findings of the Regmi et al study (2010).[15] The higher incidence of hypothyroidism in females may be caused by estrogen, which is thought to be an antagonist of FT3 and FT4 since it competes with them for receptor protein binding sites.[16] The present study reveals that serum calcium was significantly decreased (p<0.001) in both the SCH [8.7 (8.17 -9.66)] and OHY [8.51 (7.91 – 9.17)] compared to the euthyroid group [9.7 (9.01 – 10.12)], as well as in hypothyroid participants' serum calcium, was negatively correlated with serum TSH (r: -0.275, p = 0.02) and was statistically significant. The findings of our study was in consistent with the similar studies done by Dhungana A et al[6] and Saxena S et al.[10] The possible explanation of hypocalcemia in hypothyroidism is due to decreased outflow of calcium from the cells and due to increased production of calcitonin in hypothyroidism, which promotes increased tubular excretion of calcium[17] as well as due to depressed bone turnover due to decreased thyroid hormone since thyroid hormones acts on osteoblast to stimulate osteoclastic bone resorption via nuclear receptors.[8,9]

In the current study, serum phosphorus was increased in both the SCH [3.50 (3.05 – 3.89)] and OHY [3.73 (2.91 – 3.98)] compared to the euthyroid group [3.12 (2.91 – 3.37)] and was statistically significant. This finding was in agreement with the study conducted by Saxena S. et al[10] and Dhungana A et al.[6] However, In contrast to our study Modi A et al[9] reported a significant decrease in serum phosphorus in hypothyroidism, and possibly this could be due to decreased bone turnover because in hypothyroidism the effect of thyroid hormone on osteoblast diminishes resulting in decreased osteoclastic bone resorption.[9] In our study, in hypothyroid participants, serum phosphorus was positively correlated with serum TSH, but was not statistically significant (r value = 0.166, p = 0.186), which is similar to the study done by Bharti A et al[18] where they also reported a positive correlation of serum phosphorus with serum TSH. In contrast to our study, Modi et al[9] reported a significant negative correlation of serum phosphorus with serum TSH (r value = -0.69, p value < 0.05). In our study serum phosphorus was increased and the possible reason behind this is due to increased calcitonin in hypothyroidism which is responsible for increased tubular reabsorption of phosphorus.[17] The small sample size of our hospital-based study is a limitation. Clarifying the relationship between calcium, phosphorus, and TSH can be made easier with a larger sample size and a general population investigation. Additionally, further examination of confounding variables, such as vitamin D, parathyroid hormone, and calcitonin, would have been beneficial for a better understanding of mineral metabolism and balance.

CONCLUSION

Our study concludes that serum calcium levels were significantly decreased while serum phosphorus levels were significantly increased in hypothyroid individuals compared to euthyroid healthy participants. Serum calcium and serum TSH showed a strong negative association in hypothyroidism, whereas serum phosphorus and serum TSH showed a positive correlation in hypothyroidism. So, our study recommends that hypothyroid individuals should have their serum calcium and phosphorus levels routinely checked to detect and treat the disease resulting from the malfunction in mineral metabolism and prevent the additional consequences associated with it.

REFERENCES

1. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol. 2018;14(5):301–16.
2. Sharma P, Magar NT. Prevalence of thyroid disorder in residents of Western region of Nepal. Int J App Sci Biotech. 2021 Sep 29;9(3):169-75.
3. Mahato RV, Jha B, Singh k, Yadav Bk, Shah SK, Lamsal M. Status of thyroid disorders in central Nepal: A tertiary care hospital based study. Int J App Sci Biotech. 2015; 3: 119-22.
4. Aryal M, Gyawali P, Rajbhandari N, Aryal P, Pandeya DR. A Prevalence of thyroid dysfunction in Kathmandu University Hospital, Nepal. Biomed Res 2010; 21(4): 411-5.
5. Hallengren B. Hypothyroidism- clinical findings, diagnosis, therapy. Thyroid tests should be performed on broad indications. Lakartidningen 1998; 95: 4091-6.
6. Dhungana A, Shreevastva NK, Pant S, Pokharel BR. A study of serum calcium, phosphorous and magnesium level in hypothyroid cases. J Pathol Nep 2022;12(1):1933-7.
7. Jha RK, Kondhalkar AA, Panchbudhe SA, Jha RK. Study of Calcium, Magnesium and Phosphorus in Hypothyroidism Patients in Vidarbha Region. Biosc.Biotech.res.Comm 2021; 14 (7): 99- 103
8. Sultana S, Jahan MA, Ahmed SMU, Sultana R, Ara FF. Calcium Imbalance and Hypothyroidism: Exploring the Relationship. KYAMC Journal 2024; 14(04): 194-197.
9. Modi A, Sahi N. Effect of thyroid hormones on serum calcium and phosphorous. Int J. Clin. Biochem Res. 2018; 5:570-3.
10. Saxena S, Srivastava PC, Katyal R, Das B, Pannu SJ. Evaluation of mineral status in hypothyroidism in a tertiary care centre. Int J Res Med Sci. 2020 Feb;8(2):667-71.
11. Sabuncu T, Aksoy N, Arikan E, Ugur B, Tasan E, Hatemi H. Early changes in parameters of bone and mineral metabolism during therapy for hyper-and hypothyroidism. Endocrine research. 2001 Jan 1;27(1-2):203-13.
12. Jat RK, Panwar AK, Agarwal P, Sharma C, Bansal DP, Pareek A, Tyagi A, Mathur M, Agarwal P, Sharma Sr C, Pareek Sr A. Assessment of serum minerals in subclinical hypothyroid and overt hypothyroid patients. Cureus. 2021 Aug 6;13(8).
13. Al-Hakeim HK. Serum levels of lipids, calcium and magnesium in women with hypothyroidism and cardiovascular diseases. Journal of laboratory physicians. 2009 Jul;1(02):049-52.
14. Al-Tonsi AA, Abdel-Gayoum AA, Saad M. The secondary dyslipidemia and deranged serum phosphate concentration in thyroid disorders. Experimental and molecular pathology. 2004 Apr 1;76(2):182-7.
15. Regmi A, Shah B, Rai BR, Pandeya A. Serum lipid profile in patients with thyroid disorders in central Nepal. Nepal Med Coll J. 2010;12(4):253–6
16. Vasudevan N, Ogawa S, Pfaff D. Estrogen and thyroid hormone receptor interactions: physiological flexibility by molecular specificity. Physiol Rev. 2002;82(4):923–44.
17. Sridevi D, Dambal AA, Sidrah AS, Padaki SK. A study of serum magnesium, calcium and phosphorus in hypothyroidism. Age. 2016;35(8.85):35-68.
18. Bharti A, Shrestha S, Rai R, Singh MK. Assessment of serum minerals and electrolytes in thyroid patients. Int J Adv Sci Res. 2015;1(06):259-63.

Ocular Findings in Patients with Chronic Kidney Disease: A Hospital Based Cross-Sectional Study

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ABSTRACT

Introduction: Chronic kidney disease affects every organ system including the eye. **Aims:** To study the prevalence of anterior and posterior segment ocular findings in patients with chronic kidney disease. **Methods:** This was a hospital based cross-sectional study conducted among 86 patients of chronic kidney disease of all ages and either gender from June 2024 to November 2024. Standard proforma was used to collect socio-demographic and clinical variables of the patients. Detailed ocular examination including fundus evaluation was done and diabetic retinopathy and hypertensive retinopathy was graded according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) classification and Keith-Wegener-Barker classification respectively. **Results:** The mean age of the study sample was 60.73 (±14.80) years with male preponderance (62.79%). The commonest cause of chronic kidney disease was both (diabetes and hypertension) (45.35%) followed by hypertension (40.70%). The most prevalent anterior segment ocular finding was pingecula (60.47%) followed by eyelid edema (36.05%), cataract (31.40%) and conjunctival pallor (27.91%). Retinopathy (72.09%) was the most prevalent posterior segment ocular finding. Among retinopathy, the prevalence of hypertensive retinopathy, diabetic retinopathy and both retinopathy (hypertensive and diabetic retinopathy) was 51.61%, 30.64% and 17.74% respectively. The prevalence of vitreous haemorrhage, tractional retinal detachment and maculopathy was 1.16%, 2.33% and 9.67% respectively. **Conclusion:** There is high prevalence of ocular findings in the chronic kidney disease. Regular ocular examination is mandatory for early detection and treatment to prevent ocular morbidity and blindness in chronic kidney disease.

Keywords: Chronic kidney disease, Cross- sectional studies, Diabetic retinopathy, Hypertensive retinopathy, Morbidity

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INTRODUCTION

Chronic kidney disease (CKD) is defined as decreased kidney function or presence of kidney damage for three or more months. Chronic kidney disease is an irreversible[1] and progressive process which ultimately results in end stage renal disease. It is associated with several diseases, including hypertension[2] and diabetes mellitus.[3] The eyes are the window to various systemic conditions in the body. The kidney and retina develop during the same embryonic stage around the fourth to sixth week of gestation, thus sharing a strong correlation between eye and kidney diseases.[4] The kidney and eye share developmental, structural, physiological, and pathological pathways.[5-7] Chronic kidney disease affects almost all organs of the body including eyes.[8] The various ocular findings in the chronic kidney disease are lid edema, conjunctival pallor, conjunctival and corneal calcification[9], inflammatory reactions of conjunctiva, episclera,[10,11] pingecula,[12] recurrent subconjunctival hemorrhage, rubeosis iridis, cataract, diabetic retinopathy and hypertensive retinopathy.[13,14] Deterioration of vision in CKD is due to worsening of hypertensive or diabetic retinopathy, ischemic optic neuropathy, central retinal vein occlusion and cortical blindness.[15] Limited studies of ocular findings in chronic kidney disease have been conducted in Nepal. The findings of this study would help for future planning to reduce the burden of ocular morbidities and blindness among CKD patients. The objective of this study was to determine the prevalence of anterior and posterior segment ocular findings in patients with chronic kidney disease.

METHODS

This was a hospital based cross-sectional study conducted in Ophthalmology Outpatient Department (OPD) of Manipal Teaching Hospital, Pokhara, Nepal from June 2024 to November 2024. Ethical approval was taken from the Institutional Review Committee of the Manipal College of Medical Sciences, Pokhara (Reference number: MCOMS/IRC/624). Informed consent was taken from all the patients. The sample size was calculated by using the formula 3.84 pq/d^2 ((Where, n=sample size, p= prevalence=94.05[16] q=100-p=5.95, d= desired level of precision i.e., 5% for this study). The sample size according to this formula was 85.95. Hence, this study was conducted among 86 respondents.

Non-probability convenient sampling method was used for the selection of cases. The inclusion criteria were the patients with chronic kidney disease of all ages and either gender who presented to Ophthalmology OPD or referred from Nephrology Unit of Internal Medicine. Patients of acute kidney injury were excluded from the study. Those patients who do not give consent were also excluded from the study. Predesigned proforma was used to collect the sociodemographic and clinical variables of the patients. Detailed ocular examination was done including recording of visual acuity using Snellen's letter chart or E-chart. Anterior segment was assessed with slit lamp. Fundus examination was done under mydriasis with tropicamide 1% with direct ophthalmoscope and slit lamp biomicroscope using +90D lens. Diabetic retinopathy and hypertensive retinopathy was graded according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) classification[17] and Keith-Wegener-Barker classification[18] respectively.

The entry and analysis of the data was done in Epi-info version 7. The statistical methods used were mean, frequency and percentage.

RESULTS

A total of 86 chronic kidney disease patients were included in this study. Our study showed male preponderance 54 (62.79%) as compared to female 32 (37.21%). The mean age was 60.73 (±14.80) years. The commonest cause of chronic kidney disease was both (diabetes and hypertension) 39 (45.35%) followed by hypertension 35 (40.70%) and diabetes 12 (13.95%). More than half 61 (70.93%) patients were on treatment, 31 (50.82%) drugs and 30 (49.18%) dialysis while 25 (29.07%) were not on treatment. Majority of patients had normal vision 66 patients (76.74%) followed by impaired vision 10 (11.63%) and legally blind 10 (11.63%).

Table I showed that Pingecula 52 (60.47%) was the commonest anterior segment ocular finding followed by eyelid edema 31 (36.05%), cataract 27 (31.40%), conjunctival pallor 24 (27.91%).

Majority of the CKD patients had retinopathy 62 (72.09%). Among retinopathy, hypertensive retinopathy was found in 32 (51.61%), diabetic retinopathy in 19 (30.64%) and both retinopathy (hypertensive and diabetic retinopathy) in 11 (17.74%). The prevalence of vitreous haemorrhage, tractional retinal detachment and maculopathy was 1.16%, 2.33% and 9.67% respectively (Table II).

Table III showed that Grade II hypertensive retinopathy 20 (46.51%) was most prevalent. Table IV showed that out of total of 30 diabetic retinopathy patients, NPDR was noted in 25 (83.33%), PDR in 5 (16.66%). Majority had moderate NPDR 13 (43.33%).

Anterior segments ocular findings	Number (%)
Eye lid edema	31 (36.05%)
Conjunctival congestion	4 (4.65%)
Conjunctival pallor	24 (27.91%)
Pingecula	52 (60.47%)
Pterygium	7 (8.14%)
Rubeosis iridis (NVI)	4 (4.65%)
Cataract	27 (31.40%)
Pseudophakia	14 (16.28%)

Table I: Frequency of anterior segment ocular findings in CKD patients

Posterior segment ocular findings		Number (%)
Retinopathy	Hypertensive retinopathy	32 (51.61%)
	Diabetic retinopathy	19 (30.64%)
	Both retinopathy	11 (17.74%)
	Total	62 (72.09%)
Maculopathy		6 (9.67%)
Vitreous haemorrhage		1 (1.16%)
Tractional retinal detachment		2 (2.33%)

Table II: Frequency of posterior segment ocular findings in CKD patients

Grade of hypertensive retinopathy	Number (%)
Grade I	17 (39.53%)
Grade II	20 (46.51%)
Grade III	6 (13.95%)
Grade IV	0
Total	43 (100%)

Table III: Frequency of hypertensive retinopathy in CKD patients

Classification of diabetic retinopathy		Number (%)
Non-proliferative diabetic retinopathy (NPDR)	Mild NPDR	9 (36.00%)
	Moderate NPDR	13 (52.00%)
	Severe NPDR	3 (12.00%)
	Very severe NPDR	0
	Total	25 (83.33%)
Proliferative diabetic retinopathy (PDR)		5 (16.66%)
Total		30 (100%)

Table IV: Frequency of diabetic retinopathy in CKD patients

DISCUSSION

In this study, the mean age of the study sample was 60.73 years. Different other studies noted the mean age of patients as 45.2 years, 55.9 years, 48.3 years and 50.95 years.[19,20,21,23]

In the current study, male had more prevalence of chronic kidney disease (CKD) as compared to female. Similarly, other studies also supported this finding.[16,19,20,21] However, two different studies noted CKD was high in female.[22,23] This variation may be explained by differential distribution in risk factors (e.g. genetic predisposition, dietary factors and lack of physical activities). High prevalence of CKD in male could be because the kidney function in males have faster rate of deterioration.

76.74% of the total cases had normal vision. Different other studies also noted the similar findings.[19,20,21,23] However, vision is not only the indicator of the ocular status even in the severe form of diabetic retinopathy and hypertensive retinopathy may have normal vision until macula is involved.[24] In our study, the prevalence of eyelid edema was 36.05%. Our results showed higher prevalence of eyelid edema than reported in Maharashtra, India (2.38%)[16] and Kerala, India (3.5%).[20] However, our study noted lower prevalence of eyelid edema than reported in Bharatpur, Nepal (60.67%)[19] and Kathmandu, Nepal (63.0%).[21] The possible cause of eyelid edema might be deranged renal function which prevents efficient excretion of salt and water from the body thus causing retention.[20] The fluid retention leads to generalized swelling comprising of pedal edema, facial puffiness and lid edema. In the present study, the prevalence of conjunctival pallor was 27.91%. Two studies conducted in India and Nepal showed the high prevalence of conjunctival pallor as 56.9% and 75.6% respectively.[20,21] Conjunctival pallor might be due to low haemoglobin level in chronic kidney disease patients.

The prevalence of cataract was 31.40% in our study. Different other studies found the prevalence of cataract as 13%, 18% and 61.4% respectively.[19,21,23] The possible cause of cataract might be due trapping of urea in the lens with subsequent chronic accumulation and development of an osmotic cataract.[25] The other mechanism can be due to oxidative stress in CKD patients may lead to carbamylation of lens protein.[26]

This study showed the prevalence of pingecula as 60.47%. Our study found the high prevalence of pingecula than reported in India (12.2%),[20] Bharatpur, Nepal (30.67%)[19] and Kathmandu, Nepal (39.4%).[21] Pingecula might be related to inflammatory reactions of conjunctiva which is associated with an increase in calcium.[26]

Our study showed that majority of chronic kidney disease patients had retinopathy. Among retinopathy, the prevalence of hypertensive retinopathy was high followed by diabetic retinopathy and both retinopathy (hypertensive and diabetic retinopathy). The studies conducted in Nepal, India and Bangladesh also showed the similar finding as ours.[19,20,28] However, one study conducted in Kathmandu, Nepal found that the prevalence of diabetic retinopathy was high.[21] The high prevalence of hypertensive retinopathy could be due the effects of retained nitrogen products.

In our study, among hypertensive retinopathy patients, Grade II hypertensive retinopathy was most prevalent. Many other studies have supported this findings.[20,28,29] However, two different studies conducted in Bharatpur, Nepal and Kathmandu, Nepal showed high prevalence of grade I and grade III hypertensive retinopathy respectively.[19,21]

We found that the prevalence of Non- proliferative diabetic retinopathy (NPDR) was more than Proliferative diabetic retinopathy (PDR) and among NPDR, the prevalence of moderate NPDR was high. Different studies have also found the similar findings.[19,21] However, two different studies have showed the high prevalence of mild NPDR.[20,29]

LIMITATIONS

The causal association could not be measured due to cross-sectional design of the study. The result of this study could not be generalized as this is a single hospital based study. Hence, further large scale analytical study in different centers with large sample size is required.

CONCLUSION

There is high prevalence of anterior and posterior segment ocular findings in chronic kidney disease patients. There is a need to educate the chronic kidney disease patients about need to have regular ocular examination for the early diagnosis and treatment of ocular abnormalities to prevent ocular morbidities and blindness. The study recommends holistic management of chronic kidney disease patients jointly by physician, nephrologists and ophthalmologist to improve the quality of life.

REFERENCES

1. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. Harrison's Principles of Internal Medicine. 20thed. New York: McGraw-Hill Education; 2018.
2. Tedla F, Brar A, Browne R, Brown CD. Hypertension in chronic kidney disease: navigating the evidence. Int J Hypertens. 2011:2011:132405.
3. Allison SJ. Urea inhibits insulin secretion in CKD. Nat Rev Nephrol. 2016 Oct;12(10):581.
4. Bodaghi B, Massamba N, Izzedine H. The eye: A window on kidney disease. Clin Kidney J. 2014 Aug;7(4):337-8.
5. Izzedine H, Bodaghi B, Launay-Vacher V, Deray G. Eye and kidney: From clinical findings to genetic explanations. J Am Soc Nephrol. 2003 Feb;14(2):516 -29.
6. Wilkinson- Berka JL, Agrotis A, Deliyanti D. The retinal renin angiotensin system: Roles of angiotensin II and aldosterone. Peptides. 2012 Jul;36(1):142-50.
7. Zipfel PF, Heinen S, Józsi M, Skerka C. Complement and diseases: Defective alternative pathway control results in kidney and eye diseases. Mol Immunol. 2006 Jan;43(1-2):97- 106.
8. Gao B, Zhu L, Pan Y, Yang S, Zhang L, Wang H. Ocular fundus pathology and chronic kidney disease in a Chinese population. BMC Nephrol. 2011 Nov 17;12:62.
9. Dursun D, Demirhan B, Oto S, Aydin P. Impression cytology of the conjunctival epithelium in patients with chronic renal failure. Br J Ophthalmol. 2000 Nov;84(11):1225-7.
10. Duane TD, Jaeger EA. Duane's clinical ophthalmology. 5th ed. New York: Harper and Row;1987. p.1-2.
11. Ryan SJ, Schachat AP. Medical Retina. 4th ed. Philadelphia: Elsevier Mosby; 2006. p. 1271-8.
12. Peyman GA, Sanders DR, Goldberg MF. Principles and Practice of Ophthalmology. New Delhi: Jaypee Brothers;1987. p.1205-35.
13. Evans RD, Rosner, M. Ocular abnormalities associated with advanced kidney disease and hemodialysis. Semin Dial. 2005 May-Jun;18(3):252-7.
14. Patel DV, Snead MP, Satchi K. Retinal arteriolar calcification in a patient with chronic renal failure. Br J Ophthalmol. 2002 Sep; 86(9):1063.
15. Stein JH, Hulton JJ, Kohler PO. Internal Medicine. 3rd ed. New York: Little Brown & Company; 1990. p. 809-10.
16. Sapkal D, Gadekar SA, Bhamdari MS, Deshpande SA. To study ocular findings in chronic disease patients attending a tertiary care hospital in Maharashtra. Indian Journal of Clinical and Experimental Ophthalmology. 2021;7(2):410-4.
17. Early Treatment Diabetic Retinopathy Study Research Group. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics: ETDRS report number 7. Ophthalmology. 1991 May;98(5 Suppl):741-56.
18. Downie LE, Hodgson LAB, Dsylva C, McIntosh RL, Rogers SL, Connell P, et al. Hypertensive retinopathy: comparing the Keith-Wagener-Barker to a simplified classification. J Hypertens. 2013 May;31(5):960–5.
19. Dahal P, Gauli S. Ocular findings in the chronic renal failure. Journal of College of Medical Sciences-Nepal. 2014;10(2):18-26.
20. Thulasidas M, Amin H. Ocular evaluation in patients with chronic kidney disease-A hospital based study. Open Access Journal of Ophthalmology. 2018 Jan;3(5):000164.
21. Bajracharya L, Shah DN, Raut KB, Koirala S. Ocular evaluation in patients with chronic renal failure- a hospital based study. Nepal Med Coll J. 2008 Dec;10(4):209-14.
22. Khanom T, Hossain MS, Mizan MSB, Tanveer MS, Khatun D. Ocular status with chronic kidney disease- a hospital based two year study on 150 cases. Annals of International Medical and Dental Research. 2023 Apr;9(2):127-38.
23. Mansour DE, EI-Bayomi AM, EI- Azab AM. Abnormal ocular findings in chronic renal failure patients on hemodialysis. The Egyptian Journal of Hospital Medicine. 2018 Jul;72(11):5640-6.
24. Bourquia A, Zaghloul K, Berrada S, Essamadi JE, Ramdani B, Ben Youssef S, et al. Ophthalmologic manifestations in patients under chronic hemodialysis. Ann Med Interne (Paris). 1992;143(1):18-21.
25. Berlyne GM, Ari JB, Danovitch GM, Blumenthal M. Cataracts of chronic renal failure. Lancet. 1972 Mar 4;1(7749);509-11.
26. Klein BEK, Knudtson MD, Brazy P, Lee KE, Klein R. Cystatin C, other markers of kidney disease and incidence of age–related cataract. Arch Ophthalmol. 2008 Dec;126(12):1724-30.
27. Demco TA, McCormick AQ, Richards JS. Conjunctival and corneal changes in chronic renal failure. Can J Ophthalmol. 1974 Apr:9(2):208-13.
28. Ahsan MK, Alam MR, Khanam A, Ahmed AHH, Faroque MO, Hadiuzzaman KBM, et al. Ocular fundus abnormalities in pre-dialytic chronic kidney disease patients. Journal of Biosciences and Medicines. 2019 Nov;7(11):20-35.
29. Khamar DS, Bhandari A. Study of ocular manifestations in a patient with chronic kidney disease in tertiary care rural hospital. International Journal of Advanced Research. 2024 Jan;12(1):324-52.

Retrospective Analysis of EEG Patterns in the Patients Referred for EEG at a Tertiary Care Hospital in Western Nepal

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ABSTRACT

Introduction: Electroencephalography is a non-invasive neurophysiological test that records electrical activity in the brain. It can help in the diagnosis and monitoring of various clinical conditions, like seizures and sleep disorders. Extensive research on electroencephalographic patterns is scarce, especially in Western Nepal. The study will also help to avoid the consequences of misinterpreting different waveforms. **Aims:** To analyze various normal and abnormal electroencephalographic wave patterns. **Methods:** This was an observational retrospective study analyzing electroencephalographic reports of the patients referred for electroencephalography in the Department of Psychiatry, Nepalgunj Medical College Teaching Hospital, Kohalpur, from January 2023 to December 2024. Total 290 patients who underwent a 20-minute electroencephalography, meeting the study criteria were selected. Descriptive statistics were used to analyze demographic data and electroencephalographic findings. **Results:** Out of 290 patients, 57.9% were male. The most common condition referred for electroencephalographic evaluation was seizure disorder (51%), followed by psychogenic non-epileptic seizure (24.1%). Patients with normal electroencephalographic waveforms were 79%, whereas 21% had abnormal electroencephalographic waveforms. Among normal variant waveforms, wicket waves were seen more frequently (7.42%), particularly in children and adolescents. Polyspike waves were the most frequently observed (47.54%) among the abnormal waveforms. **Conclusion:** The EEG waveforms were normal in most cases, while a few had abnormal EEG findings. The normal variants must not be misinterpreted as epileptiform discharges to avoid the consequences of misdiagnosis.

Keywords: Electroencephalography, Nepal, Normal Variant Waveforms, Polyspike, Wicket waveforms

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INTRODUCTION

Electroencephalography (EEG) began as a diagnostic tool when a German psychiatrist, Hans Berger, introduced it in 1924. An EEG is a non-invasive electrophysiological method that measures brain electrical signals to detect various neurological disorders. However, in more than half of the patients with a provisional diagnosis of epilepsy, the initial EEG does not show epileptiform activity, and the paroxysmal events are due to its low sensitivity.[1] Its sensitivity depends on various factors like age, recording procedures, and activation procedures such as hyperventilation and photic stimulation.[2] An abnormal EEG finding in a person without a history of seizure and, conversely, a normal EEG finding in seizure patients are possible.[3] Normal variant waveforms are mostly unrecognized and are misdiagnosed as epileptiform discharges in one-third of the patients.[4] A single normal EEG recording does not exclude the presence of pathology because electrographic changes are often transient.[5] It can help in the diagnosis and monitoring of various neurological conditions, including epilepsy and sleep disorders. Moreover, there is a paucity of research analyzing EEG findings in tertiary care settings in Nepal, particularly in the western region.[3] Studies of EEG abnormalities can lead to improved neurological diagnosis and management strategies. This study will address the knowledge gap regarding EEG patterns and also help to avoid the consequences of misinterpretation of different EEG waveforms. This study aims to analyse various normal and abnormal EEG wave patterns in patients referred from various departments within the tertiary care hospital.

METHODS

This was an observational retrospective study among the referred patients from various departments who underwent

EEG from January 2023 to December 2024 in Nepalgunj Medical College Teaching Hospital, Kohalpur. The calculated sample size was 290, considering the prevalence of EEG abnormalities in a tertiary care hospital at 18.69%[6] using a 4.5% margin of error[7] and 95% confidence interval. Ethical approval was obtained from the Institutional Review Committee (Ref. 60/081-082), Nepalgunj Medical College Teaching Hospital, Kohalpur, and permission to use medical records from the respective hospital departments. However, patient confidentiality was strictly maintained by anonymizing data before analysis. After obtaining ethical approval, the study was started. A convenience sampling technique was used. Data were retrieved from the hospital database. Demographic details, clinical diagnoses, and EEG-related details were collected from medical records. All patients referred from various departments for EEG were included in the study. Patients with incomplete, inadequate data and patients with artifacts affecting EEG interpretation were excluded. Descriptive statistics were used to summarize demographic data and EEG findings. Data were analyzed using SPSS version 25.0.

RESULTS

A total of 290 patients were included in the study (Table I). The majority of patients (53.8%) were in the age group of 1–18 years, followed by 33.1% who were 18 years or older, and 13.1% who were under one year of age. Males accounted for 57.9% of the sample, while females represented 42.1%. In terms of residence, 60.7% of the patients were from urban areas, whereas 39.3% were from rural areas. The most common religion among the patients was Hinduism (77.6%), followed by Christianity (11%), Buddhism (10.7%) and Islam (0.7%). Regarding the referring departments, half of the patients (50%) were referred from the Pediatrics department, 37.2% from Neurosurgery, 6.9% from Medicine and 5.9% from Psychiatry. Clinically, seizure was the most common diagnosis (51%), followed by psychogenic non-epileptic seizure (24.1%), febrile seizure (19.3%), primary headache (3.1%), and traumatic brain injury (2.4%). Based on waveform analysis, 79% of patients exhibited normal waveforms, whereas 21% showed abnormal waveforms.

Variable	Categories	Frequency (Percentage)
Age	<1 year	38 (13.10)
	1-18	156 (53.80)
	≥18	96 (33.10)
Sex	Male	168 (57.90)
	Female	122 (42.10)
Residence	Rural	114 (39.30)
	Urban	176 (60.70)
Religion	Hindu	225 (77.60)
	Buddhist	31 (10.70)
	Islam	2 (0.70)

Table I: Demographic and clinical profiles of the patients

Normal variant Waveform	Age Groups			Total (%)
	<1	1-18	>18	
Positive occipital sharp transients	1	4	1	6 (2.62)
6 Hz spike and wave	0	2	0	2 (0.87)
14 and 6 Hz spikes	0	4	0	4 (1.75)
Vertex sharp Transients	2	0	0	2 (0.87)
Benign Epileptiform Transients of Sleep	2	10	1	13 (5.69)
Wicket waves	2	13	2	17 (7.42)
Rhythmic mid-temporal theta of drowsiness	0	2	0	2 (0.87)
Subclinical rhythmic electroencephalographic discharges of acute	0	0	2	2 (0.87)
None	16	91	74	181 (79.04)

Table II: Normal Variant Waveform in relation to age

A total of 229 EEG recordings were analysed across various age groups to identify the distribution of normal EEG waveforms (Table II). The majority of patients (79.04%) exhibited no normal variant waveforms. Among the normal variants, wicket waves were the most common, observed in 17 patients (7.42%), with the highest occurrence particularly in children and adolescents (1–18 age group). Benign Epileptiform Transients of Sleep (BETS) were found in 13 patients (5.69%), predominantly in the 1–18 age group, followed by the <1 year and >18 age groups. Positive Occipital Sharp Transients (POSTs) were observed in 6 patients (2.62%) across all age groups. Whereas 14 and 6 Hz spikes were seen in 4 patients (1.75%), exclusively in the 1–18 age group. Vertex sharp transients were present in 2 patients (0.87%), all under the age of one. Other waveforms observed included 6 Hz spike and wave, Rhythmic Mid-Temporal Theta

of Drowsiness (RMTD), and Subclinical Rhythmic Electroencephalographic Discharges of Adults (SREDA), each identified in 2 patients (0.87%). Overall, normal variant waveforms were more frequently seen in the 1–18 age group compared to the other age categories.

Abnormal EEG waveform	Total (Percentage)
3 Hz and spike wave	5 (8.19)
Poly spike-waves	29 (47.54)
Generalized spike and waves	1 (1.64)
Lateralized periodic discharges	4 (6.56)
Centro-temporal spikes	1 (1.64)
Generalized periodic discharges	3 (4.91)
Continuous spike-wave during sleep	2 (3.28)
Slow spike-waves	13 (21.32)
Slowing temporal intermittent rhythm	1 (1.64)
Hypsarrhythmia	2 (3.28)

Table III: Distribution of abnormal EEG waveforms

A total of 61 (21%) EEG records with abnormal waveforms were analysed (Table III). Among the patients with abnormal EEG findings, the most frequently observed waveform was poly spike-waves, present in 29 patients (47.54%). This was followed by slow spike-waves in 13 patients (21.32%). Other notable abnormal patterns included 3 Hz spike and wave discharges in 5 patients (8.19%) and Lateralized Periodic Discharges (LPDs) in 4 patients (6.56%). Generalized Periodic Discharges (GPDs) were observed in 3 patients (4.91%), while continuous spike-wave during sleep and hypsarrhythmia were each seen in 2 patients (3.28%). Less commonly detected patterns included generalized spike and wave, centro-temporal spikes, and slowing temporal intermittent rhythm, each found in 1 patient (1.64%). These findings suggest a predominance of epileptiform discharges, particularly poly spike waves, among the patients with abnormal EEG waveforms.

DISCUSSION

This study aimed to analyse the distribution of normal and abnormal EEG waveform patterns among patients undergoing EEG evaluation at a tertiary care hospital in Western Nepal. Our findings revealed that 79% of the EEGs were normal, while 21% showed abnormalities among 290 patients. This result is consistent with the findings of Ko et al[8], who reported abnormal EEGs in 21.3% of their study population. In contrast, a study conducted in South India by Priyavathani et al[9] reported a higher prevalence of abnormal EEGs at 33.9%. This variability may be attributed to differences in clinical settings, diagnostic protocols, and patient demographics. Among the normal variant waveforms, wicket waves were the most commonly observed (7.42%), followed by Benign Epileptiform Transients of Sleep (BETS) (5.69%), Positive Occipital Sharp Transients (POSTs) (2.62%) and 14 and 6 Hz spikes (1.75%). Other normal variants observed at lower frequencies (0.87% each) included 6 Hz spike-and-wave discharges, vertex sharp transients, rhythmic mid-temporal theta of drowsiness (RMTD) and subclinical rhythmic electroencephalographic discharges of adults (SREDA). Our findings show some similarity to those reported by Radhakrishnan et al[10] who found Benign Epileptiform Transients of Sleep (BETS) in 8.2% of subjects, wicket waves in 1%, 14 and 6 Hz positive spikes in 5.7%, 6 Hz spike-waves in 2.8%, and RMTDs in 0.8%. In a much larger study by Santosh kumar et al[11] involving 35,249 subjects, Benign Epileptiform Transients of Sleep (BETS) were reported in 1.85%, wicket waves in only 0.03%, 14 and 6 Hz positive spikes in 0.52%, 6 Hz spike-and-wave discharges in 1.02%, RMTDs in 0.12% and SREDA in 0.07%. Our observation that SREDA was rare aligns with the findings of Azman et al[12] and Van Cott AC[13] who reported a prevalence of only 0.06% and 0.05%, respectively. Similarly, our data on RMTDs fall within the range of 0.1% to 2.1% reported in young adults by Macorig et al.[14]

In our study, the analysis of abnormal EEG patterns revealed that polyspikes were the most frequently observed abnormality, present in 47.54% of cases. Polyspike discharges are typically associated with generalized epilepsy syndromes, particularly juvenile myoclonic epilepsy[15] and other idiopathic generalized epilepsies. Their high frequency in this study may reflect the underlying diagnostic profile of the referred population. Following polyspikes, slow spike-and-wave discharges were the second most common abnormality, seen in 21.32% of cases. This pattern is often linked to symptomatic or cryptogenic generalized epilepsies, such as Lennox-Gastaut syndrome, and indicates more severe epileptic encephalopathies. The presence of 3 Hz spike-and-wave discharges in 8.19% of patients further supports the predominance of generalized epilepsy forms in our cohort, as this pattern is characteristic of typical absence seizures. Less frequently observed patterns included lateralized periodic discharges (LPDs) (6.56%) and generalized periodic discharges (GPDs) (4.91%), both of which are often associated with acute structural or metabolic brain insults, such as encephalitis, stroke, or hypoxic injury. The detection of continuous spike-wave during sleep (CSWS) and hypsarrhythmia in 3.28% of cases each highlights the presence of severe childhood-onset epileptic syndromes, such as electrical status epilepticus during slow-wave sleep (ESES) and West syndrome respectively.

Finally, generalized spike-and-wave discharges and temporal intermittent rhythmic slowing were each observed in 1.64% of abnormal EEGs. While generalized spike-and-wave activity further supports the diagnosis of idiopathic generalized epilepsy,

temporal intermittent slowing is a nonspecific finding that may indicate focal cerebral dysfunction, particularly in the temporal lobe.[16]

LIMITATIONS

The study was conducted in a single tertiary care hospital, which may not reflect the EEG pattern in other regions of Nepal. A relatively small sample size in our study may limit its generalizability. The retrospective nature of this study may limit the reliability of our findings due to inconsistency or missing data. Moreover, inter-observer variability in EEG interpretation might have introduced subjective bias.

CONCLUSION

The EEG waveforms were normal in most cases, while a few had abnormal EEG findings. Normal variant EEG waveforms were seen in many cases, particularly in children and adolescents. The normal variants must not be misinterpreted as epileptiform discharges to avoid the consequences of misdiagnosis. Our findings emphasize the need for continued EEG evaluation to support diagnosis and management. Twenty-four-hour EEG recording or Video-EEG monitoring (VEEG) may be more useful than routine EEG recording.

REFERENCES

1. Bhagat R. Clinical Pattern of Epilepsy and their Electroencephalogram Findings. J Neurol Neurophysiol [Internet]. 2015 [cited 2025 Mar 13];06. Available from: https://www.omicsonline.org/open-access/clinical-pattern-of-epilepsy-and-their-electroencephalogram-findings-2155-9562-1000335.php?aid=64882

2. Noachtar S, Rémi J. The role of EEG in epilepsy: A critical review. Epilepsy & Behavior [Internet]. 2009 [cited 2025 Mar 13];15:22–33. Available from: https://www.sciencedirect.com/science/article/pii/S1525505009000924

3. Sharma B, Shrestha R, Lamichhane RP. A Study on Electroencephalography Findings of Patients Visiting the Psychiatric Clinic: An Experience at A Tertiary Care Center in Western Nepal. Journal of Lumbini Medical College [Internet]. 2021 [cited 2025 Mar 13];9:3 pages-3 pages. Available from: https://jlmc.edu.np/index.php/JLMC/article/view/406

4. Prevalence of benign epileptiform variants from an EEG laboratory in India and frequency of their misinterpretation | Request PDF. ResearchGate [Internet]. 2024 [cited 2025 Mar 23]; Available from: https://www.researchgate.net/publication/348344929_Prevalence_of_benign_epileptiform_variants_from_an_EEG_laboratory_in_India_and_frequency_of_their_misinterpretation

5. Nayak CS, Anilkumar AC. EEG Normal Waveforms. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Mar 13]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK539805/

6. Ostwal P, Dabadghao V. Spectrum of electroencephalographic abnormalities in a cohort of patients from a teaching tertiary care hospital in Western India. Med J DY Patil Univ [Internet]. 2016 [cited 2025 Apr 3];9:51. Available from: http://www.mjdrdypu.org/text.asp?2016/9/1/51/172429

7. Poudel R, Aich TK, Panta P, Khan TA, Bhandary K. Utilization of EEG in A Teaching Hospital: A Descriptive Cross-Sectional Study. J Psychiatr Assoc Nepal [Internet]. 2021 [cited 2025 May 15];10:18–21. Available from: https://www.nepjol.info/index.php/JPAN/article/view/49000

8. Ko YJ, Han JH, Cho A, Yoo H, Kim H. Abnormal Electroencephalogram Findings and Its Correlation With Clinical Features From Pediatric Patients in Psychiatric Clinic. Clin EEG Neurosci [Internet]. 2024 [cited 2025 Apr 4];55:636–42. Available from: https://journals.sagepub.com/doi/10.1177/15500594241256170

9. Priyavathani J. B, Pothapregada S, Varadhan A, Thirunavukarasu SC. A study of prevalence of abnormal EEG and its association between various clinical presentations of atypical febrile seizures. Int J Contemp Pediatr [Internet]. 2020 [cited 2025 May 6];8:120. Available from: https://www.ijpediatrics.com/index.php/ijcp/article/view/3860

10. Radhakrishnan K, Santoshkumar B, Venugopal A. Prevalence of benign epileptiform variants observed in an EEG laboratory from South India. Clin Neurophysiol [Internet]. 1999 [cited 2025 Mar 23];110:280–5. Available from: https://doi.org/10.1016/s1388-2457(98)00002-9

11. Santoshkumar B, Chong JJR, Blume WT, McLachlan RS, Young GB, Diosy DC, et al. Prevalence of benign epileptiform variants. Clin Neurophysiol. 2009;120:856–61.

12. Azman Iste F, Tezer Filik FI, Saygi S. SREDA: A Rare but Confusing Benign EEG Variant. J Clin Neurophysiol. 2020;37:225–30.

13. Van Cott AC. Epilepsy and EEG in the tElderly. Epilepsia [Internet]. 2002 [cited 2025 Mar 13];43:94–102. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1528-1157.43.s.3.10.x

14. Macorig G, Crespel A, Nilo A, Tang NPL, Valente M, Gigli GL, et al. Benign EEG variants in the sleep-wake cycle: A prospective observational study using the 10-20 system and additional electrodes. Neurophysiol Clin. 2021;51:233–42.

15. Emmady PD, Anilkumar AC. EEG Abnormal Waveforms. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Mar 19]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK557655/

16. Pelliccia V, Mai R, Francione S, Gozzo F, Sartori I, Nobili L, et al. Ictal EEG modifications in temporal lobe epilepsy. Epileptic Disord [Internet]. 2013 [cited 2025 Mar 13];15:392–9. Available from: https://doi.org/10.1684/epd.2013.0615

Knowledge and Practice Regarding Breastfeeding among Physician Mothers in Tertiary Care Centre

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ABSTRACT

Introduction: During medical school and residency training, physicians are taught that breastfeeding is the preferred feeding for all infants. Evidence is accumulating that while physician mothers have a high rate of breastfeeding initiation, they face significant obstacles to sustained breastfeeding. **Aims:** This study aimed to assess personal breastfeeding intentions and behavior of a diverse group of physician mothers from various medical specialties. **Methods:** This study was a questionnaire-based descriptive cross-sectional study conducted among physician mothers in a tertiary care center located in Kathmandu, Nepal between October 2024 to April 2025. The questionnaire contained 35 items about maternal demographics, breastfeeding practices, environmental factors, and breastfeeding advocacy. Descriptive statistics, frequency tables, and percentages were calculated using SPSS. **Results:** Ninty-two physician mothers participated in the study. Majority of them had fairly adequate knowledge towards various correct breastfeeding practices, however only 12% were able to successfully breastfeed exclusively whereas most of the mothers chose to give a combination of formula and breastfeeding. Only 73 (79.3%) doctors reported that they felt they actively promote breastfeeding among their women patients. **Conclusion:** Even mothers who are medical professionals experience, and often cannot overcome, difficulties with breastfeeding. Women in medicine need enhanced breastfeeding support and services/resources. Advocacy is needed, in our work environments, for better breastfeeding support not only for our physician colleagues, but also for all lactating employees within our institutions.

***Keywords*:** Breastfeeding, Knowledge, Physician Mothers

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INTRODUCTION

Breastfeeding is the universally recommended modality of infant feeding.[1] Current recommendations are exclusive breastfeeding (EBF) for the first 6 months of life, followed by continued breastfeeding throughout at least for the first two years.[1,2] Exclusive breastfeeding (EBF) is defined as infant receiving only breast milk and no other liquids or solids except vitamins, minerals, or medications.[1] Breastfeeding is also considered to be the most effective health measure to reduce child mortality. It is known that one's physician's breastfeeding advice effectively increases mothers' breastfeeding initiation and continuation.[3] Despite excellent breastfeeding initiation rates, female physicians seem to also be at risk of premature breastfeeding cessation before achieving their own individual breastfeeding duration (BFD) goal.[4] Female physicians have some particular challenges in balancing work and family issues, partly owing to workload, call duty and remuneration issues. The most common reasons to wean children often are return to work, diminishing milk supply, and lack of time to express milk. It has been reported that residents and physicians with personal experiences of breastfeeding were more confident providing support and advice to breastfeeding patients.[5] However, the strongest predictor of physicians' clinical breastfeeding advocacy is their personal breastfeeding behavior.[6] It is known that physician mothers' breastfeeding behavior impacts their anticipatory guidance to their patients, which in turn influences patients' breastfeeding initiation and continuation. Therefore, studying physician mothers' breastfeeding behavior is important, as it impacts not only the well-being of themselves and their families, but eventually the well-being of their patients and patients' families, impacting their anticipatory guidance to patients and, therefore, influences patients' breastfeeding behavior. Hence this study aims to assess per-

sonal breastfeeding intentions and behavior of a diverse group of physician mothers from various medical specialties in a tertiary care center.

METHODS

This study was a questionnaire-based descriptive cross-sectional study conducted among physician mothers in a tertiary care center located in Kathmandu, Nepal. Criteria for participation consisted of being a female doctor having at least one biological child. Eligible participants were included whether they were in training (resident or fellow) or had completed training (faculty at the study center). Participants were included regardless of their infant-feeding methods (formula, breast milk, or combination). All physician mothers who gave consent were eligible for the study and those who did not respond were excluded from the study. The duration of the study was six months from October 2024 to April 2025 after ethical approval. The initial questionnaire was developed and piloted among a dozen physicians after review of instruments used in previous similar breastfeeding studies. The questionnaire was then converted to an online format that contained 35 items about maternal demographics, breastfeeding practices, environmental factors, and breastfeeding advocacy. The questionnaire was then sent as a self-designed Google Form to the doctors enrolled in the study electronically (via E-mail, WhatsApp, Viber, and Messenger). Ethical clearance was taken from the Institutional Review Committee of Kathmandu Medical College (Ref. 16102024/11). Convenience sampling technique was employed to select participants. The total sample size calculated after adding a non-response rate of 10 %, sample size was 78. All doctors who filled out the survey gave digital consent to take part in the survey. The questionnaire included a combination of both open and closed-ended questions and consisted of two parts. The first part included the maternal demographics like age and the second part consisted of breastfeeding advocacy and the breastfeeding practices followed by these doctor mothers. This included whether they were familiar with the right time of breastfeeding initiation, understanding of exclusive breastfeeding, weaning practices, reasons and challenges for discontinuation of breastfeeding. The data were entered and analyzed with IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics, frequency tables, and percentages were used.

RESULTS

A total of 92 physician mothers participated in the study. The mean participant age at the time of the study was 34.3 years and Table I summarizes maternal demographic characteristics. Majority of participants reported living in a joint family (63.1%). Participants came from a variety of specialties and most had completed their medical training. The participants had one to three children, ranging from 52 days to 28 years of age (mean of 6.4 years), at the time of the study.

Variable	n	Percentage (%)
1. Participant's age		
20-29	12	13.0
30-39	49	53.3
40-49	27	29.4
50+	4	4.3
2. Type of Family		
Nuclear	34	36.9
Joint	58	63.1
3. Medical Speciality		
Anesthesiology	5	5.4
Basic Sciences	29	31.5
Dermatology	3	3.3
Emergency Medicine	4	4.3
ENT	3	3.3
General Surgery	1	1.1
Internal Medicine	2	2.2
Microbiology	4	4.3
Ophthalmology	3	3.3
Obstetrics-Gynecology	7	7.6
Pathology	2	2.2
Paediatrics	4	4.3
Psychiatry	3	3.3
Radiology	3	3.3
Residents	19	20.6
4. Number of Children		
1	55	59.8
2	36	39.1
3	1	1.1

Table I: Characteristics of Study Participants (n=92)

Most of the children (n = 74; 80.4%) were born after the participants had completed their medical training (Table II). The majority of them (71.7%) had extended their maternity leave however reported to have to take unpaid leave. Of the 92 responses, only 12% were able to successfully breastfeed exclusively whereas most of the mothers chose to give a combination of formula and breastfeeding (73.9%). The study also found that there is poor flexibility of schedule for breastfeeding doctors on return to work with 1/3rd participants having to go back to night duties.

Only 73 (79.3%) doctors reported that they felt they actively promote breastfeeding among their women patients (Table III). Of the 92 respondents to the question, 53 (57.6%) reported that they actively promote breastfeeding among female house staff (colleagues, staff, residents) and only 13% reported strongly encouraging new mothers to breastfeed.

Practice Component	Frequency	Percentage (%)
1. Maternal career stage at the time of childbirth		
During training	18	19.6
After job enrollment	74	80.4
2. Did you extend your maternity leave?		
Yes	66	71.7
No	26	28.3
3. Infant feeding method		
Exclusive breastfeeding till 6 months	11	12.0
Mixed feeding	68	73.9
No breastfeeding at all	13	14.1
4. Schedule of work after maternal leave		
Full-Time	87	94.6
Half-time	4	4.3
Did not return	1	1.1
5. Did you have flexibility of schedule upon return to work?		
Yes	29	31.5
No	32	34.8
Somewhat	31	33.7
6. Were you put on night duties?		
Yes	38	41.3
No	54	58.7
7. How would you scale your mental health during breastfeeding period?		
Severely depressed	3	3.3
Depressed	62	67.4
Not depressed	27	29.3
8. How would you rate your energy level during breastfeeding period?		
Often Tired	75	81.5
Sometimes Tired	17	18.5
Rarely Tired	0	0
9. How would you rate your stress level during breastfeeding period?		
Very Stressed	67	72.8
Sometimes Stressed	23	25.0
Rarely Stressed	2	2.2
10. Did you pump milk in the workplace?		
Yes	34	37.0
No	58	63.0
11. Did you have sufficient time to express milk during work hours?		
Did not express	58	63.0
Never	11	12.0
Occasionally	9	9.8
Sometimes	12	13.0
Often	2	2.2
Always	0	0
12. Did you have access to an appropriate place to express milk at work?		
Did not express	58	63.0
Never	4	4.3
Occasionally	10	10.9
Sometimes	7	7.6
Often	9	9.9
Always	4	4.3
13. Were your colleagues supportive of your breastfeeding efforts?		
Always opposed my efforts	8	8.7
Usually opposed my efforts	39	42.4
Neither supportive nor oppositional	5	5.4
Usually supportive	17	18.5
Always supportive	16	17.4
Colleagues were not aware	7	7.6
14. Was discontinuing of breastfeeding due to demands at work?		
Yes	73	79.3
No	19	20.7
15. Were you satisfied with the duration that you were able to breast-feed?		
Yes	25	27.2
No	67	72.8

Table II: Characteristics of Pregnancies and Infant Feeding (n=92

Advocacy Components	n	Percentage (%)
1. Awareness of country's maternal leave policy		
Yes	37	40.2
No	55	59.8
2. Awareness of breastfeeding law for working women		
Yes	14	15.2
No	78	84.8
3. Frequency of talking to a new breastfeeding mother		
Usually	26	28.3
Sometimes	19	20.7
Rarely	11	11.9
Never	36	39.1
4. How strongly do you encourage a new mother to breastfeed?		
Strongly encourage	12	13.0
Encourage	65	70.7
Neither encourage nor dis-courage	15	16.3
Discourage	0	0
5. Do you feel you actively promote breastfeeding in your women patients?		
Yes	19	20.7
No	73	79.3
6. Do you actively encourage breastfeeding in your female colleagues, staff, juniors?		
Yes	53	57.6
No	39	42.4

Table III : Breastfeeding Advocacy (n=92)

Table IV shows a fairly adequate knowledge among physician mothers towards various correct breastfeeding practiceswith p-value 0.001. Most of the respondents had the right knowledge on the importance of starting breastfeeding early and of rooming in the mother and baby together (88%). It was interesting to note than half of the participants were of the opinion that bottle feeding was not harmful, and majority also believed it was okay to use pacifiers (58.7%). However, 80.4% were aware of the consequences of pre-lacteal feeds and 100% participants knew that the first breast milk, colostrum, contains antibodies and is beneficial for the baby. Approximately half of the respondents 48 (52.2%) had knowledge about the correct technique of burping and knew the right age of starting semi-solids (n = 51, 55.4%).

Advocacy Components	n	Percentage (%)
1. Believes breastfeeding should be started as early as possible	87	94.6
2.Believes colostrum is beneficial	92	100
3.Believes babies should not be given pre-lacteal feeds	74	80.4
4. Believes in rooming in	81	88.0
5. Believes in demand feeding	64	69.6
6. Knows the correct frequency of feeding	49	53.3
7. Believes feeding bottles are harmful	52	56.5
8. Does not believe in the use of pacifier	38	41.3
9. Knows the correct technique of burping	48	52.2
10. Knows the right age of starting semi-solids	51	55.4

Table IV: Beliefs of Physician Mother's Breastfeeding Practices (n=92)

DISCUSSION

The benefits of breastfeeding for both women and infants are well established.[7] Despite recommendations from the World Health Organization, initiating and sustaining lactation remains a challenge for many women.[8] Several studies that have examined the breast-feeding practices of physicians have found that the quality and quantity of counseling and support that they provide is related to their own self-perceptions regarding their effectiveness in breastfeeding.[9] It is reported that primary care physicians, specifically those specializing in internal medicine, paediatrics, obstetrics-gynecology, with personal or spousal experience were more self-confident in providing breast-feeding promotion and support.[10] However, physicians who are mothers face substantial challenges that may undermine efforts to sustain lactation after they return to work. It also has been demonstrated that the career satisfaction of physicians who are mothers was negatively affected by the short duration of maternity leave, associated financial losses, and inflexible work schedules.

In this study, all of the physician mothers were reasonably aware of the benefits of breastfeeding however the level of knowledge regarding national breastfeeding policy and workplace policy was poor. 72.8% respondents reported to be unsatisfied with the duration that they were able to breastfeed and 79.3% of them stated work-related demands as the reason for discontinuation of breastfeeding.

Consistent with other physician studies[11,12,13] we found high breastfeeding initiation rates in this study. However, our data also demonstrate that while 96% of infants were breastfed at birth and intent to breastfeed for at least 12 months, only 12% of infants were exclusively breastfed till 6 months of age. This discrepancy and the work-related factors associated with exclusive breastfeeding suggest that work-related factors not only influence physician mothers' breastfeeding behavior but also might have a larger impact than their education and intentions on their breastfeeding advocacy on their patients and colleagues, family members and juniors.

Similar to other studies[14,15] reporting that discontinuation of breastfeeding was due to work-related demands was associated with shorter duration of both exclusive and any breastfeeding. Maternal level of energy while breastfeeding, maternal satisfaction on achieving breastfeeding goals, availability of time to express milk at work, access to appropriate place at the workplace to express milk at work, and perceived level of support for breastfeeding efforts from colleagues are factors related to discontinuity of breastfeeding amongst physician mothers. Their own breast-feeding success might enhance the potential of female physicians as advocates and sources of credible information regarding breast-feeding.

LIMITATIONS

Results of the study reflects only a small population of physician mothers and some of the participants' nature of work does not put them directly in contact with breastfeeding patients for advocacy.

CONCLUSION

Modifiable, work-related factors such as providing longer paid maternal leave, accommodating schedules to allow for pumping, and establishing a dedicated private space may improve the ability of physicians who are mothers to continue lactation after they return to work. With a breastfeeding conducive environment physician mothers' it further positively impacts their anticipatory guidance to their patients, which in turn influences patients' breastfeeding initiation and continuation.

REFERENCES

1. American Academy of Pediatrics. Infant Food and Feeding. 2019.

2. World Health Organisation& UNICEF (2017). Global Breastfeeding Scorecard: Tracking Progress for Breastfeeding Policies and Programmes. New York: UNICEF.

3. Lawrence RA. Practices and attitudes toward breast-feeding among medical professionals. Pediatrics 1982;70:912–20

4. Sattari M, Levine D, Bertram A, et al. Breastfeeding intentions of female physicians. Breastfeed Med 2010;5:297–302.

5. Freed GL, Clark SJ, Sorenson J, Lohr J, Cefalo R, Curtis P. National assessment of physicians' breastfeeding knowledge, attitudes, training, and experience. JAMA 1995;273(6):472-6.

6. Brodribb W, Fallon A, Jackson C, et al. The relationship between personal breastfeeding experience and the breastfeeding attitudes, knowledge, confidence and effectiveness of Australian GP registrars. Matern Child Nutr 2008;4:264–274.

7. Victora CG, Bahl R, Barros AJD, et al; Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet. 2016;387(10017):475-490.

8. Section on Breastfeeding. Breastfeeding and the use of human milk. Pediatrics. 2012;129(3):e827-e841.

9. Melnitchouk N, Scully RE, Davids JS. Barriers to Breastfeeding for US Physicians Who Are Mothers. JAMA Intern Med. 2018 Aug 1;178(8):1130-32.

10. S Preventive Services Task Force. Primary Care Behavioral Counseling Interventions to Support Breastfeeding: US Preventive Services Task Force Recommendation Statement. JAMA. Published online April 08, 2025. doi:10.1001/jama.2025.3650

11. Sattari M, Levine D, Bertram A, et al. Breastfeeding intentions of female physicians. Breastfeed Med 2010;5:297–302.

12. Miller N, Miller D, Chism M. Breastfeeding practices among resident physicians. Pediatrics 1996;98:434–37.

13. Orth TA, Drachman D, Habak P. Breastfeeding in obstetrics residency: Exploring maternal and colleague resident perspectives. Breastfeed Med 2013;8:394–400.

14. Arthur CR, Saenz RB, Replogle WH. Personal breast-feeding behaviors of female physicians in Mississippi. South Med J 2003;96:130–35.

15. Riggins C, Rosenman MB, Szucs KA. Breastfeeding experiences among physicians. Breastfeed Med 2012;7:151–54.

ORIGINAL ARTICLE

Preoperative Lignocaine Nebulization for Attenuation of the Pressor Response of Laryngoscopy and Tracheal Intubation in Patients Undergoing Laparoscopic Cholecystectomy Under General Anesthesia

Shakya S[1], Shakya A[2], Paudel B[3]

ABSTRACT

Introduction: Laryngoscopy and intubation during laparoscopic cholecystectomy under general anesthesia can cause a pressor response, resulting in hemodynamic instability. Preoperative lignocaine nebulization provides topical anesthesia by inhibiting sodium channels and may offer better mucosal coverage than intravenous administration. **Aims:** To assess the effect of lignocaine nebulization on pressor response, hemodynamic stability, and related complications. **Methods:** This double-blinded comparative study was conducted from August to December 2024, involving 100 patients undergoing elective surgery under general anesthesia with physical status score I or II (American Society of Anesthesiologists). Patients were randomized into two groups for nebulization: Group A (n=50) received 2% lignocaine (3 mg/kg, volume adjusted with saline), while Group B (n=50) received an equivalent volume of 0.9% normal saline. Parameters analyzed included age, gender, weight, ASA physical status, SpO2, heart rate and mean arterial pressure. Statistical analysis was performed using Student's t-test and Chi-square test; $p<0.05$ was considered significant. **Results:** Both groups were comparable in terms of age, gender, physical status and mean duration of surgery. In group A, the baseline Heart Rate was 89.34 ± 12.12 per minute while in group B 88.26 ± 10.98 per minute. Two minutes after intubation, it increased and started declining from the 4th minute in both the groups. However, there were significant statistical difference between two groups at 2 and 4 minutes respectively (p = 0.001 and 0.038). Mean arterial pressure (MAP) also rose in both groups at 2 minutes, but the increase was significantly greater in group B (p=0.001). This difference remained significant at 4 minutes (p=0.001), with no significant variation observed from the 6th minute onward. **Conclusion:** Preoperative lignocaine nebulization effectively blunts the pressor response to laryngoscopy and intubation, enhancing hemodynamic stability and perioperative safety.

Keywords: Hemodynamic, Laryngoscopy, Lignocaine nebulization, Pressor response, Intubation

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INTRODUCTION

Laparoscopic cholecystectomy is a commonly performed surgical procedure, typically conducted under general anesthesia with endotracheal intubation. However, laryngoscopy and tracheal intubation can lead to a sympathetic response known as the pressor response, characterized by an increase in blood pressure and heart rate. This response can be detrimental, especially in patients with cardiovascular disease or hypertension. Forbes and Dally reported a case of acute ischemia even in a previously healthy, normotensive patient whose blood pressure reached 190/130 mmHg,[1] indicating the importance of suppressing pressor response. Attenuation of pressor responses could be possible either by deepening the plane of anesthesia[2] or by the use of drugs, or by using advanced airway devices.[3] The attenuation of pulse and blood pressure fluctuations may be attributed to lignocaine's local anesthetic action, which inhibits sodium channels and reduces afferent neuronal transmission from the oropharynx and larynx, thereby blunting sympathetic nervous system activation.[4,5] This study was done to determine whether preoperative lignocaine nebulization can effectively attenuate the pressor response of laryngoscopy and tracheal intubation and to assess its impact on hemodynamic stability, postoperative complications in patients under-

going laparoscopic cholecystecomy under general anesthesia.

METHODS

This Hospital based prospective, double-blinded comparative study was carried out in the Department of Anesthesiology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Nepal, from August 2024 to December 2024 after approval from the Institutional Review Committee. Patients aged 18–65 years of any gender, classified as American Society of Anesthesiologists (ASA) I or II, and scheduled for elective laparoscopic cholecystectomy under general anesthesia were included after obtaining written informed consent. Exclusion criteria included: known allergy to lignocaine, hypertension, diabetes mellitus, COPD, cardiovascular, renal, hepatic, or neurological diseases, or an abnormal coagulation profile. The sample size was calculated with an α error of 5% and β error of 20%[6] resulting in 100 patients. Patients (N = 100) were randomly assigned to one of two groups (n = 50 per group) using a sealed opaque envelope method.

Group A (Lignocaine group): Nebulized with 2% lignocaine at 3 mg/kg (total volume adjusted with saline) for 10 minutes before induction using a fitting face mask with Nebulizer Nebufish model of Explore Medical Accessories.

Group B (NS group): Nebulized with an equivalent volume of 0.9% normal saline.

The patient and the anesthesiologist recording the outcomes were blinded to group allocation. A separate anesthesiologist or nurse, not involved in the study, prepared and administered the study drugs. All the patients included for the study were admitted to the hospital day before surgery. They all underwent complete pre-anaesthetic evaluation including detailed history taking, physical examination and routine pre-operative investigations. All the patients fasted for 6 hours were received and identified in the operation theater on the day of surgery. An intravenous line was established with an 18G intravenous cannula in a large vein on the dorsum of the hand or forearm. All patients were attached with standard monitors with heart rate (HR), non-invasive blood pressure (NIBP), respiratory rate (RR), arterial hemoglobin oxygenation by pulse oximeter (SPO2) and electrocardiography (ECG) before the procedure was started and recorded. All patients were pre-oxygenated with 100% oxygen for 3 minutes and midazolam in the dose of 2mg and fentanyl 2mcg/kg was given as well. Anaesthesia was induced using Propofol injection in the dose of 1 mg/kg. Endotracheal intubation was facilitated using Vecuronium in the dose of 0.08mg/kg IV. Laryngoscopy and endotracheal intubation was done with Machintosh laryngoscope. Anesthesia was maintained with 100% oxygen, Isoflurane (1-2%), and intermittent doses of vecuronium.

Following parameters were recorded:

•Baseline parameters and Changes in HR, SBP, DBP and mean arterial pressure at 1, 2, 4 upto 10 min after intubation

•Occurrence of Arrhythmias noted if any during laryngoscopy and intubation.

After the end of the surgery, residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and endotracheal tube was removed once the patient resumed spontaneous breathing.

Statistical Analysis

Data thus recorded and collected were analyzed by standard statistical tests such as Chi square test and Students t-test with SPSS version 20. The p value < 0.05 were considered statistically significant.

RESULTS

Both groups were comparable with regards to age, gender, weight, ASA physical status, mean duration of surgery. There was no statistically significant difference between groups (p > 0.05). (Table I)

Variables	Group A	Group B	p-value
Age (years)	41.80 ± 15.29	44.12 ± 14.57	0.439
Gender			
Male	17 (34)	12 (24)	0.378
Female	33 (66)	38 (76)	
Weight (Kg)	53.86 ±7.14	51.94±4.80	0.118
Physical Status			
ASA I	39 (78)	35 (70)	0.495
ASA II	11 (22)	15 (30)	
Duration of Surgery (min)	81.40 ±19.27	76±16.41	0.135

Table I: Study population demographic data

In group A, the baseline HR was 89.34 ± 12.12 bpm while in group B 88.26 ± 10.98 bpm. Two minute after intubation, it was increased and it started declining from the 4th minute in both the groups. However, there was significant statistical difference between two groups at 2 and 4 minutes respectively (p value of 0.001 and 0.038). Figure 1

Similar results were seen with Systolic, Diastolic and Mean Arterial Pressure. There was significant difference between the two groups (p value of 0.001 and 0.001) while using Students t-test in mean arterial pressure at 2 and 4 minutes after intubation. Figure 2

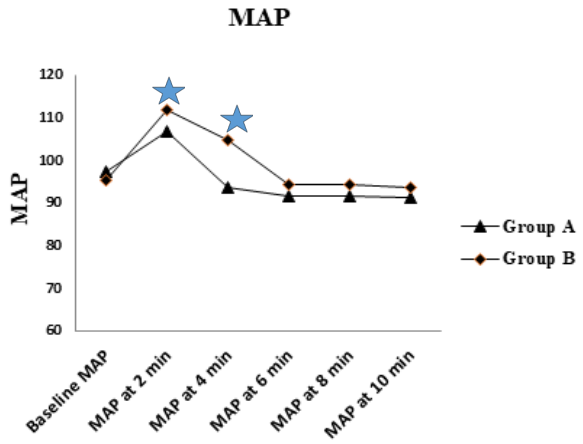

Figure 1: Mean Heart Rates (beats per min) of the two study groups at different time intervals

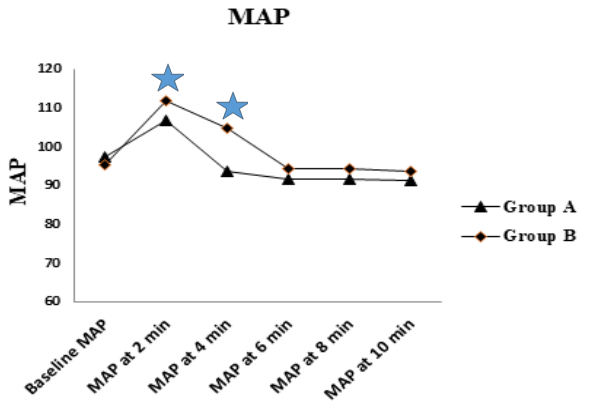

Figure 2: MAP (mmHg) of the two study groups at different time intervals

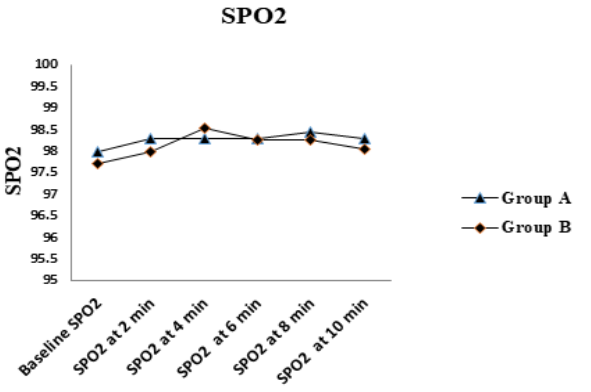

Figure 3: SPO2 of the two study groups at different time intervals

There was no significant difference between groups regarding SpO2 at all assessed times ($p > 0.05$) intraoperatively. Figure 3 In both groups, no any side effect or complication was observed.

DISCUSSION

Direct laryngoscopy and intubation are noxious stimuli that can provoke adverse cardiovascular and other system changes. It induces hemodynamic alterations within seconds, subsequently causing an elevation in heart rate and blood pressure upon tracheal intubation.[7] Hence, suppressing hypertensive responses during airway manipulation is a crucial prerequisite for proper general anesthesia. Lignocaine given by nebulization, has a good safety profile.[8] It can be easily administered non-invasively and is generally well tolerated. It has a rapid onset of action, a short duration, minimal side effects and is cost-effective.

We selected 10 ml of 2% lignocaine for nebulization in the patients. Woodruff et al conducted a study on awake fiber-optic intubation and observed that 2% and 4% nebulized lignocaine had similar haemodynamic responses to topicalization and airway manipulation. However, there was a delay in the return of airway reflexes in short duration surgeries with 4% concentration.[10] The dose of 10 ml was chosen in order to ensure comparability between two groups. It is suggested that 50% of the mists were lost around the patient's mouth during expiration and breath holding.[11]

We used continuous nebulization; therefore, the estimated loss of nebulized lignocaine was greater than 50%. In our study, patients were nebulized with 10 ml of 2% lignocaine using a standard gas-driven nebulizer, 15 minutes prior to attempting laryngoscopy. There was an increase in heart rate and mean arterial pressure at 2 and 4 minutes, which gradually declined below baseline from 6 minutes onward following intubation in both groups. The mean rise in heart rate and mean blood pressure were comparatively lesser in the nebulize group, which was statistically significant when compared to normal saline group. There were no episodes of bradycardia in any of our study groups.

Agrawal et al (2022)[12] conducted an observational study in 50 patients within the age group of 18-65 years undergoing elective surgery under general anaesthesia randomly allocated into two groups: Group L (n=25) nebulized with 5 ml lignocaine (2%) and Group C (n=25) nebulized with 5 ml normal saline, 15 minutes before surgery. Their study indicated a significant reduction in heart rate and mean arterial pressure in the lignocaine group compared to the control group at intubation 2, 5 and 10 minutes after intubation respectively further supporting the use of lignocaine nebulization in managing hemodynamic responses during intubation as highlighted by our study results.

Similarly, Nabil et al (2023)[13] conducted a randomized double blind study on 110 patients with severe preeclampsia who underwent caesarean delivery under general anaesthesia. They found that patients who received preoperative nebulization with 2% lignocaine (4.5 mg/kg, up to 400 mg) had significantly lower systolic blood pressure and heart rate at 1, 3 and 5 minutes after intubation compared to those who received normal saline. These findings were consistent with our study.

Another study by Baloch et al (2023)[14] included 90 patients and compared three groups: intravenous lignocaine, nebulized lignocaine, and saline. Both the intravenous and nebulized lignocaine groups had better control of heart rate and blood pressure during intubation than the saline group. Nebulized lignocaine was nearly as effective as the intravenous route.

Verma et al (2022)[15] also studied 94 patients undergoing head and neck surgery. One group received 4% lignocaine via nebulization, while the other received saline. The lignocaine group had a smaller rise in blood pressure and heart rate after intubation, with values returning to normal within 10 minutes.

In the current study we observed the most common ECG abnormality as Sinus Tachycardia. However, there were no any other arrhythmia and side effects observed in both the groups. All the patients were satisfied with the procedures they underwent. The occurrence of sinus arrhythmia as a minor side effect in both groups suggests that this rhythm disturbance may not be directly attributable to the intervention. Sinus arrhythmia, characterized by phasic variations in heart rate with respiration, is a common benign finding during anesthesia, often linked to vagal stimulation during laryngoscopy, mechanical ventilation, or pneumoperitoneum in laparoscopic procedures.[16,17]

While systemic lignocaine administration has been associated with arrhythmogenic effects at high doses (e.g.ventricular arrhythmias), lignocaine nebulization typically achieves lower plasma concentrations, minimizing such risks.[18,19] Studies by Kim et al (2020) and Gupta et al (2021) similarly reported sinus arrhythmia as a transient, hemodynamically insignificant event during intubation, unrelated to lignocaine use.[20,21]

The clinical implications of this study are significant, particularly in laparoscopic procedures where hemodynamic stability is critical in minimizing perioperative complications. The simplicity of nebulization makes it a practical option in resource-limited settings like ours.

LIMITATIONS

Limitations of this study includes it's lack of comparison with other pharmacological agents, such as opioids or beta-blockers, which are also used to attenuate pressor responses. Future studies should explore optimal dosing regimens in various other surgeries in different settings.

CONCLUSION

This study showed that the preoperative lignocaine nebulization represents an effective strategy to attenuate the hemodynamic stress response to laryngoscopy and intubation. Its integration into routine general anesthesia practice could enhance patient safety, particularly in high-risk populations.

REFERENCES

1. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth. 1970;42(7):618-24.
2. Nair GC, Singh H, Singh P. Vital signs and electrocardiography during intubation. Indian J Anaesth. 1965;40:40-57.
3. Bedford RF, Marshal K. Cardiovascular responses to endotracheal intubation during four anaesthetic techniques. Acta Anaesthesiol Scand. 1984;28:563-6.
4. Miller DR, Woo PY. Intravenous lignocaine for attenuation of the haemodynamic response to laryngoscopy and tracheal intubation: a systematic review. Anaesth Analg. 2018;126(3):1029-37.
5. Kautto UM. Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. Acta Anaesthesiol Scand. 2017;21(3):217-21.
6. Mostafa SM, Wiles JR, Dowd T, Bates R, Bricker S. Effects of nebulized lignocaine on intraocular pressure responses to tracheal intubation. Br J Anaesth.1990;64(4):515-7.
7. Birnbach DJ, Browne IM. Anesthesia for obstetrics. In: Miller RD, editor. Miller's Anesthesia. 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010. p. 1144-77.
8. Brouton L, Lazo J, Parker K, editors. Goodman & Gillman's The Pharmacological Basis of Therapeutics. 11th ed. New York: McGraw-Hill Companies; 2006.
9. Yuki N, Kikuchi H, Honda Y. Nebulized lignocaine for blunting haemodynamic response to laryngoscopy: a randomized controlled trial. J Clin Anesth. 2019;52:45-50.
10. Woodruff C, Wieczorek PM, Schricker T, Vinet B, Backman SB. Atomised lidocaine for airway topical anaesthesia in the morbidly obese: 1% compared with 2%. Anaesthesia. 2010;65:12-7.
11. Chinn WM, Zalavala DC, Ambre J. Plasma levels of lidocaine following nebulized aerosol administration. Chest. 1977;71:346-8.
12. Agrawal A, Shah A, Mehta M, Chauhan D. An observational study to evaluate pressor response to laryngoscopy and tracheal intubation after pre-operative nebulization of lignocaine. Int J Health Sci (Qassim). 2022;6(S2):9133-43.
13. Nabil F, Gharib AA, Gadelrab NA, Osman HM. Preoperative lignocaine nebulization for attenuation of the pressor response of laryngoscopy and tracheal intubation in patients with severe preeclampsia undergoing caesarean section delivery: A randomised double-blind controlled trial. Indian J Anaesth. 2023;67(6):515-22.
14. Baloch AA, Kalim N, Hassan A, Kumar V, Ahmad Z et al. Comparative study on the effects of lignocaine nebulization with I/V lignocaine on stress response to laryngoscopy and tracheal intubation. PJMHS. 2023;17(9):1796. Doi: 10.53350/pjmhs20231796.
15. Verma R, Gaurav S, Verma H, Verma S, Kuswaha B et al. A prospec¬tive study evaluating the effect of nebulised lidocaine on haemodynamic responses during nasotracheal intubation. Indian J Clin Anaesth. 2022;9(4):439-444.
16. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Cohen NH. Miller's Anesthesia. 9th ed. Elsevier; 2020. p. 1532-5.

17. Staikou C, Stamelos M, Stavroulakis E. Impact of anaesthetic drugs and adjuvants on ECG parameters. Anaesth Intensive Care. 2014;42(1):17-26.

18. Butterworth JF, Mackey DC, Wasnick JD. Local anesthetics. In: Morgan & Mikhail's Clinical Anesthesiology. 6th ed. McGraw-Hill; 2018. p. 297-9.

19. Yuki N, Kikuchi H, Honda Y. Nebulized lignocaine for blunting haemodynamic response to laryngoscopy: a randomized controlled trial. J Clin Anesth. 2019;52:45-50.

20. Kim SH, Kim HJ, Lee SJ. Perioperative sinus arrhythmia during laparoscopic cholecystectomy: incidence and implications. Surg Laparosc Endosc Percutan Tech. 2020;30(2):178-81.

21. Gupta S, Rajderkar S, Deshmukh S. Vagally mediated arrhythmias during pneumoperitoneum: a prospective observational study. Indian J Anaesth. 2021;65(3):213-8.

Status of C-Reactive Protein, Cellular and Clinical Parameters in Neonates with Risk of Sepsis in Tertiary Center of Mid-Western Nepal

Sapkota S[1], Danai A[2], Malla P[3], Sah B[1]

ABSTRACT

Introduction: Neonatal sepsis refers to a bloodstream infection which impacts infants under 28 days of age. Symptoms may encompass irregular vital signs and respiratory discomfort. C-reactive protein served as a vital diagnostic marker; nevertheless, its low sensitivity in early identification necessitates periodic assessments for accurate diagnosis and therapy monitoring. **Aims**: This study assessed C-reactive protein levels, cellular parameters, and clinical indicators in neonates predisposed to sepsis at a tertiary care facility. **Methods:** Hospital based prospective study, conducted on 150 neonates in paediatrics and biochemistry department of Nepalgunj Medical College from June 2024 to October 2024. C-reactive protein, whole blood count, platelets count, Immature/total neutrophil ratio were calculated along with the clinical findings suggesting sepsis were recorded. Major neonatal anomalies and prior antibiotic use led to exclusion. **Results:** Among 150 at-risk neonates, 65.3% were male, 46% were preterm and 45.3% had low birth weight. Elevated C-reactive protein (>6 mg/L) was found in 84.7%, with 68% showing tachypnea and 53.3% delayed capillary refill. Temperature variability (90%) and tachycardia (70%) were common. Laboratory findings showed high C-reactive protein (mean 16.8 mg/L), neutrophil predominance (61%), and raised Immature to total neutrophil ratio (0.25). Late-onset cases had more severe clinical and inflammatory profiles than early-onset cases. **Conclusion:** C-reactive protein, as a biochemical marker, was observed in the majority of neonates at risk of sepsis, while temperature variability, tachycardia and reduced urine output were common clinical features indicating systemic compromise.

Keywords: C-reactive protein, immature to total neutrophil ratio, neutrophilia, neonatal risk factors, tachypnoea, tachycardia, temperature variability

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INTRODUCTION

Neonatal sepsis is defined by the World Health Organization as a clinical syndrome marked by signs of infection in infants under 28 days old. Symptoms include temperature instability, respiratory distress, and changes in feeding behaviour. Diagnosis combines clinical assessment with laboratory evidence,like abnormal white blood cell counts.[1,2] Neonatal sepsis is classified into two groups based on when symptoms appear after birth: early-onset sepsis (EOS) and late-onset sepsis (LOS). C-reactive protein (CRP), along with clinical features like temperature variability and tachycardia, and hematological markers such as neutrophilia and elevated I/T ratio, enhances diagnostic accuracy and supports timely intervention in neonates at risk.[1,3,4] Neonatal sepsis commonly presents with respiratory signs such as grunting, nasal flaring, and cyanosis.[5-9] Neurological symptoms may include lethargy, seizures, or hypotonia, while gastrointestinal signs are also frequent. Skin findings such as petechiae or cellulitis may indicate systemic infection.[10-13] Studies done by Hisamuddin et al (2015)[11] and Jeon et al (2014)[12] had shown that CRP has moderate sensitivity and specificity and its diagnostic accuracy improves significantly when used alongside clinical and hematological parameters. The justification for this study lies in its focused evaluation of CRP in conjunction with clinical and cellular indicators to improve early detection of neonatal sepsis in a resource-limited setting. Such an integrated approach is essential for timely intervention and reducing neonatal morbidity and mortality.

METHODS

A Hospital based prospective study, conducted on 150 neonates at paediatrics and biochemistry department of Nepalgunj Medical College from June 2024 to October 2024, aimed at investigating neonates with risk of sepsis. Ethical approval was taken from institutional review committee before starting the study. Considering that the neonatal sepsis has a prevalence of 48%[9], the sample size was formulated. The present study employed an observational design to evaluate clinical, hematological, and biochemical parameters in neonates at risk of sepsis. The data collection was conducted prospectively over a defined period in a tertiary care neonatal unit. Neonates admitted with clinical suspicion of sepsis, either early-onset (≤72 hours of life) or late-onset (>72 hours), were enrolled consecutively after obtaining appropriate written consent from their parents. Baseline informations, including age, sex, gestational age and birth weight, were recorded. Detailed clinical assessments were performed by attending pediatricians, focusing on signs of systemic illness such as temperature instability, tachycardia, respiratory distress, perfusion status, and feeding behavior. Standardized criteria were used to identify symptoms such as tachypnea, cyanosis, grunting, seizures, and abdominal distension.[14] Neonates weighing <1000gm, those with any congenital anomalies and those who received antibiotics prior to the hospital admission were excluded from the study. Blood samples were collected aseptically for laboratory analysis at the time of clinical suspicion. Parameters evaluated included white blood cell count, absolute neutrophil count, platelet count, C-reactive protein (CRP) level and the immature-to-total neutrophil (I/T) ratio. Differential leukocyte counts were also performed. CBC (complete blood count) was estimated using Syxmex (6-part Hematology) analyzer and CRP was estimated using Mispa-I3 (Immunoturbidometric method). The neonates were subsequently stratified into early-onset and late-onset groups based on the timing of symptom onset, and comparative analysis of clinical and laboratory features. The data were tabulated and analyzed to determine the prevalence of key clinical signs, laboratory abnormalities, and their correlation with sepsis onset patterns.

Statistical analysis

The study used SPSS 22 for descriptive analysis and MS Excel for data management. Baseline, clinical, and laboratory data were collected and analyzed across these groups. Descriptive statistics, including means and standard deviations, were used to summarize continuous variables such as age, weight, and blood parameters, while categorical variables like symptoms and clinical signs were reported as percentages to identify trends and associations with sepsis severity and onset.

RESULTS

In the present study, the mean age of the neonates was 16.8 ± 8.5 days, with an average weight of 2.8 ± 0.6 kg. The majority of the participants were male, accounting for 65.3% of the total (Table I).

Characteristic	n	%
Mean Age (days)	16.8 ± 8.5	
Mean Weight (kg)	2.8 ± 0.6	
Male	98	65.30%
Female	52	34.67%

Table I: Baseline characteristics of the patients

Among the clinical and laboratory parameters observed in the 150 neonates at risk of sepsis, elevated C-reactive protein levels (>6 mg/L) were the most frequently recorded finding, presented in 84.7% of cases. This was followed by tachypnoea in 68% and delayed capillary refill, an indicator of poor perfusion was observed in 53.3% of neonates. Additionally, 46% were preterm and 45.3% had low birth weight (Table II).

Parameter	n	Percentage (%)
CRP > 6 mg/L	127	84.70%
Tachypnea	102	68.00%
Late Capillary Refill	80	53.30%
Gestational Age < 37 weeks	69	46.00%
Gestational Age ≥ 37 weeks	81	54.00%
Birth Weight < 2.5 kg	68	45.30%
Birth Weight ≥ 2.5 kg	82	54.70%

Table II: Risk Factors in At-Risk Neonates (n = 150)

The clinical features observed in the study population highlighted several common signs of neonatal distress or sepsis. Temperature variability was the most prevalent symptom, present in 90% of the neonates, representing potential systemic infection or impaired thermoregulation. Tachycardia was observed in 70% of the cases, reflecting a possible compensatory response to infection or hemodynamic instability. Reduced urine output was reported in 62.7% of neonates, suggesting compromised renal perfusion or dehydration. Feeding difficulty was present in 57.3%, which is a common early indicator of systemic illness in neonates. Grunting, a sign of respiratory distress, was noted in 52% of the neonates. Cyanosis, indicating hypoxia, was seen in 36% of cases. Less frequently, seizures were observed in 16% of the neonates, and abdominal distension was present in 28%, both of which may point to more severe systemic contribution or complications (Table III).

Clinical Features	n	Percentage (%)
Reduced Urine Output	94	62.70%
Temperature Variability	135	90.00%
Tachycardia	105	70.00%
Feeding Difficulty	86	57.30%
Grunting	78	52.00%
Cyanosis	54	36.00%
Seizures	24	16.00%
Abdominal Distension	42	28.00%

Table III: Clinical Features in At-Risk Neonates (n = 150)

The hematological parameters observed in the study provide insight into the inflammatory and immune status of the neonates. The mean white blood cell count was 12.3 ± 5.5 ×10³/µL, which falls within the normal range but may reflect a response to infection in some cases. The absolute neutrophil count averaged 7.3 ± 3.4 ×10³/µL, suggesting an active neutrophilic response, commonly seen in bacterial infections. Platelet count was 215 ± 78 ×10³/µL, representing generally adequate platelet levels, though variability suggests some neonates may have had thrombocytopenia. The mean C-reactive protein level was notably elevated at 16.8 ± 14.2 mg/L, reinforcing the presence of an inflammatory or infectious process in many neonates. The immature-to-total neutrophil (I/T) ratio was 0.25 ±0.15, which is higher than the normal threshold (typically <0.2), additional supporting a possible infectious etiology. Differential leukocyte counts showed a predominance of neutrophils (61% ± 16), with lymphocytes at 29% ± 12, monocytes at 5% ± 2, and eosinophils at 3% ± 1. This neutrophil predominance, along with elevated CRP and I/T ratio, strongly suggests an ongoing bacterial infection or systemic inflammatory response in the study population (Table IV).

Parameter	Mean±SD
WBC Count (×10³/µL)	12.3±5.5
ANC (×10³/µL)	7.3±3.4
Platelet Count (×10³/µL)	215±78
CRP (mg/L)	16.8±14.2
I/T Ratio	0.25±0.15
Neutrophils (%)	61±16
Lymphocytes (%)	29±12
Monocytes (%)	5±2
Eosinophils (%)	3±1

Table IV: Laboratory or cellular Parameters (Mean±SD) in At-Risk Neonates

The mean age at risk onset was 1.8 ± 0.7 days in the early-onset group and 17.2 ± 4.3 days in the late-onset group, clearly distinguishing the two categories based on timing. Late-onset cases exhibited more severe inflammatory responses, as reflected by higher CRP levels (36.4 ± 10.5 mg/L vs. 15.2 ± 5.8 mg/L), elevated WBC counts (19.0 ± 5.9 ×10³/µL vs. 12.5 ± 4.2 ×10³/µL), and increased ANC (11.2 ± 3.5 ×10³/µL vs. 6.8 ± 2.1 ×10³/µL). The I/T ratio was also markedly higher in the late-onset group (0.45 ± 0.12 vs. 0.25 ± 0.08), indicating a stronger immature neutrophil response. Late-onset cases had a higher percentage of neutrophils (72% vs. 58%) and a lower percentage of lymphocytes (18% vs. 32%), suggesting a more intense and possibly prolonged neutrophilic response. Platelet counts were lower in the late-onset group (160 ± 55 ×10³/µL) compared to the early-onset group (225 ± 65 ×10³/µL), which may reflect greater severity or progression of illness. Clinically, feeding difficulty (72% vs. 48%), cyanosis (60% vs. 30%), seizures (42% vs. 10%), and abdominal distension (56% vs. 22%) were all more common in the late-onset group, representing more pronounced systemic involvement (Table V).

Parameter	Early-Onset Risk (n = 65)	Late-Onset Risk (n = 45)
Age at Risk Onset (days)	1.8±0.7	17.2±4.3
CRP Level (mg/L)	15.2±5.8	36.4±10.5
WBC Count (x×10³/µL)	12.5±4.2	19.0±5.9
ANC (x×10³/µL)	6.8±2.1	11.2±3.5
Platelet Count (×10³/µL)	225±65	160±55
I/T Ratio	0.25±0.08	0.45±0.12
Neutrophils (%)	58±12	72±15
Lymphocytes (%)	32±10	18±7
Feeding Difficulty	48%	72%
Cyanosis	30%	60%
Seizures	10%	42%
Abdominal Distension	22%	56%

Table V: Risk Profile by Early vs. Late-Onset Sepsis Risk

DISCUSSION

In our study, the analysis of baseline characteristics of neonates at risk of sepsis showed mean age of 16.8 ± 8.5 days and weigh of 2.8 ± 0.6 kg. There was male domination over the female. Male domnation in neonates at risk of sepsis was also the significant finding in other studies done by Worku M et al, Patel U et al, Hisamuddin E et al, Jeon JH et al, the majority of neonates were presented within 10 days of birth and were of low birth weight.[9-12]

Temperature variability was seen in 90% of our neonates, making it the most common symptom. Both hypothermia and hyperthermia were common, reflecting the neonate's impaired thermoregulation during infection. This matches with findings by Ganesan et al (2016)[15], who also reported temperature instability as a frequent sign in septic neonates. Tachycardia occurred in 70% of our cases, compared to 67% reported by Ahmed et al (2005)[5], showing a similar trend. Reduced urine output (62.7%) and feeding difficulty (57.3%) were also common in our study, which was in line with the 60–65% rates observed in previous studies by Yin et al (2024)[16] and Brown et al (2019).[17] In our study, 68.00% of neonates presented with tachypnea, highlighting it as one of the important risk factor of sepsis. The prevalence was slightly higher than reported in other studies, where incidence ranged from 52.3% - 65.0% among septic neonates.[13,15,16] Symptoms like grunting (52%), cyanosis (36%), seizures (16%) and abdominal distension (28%) were also reported, with higher rates of severe symptoms like seizures and abdominal distension in late-onset cases. This was similar to the work of Selimovic et al (2010)[6], who found these signs were more frequent in severe or late-presenting cases. Reduced urine output and feeding difficulties, noted in over half of this current cohort, were indicative of systemic involvement and were consistent with other studies highlighting these as early manifestations of sepsis. Among the laboratory parameters studied, CRP was elevated (>6 mg/L) in 84.7% of our neonates, with a mean value of 16.8 mg/L. This rate was higher than the 69–77% sensitivity and specificity

reported by Jeon et al (2014) and Hisamuddin et al (2015), but could be explained by our higher CRP cut-off, use of prospective protocols, and a larger share of late-onset cases.[15] The mean white blood cell (WBC) count was 12.3 $\times 10^3/\mu L$, which falls within the normal range but slightly higher than the baseline reported by Tappero and Johnson (2010), who found mean counts of around 10 $\times 10^3/\mu L$. Our mean absolute neutrophil count (ANC) was 7.3 $\times 10^3/\mu L$, again higher than in healthy controls from other studies.[16] The immature-to-total neutrophil (I/T) ratio averaged 0.25, exceeding the normal threshold (<0.2). This finding is similar to the 0.22–0.30 range seen in other reports of septic neonates (Benitz et al, 1998).[13] Platelet counts were generally normal (mean 215 $\times 10^3/\mu L$), but late-onset cases showed a drop (160 $\times 10^3/\mu L$), supporting published evidence that thrombocytopenia is linked to advanced infection. Differential leukocyte counts showed a predominance of neutrophils (61% ± 16), with lymphocytes at 29% ± 12, monocytes at 5% ± 2, and eosinophils at 3% ± 1. This neutrophil predominance, along with elevated CRP and I/T ratio, strongly suggests an ongoing bacterial infection or systemic inflammatory response in the study population (Table IV). These values were in line with those reported by other studies, which had demonstrated the utility of these hematological markers in diagnosing neonatal sepsis.[15-17]

Late-onset sepsis (LOS) cases showed higher CRP levels (mean 36.4 mg/L vs. 15.2 mg/L in early-onset), WBC counts (19.0 $\times 10^3/\mu L$ vs. 12.5 $\times 10^3/\mu L$) and ANC (11.2 $\times 10^3/\mu L$ vs. 6.8 $\times 10^3/\mu L$). The I/T ratio and neutrophil percentage were also higher, while platelet counts were lower in LOS, reflecting a stronger inflammatory response. These patterns were nearly identical to those described by Brown et al (2019) and Yin et al (2024), who both found association of LOS with higher CRP, higher neutrophil response, and lower platelets.[13,14] Clinically, feeding difficulty (72% vs. 48%), cyanosis (60% vs. 30%), seizures (42% vs. 10%), and abdominal distension (56% vs. 22%) were all more common in LOS, echoing previous findings (Selimovic et al 2010; Benitz et al 1998) that late-onset sepsis is often more severe.[15] Our study supported the use of CRP as a helpful but imperfect tool for early sepsis detection. In our population, CRP alone was positive in over 80% of suspected cases, while other studies (Jeon et al 2014[12]; Hisamuddin et al 2015[11]) found sensitivity and specificity between 69–77%. The positive predictive value and specificity in those studies ranged from 53% to 80%. The higher rate in our data may be due to case selection or the higher threshold for CRP positivity (>6 mg/L). Other studies suggested combining CRP with other markers- such as I/T ratio, WBC, and clinical features-increases diagnostic accuracy. Our findings supported this combined approach, as most neonates with high CRP also had abnormal hematological and clinical parameters. Studies like Brown et al (2019) suggested that serial (repeated) CRP measurements may help identify trends and track severity, which could be useful in our setting for late-onset cases.[17] Our current results also align with the observation by Jeon et al (2014)[12] that positive maternal CRP predicts risk of early -onset sepsis, although we focused only on neonatal CRP. In our setting, neonatal CRP was highly informative, suggesting that routine neonatal testing may be more practical in resource-limited environments.

LIMITATIONS

One limitation of this study is we did not use Blood culture, which could have been helpful in validation. Additionally, the sample size may not adequately represent all demographic groups, possibly limiting the generalizability of the findings.

CONCLUSION

The study has concluded that risk of sepsis were higher in male babies. Common clinical features included tachycardia, temperature instability, and reduced urine output, while over 80% showed elevated CRP levels. Hematological findings has shown slightly higher WBC counts, increased I/T ratios, and declining platelet levels, indicating systemic inflammation.

REFERENCES

1. Shete VB, Ghadage DP, Muley VA, Bhore AV. Acinetobacter septicemia in neonates admitted to intensive care units. J Lab Physicians. 2009;1:73–76.
2. Mahmood A, Karamat KA, Butt T. Neonatal Sepsis: High antibiotic resistance of the bacterial pathogens in a Neonatal Intensive Care Unit in Karachi. J Pak Med Assoc. 2002;52(8):348–50.
3. Shirazi H, Riaz S, Tahir R. Role of the Hematological Profile in Early Diagnosis of Neonatal Sepsis. Ann Pak Inst Med Sci. 2010;6:152–56.
4. Tappero E, Johnson P. Laboratory evaluation of neonatal sepsis. Newborn Infant Nurs Rev. 2010;10(4):209–17.
5. Ahmed Z, Ghafoor T, Waqar T, Ali S, Aziz S, Mahmud S. Diagnostic value of C-reactive protein and haematological parameters in neonatal sepsis. J Coll Physicians Surg Pak. 2005;15(3):152–56.
6. Selimovic A, Skokic F, Bazardzanovic M, Selimovic Z. The predictive score for early-onset neonatal sepsis. Turk J Pediatr. 2010;52:139–44.
7. Benitz WE, Han MY, Madan A, Ramachandra P. Serial Serum C-reactive protein levels in diagnosis of neonatal infection. Pediat. 1998;102:41.
8. Chan Dk, Ho LY. Usefulness of C-reactive Protein in the diagnosis of neonatal sepsis. Singapore Med J. 1997;38(6):252–55.
9. Worku M, Aynalem M, Biset S, Woldu B, Adane T, Tigabu A. Role of complete blood cell count parameters in the diagnosis of neonatal sepsis. BMC Pediatr 2022; 22(1):411-20.
10. Patel U, Patel VK, Patel NP, Verma J, Ratre BK, Verma SP. C-Reactive Protein and other Hematological parameters for diagnosis of Neonatal Sepsis.Int J Mes Res. 2014;2(1):311-18.
11. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pak J Med Sci. 2015;31(3):527-31.

12. Jeon JH, Namgung R, Park MS, Park KI, Lee C. Positive maternal C-reactive protein predicts neonatal sepsis. Yonsei Med J. 2014 Jan;55(1):113-7.

13. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998 Oct;102(4):E41.

14. Anderson-Berry AL.Neonatal Sepsis Workup Updated, Rosenkrantz T, editor. 2015;

15. Ganesan P, Shanmugam P, Sattar SB, Shankar SL. Evaluation of IL-6, CRP and hs-CRP as Early Markers of Neonatal Sepsis. J Clin Diagn Res. 2016 May;10(5):DC13-7.

16. Yin W, Fang C, Fan X, Chen Y. Albumin and C-reactive protein as diagnostic markers for neonatal sepsis: a retrospective study. J Int Med Res. 2024 Mar;52(3):1-7.

17. Brown JVE, Meader N, Cleminson J, McGuire W. C-reactive protein for diagnosing late-onset infection in newborn infants. Cochrane Database Syst Rev. 2019 Jan 14;1(1):CD012126.

ORIGINAL ARTICLE

Role of Dermoscope as a Monitoring Tool in Assessing Treatment Response in Patients with Tinea Corporis: A Prospective Clinical Study

Aryal A[1], Shrestha M[2], Bhattarai N[3]

ABSTRACT

Introduction: Tinea corporis is a common superficial dermatophytic infection affecting the glabrous skin. There is a prominent gap in research concerning the use of dermoscopy for monitoring treatment response in tinea corporis. **Aims**: To evaluate dermoscopic findings and assess the treatment response in patients with tinea corporis **Methods:** A prospective clinical study was conducted at the Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, involving 115 patients with tinea corporis over a 12-month period. Baseline dermoscopic examinations were performed for all participants. Patients were treated with oral itraconazole 100 mg twice daily and then re-evaluated with dermoscopy at 2 and 4 weeks. The frequency of various dermoscopic changes was analyzed using the chi-square test. **Results:** At baseline, the most common dermoscopic findings were erythema (98.3%), brown globules (83.5%), and perifollicular scales (80%). Micropustules were the first feature to resolve, disappearing within 2 weeks. Erythema, the predominant finding, showed significant reduction by 4 weeks (P = 0.005). Other features, including dotted vessels, perifollicular scales, brown globules, peripheral peeling scales, moth-eaten scales, translucent hairs, broken hairs, black dots, and telangiectasia, significantly decreased at 2 weeks, with further reduction observed by 4 weeks. **Conclusion:** Dermoscopy is a non-invasive, bedside tool that aids in the monitoring of treatment response in tinea corporis. It is particularly useful in identifying patients who may need extended systemic antifungal therapy to achieve a full resolution of the infection.

***Keywords**:* Dermoscopy, Tinea Corporis, Treatment response

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INTRODUCTION

Tinea corporis, commonly known as 'ringworm,' is a superficial dermatophytic infection affecting glabrous skin.[1,2] The infection is chiefly caused by Trichophyton rubrum.[1] Tinea corporis is the most prevalent dermatophytosis, with a global distribution and an estimated lifetime risk of 10-20%.[3,4,5] In recent years, the incidence of dermatophytic infections has surged, with tinea corporis being the most widespread. Diagnosis is typically achieved through microscopic examination with potassium hydroxide and fungal cultures, which require approximately 3-4 weeks for results.[5] This delay can impede the prompt initiation of treatment. Furthermore, these diagnostic methods are labor-intensive and demand specialized personnel and mycological tools. Diagnosing tinea corporis can be particularly challenging due to factors such as steroid misuse or incomplete treatment. A dermoscope, a noninvasive, portable and bedside device, offers a practical solution for assessing disease activity as well as comparing treatment effects of medicines on various skin conditions by evaluating dermoscopic patterns like hair, pigment and vascular pattern.[6] Although dermoscopic features of tinea corporis have been documented in several studies with small sample sizes, there is a notable lack of research on monitoring treatment response. This study aims to address this gap by investigating dermoscopic findings and assessing the treatment response for tinea corporis.

METHODS

A prospective, clinical study was carried out at the Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke. Written informed consent was obtained from all participants before their enrollment. The study was approved by the Institutional Review Committee (IRC no. 07/080-081). The prevalence of tinea corporis at Nepalgunj Medical College and Teaching Hospital from April 2022 to April 2023 was 5.03%. Using this prevalence proportion and a margin of error of 4% with a 95% confidence interval

(CI), the sample size was determined to be 115. A convenient sampling technique was employed to select the study population. The study was conducted over 12 months, from August 2023 to August 2024. The patients who met the study criteria were enrolled. The diagnosis of tinea corporis was made clinically and then confirmed by microscopic examination using potassium hydroxide (KOH). Baseline dermoscopic examination was conducted for all cases. Dermoscopy was performed using a DermLite DL1 dermatoscope connected to an iPhone 12. All patients were treated with oral itraconazole 100 mg twice daily and were subsequently evaluated with dermoscopy at 2 and 4 weeks. The contact plate of the dermoscope was cleaned with a sanitizer to prevent cross-contamination.

Inclusion criteria

1. Patients of age 16-70 years with diagnosis of tinea corporis

2. Willing to provide written informed consent for participation

Exclusion criteria

1. Patients with elevated liver enzymes or serum bilirubin levels

2. Patients with history of topical or systemic antifungals in last three months.

3. Patients who are on topical steroids

4. Pregnant or lactating women.

5. Patients not willing to give consent for study

6. Patients with other comorbidities and immunosuppression

Statistical analysis: All the data were entered in MS-EXCEL sheet and proceeded for data analysis by using Statistical Program for Social Sciences (SPSS) version 26. The categorical data were presented as numbers (percentages). The continuous data was presented as either mean ± standard deviation or median (inter-quartile range) depending on the normality of the data distribution. Chi-square tests was used to evaluate for the statistical significance amongst independent variables. A P value less than 0.05 was considered significant.

RESULTS

Demographic features: Total 115 patients of KOH positive cases of tinea corporis were included in the study. Out of 115, 63 (54.8%) were female and 52 (45.2%) were male. Age of patients ranged from 16 to 69 years, with a mean age of 32.8 ± 13.4 years. In our study, median duration of disease was 10 weeks; it ranged from 1 week to 48 weeks. Dermoscopic features: Baseline dermoscopic findings of tinea corporis are shown in Table I. Baseline findings in decreasing order of frequency were erythema (98.3%), brown globules (83.5%), perifollicular scales (80%), peripheral peeling scales (79.1%), dotted vessels (69.6%), moth eaten scales (60.9%), translucent hairs (60%), broken hairs (31.3%), black dots (17.3%), micropustule (12.1%), and talengectasia (9.6%).

Baseline Dermoscopic features	Number of patients (N=115)	Percentage (%)
Erythema	113	98.3
Dotted vessels	80	69.6
Peripheral peeling scales	91	79.1
Perifollicular scales	92	80
Moth-eaten scales	70	60.9
Translucent hairs	69	60
Brown globules	96	83.5
Talengectasia	11	9.6
Broken hairs	36	31.3
Black dots	20	17.3
Micropustule	14	12.1

Table I: Baseline Dermoscopic findings of tinea corporis

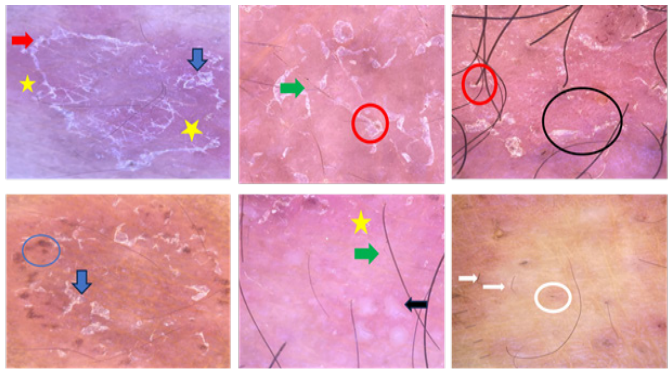

Figure 1: Baseline dermoscopic features of tinea corporis showing background erythema (yellow star), peripheral peeling scale (red arrow), moth eaten scale (blue arrow), brown globules (blue circle), translucent hair (green arrow), perifollicular scale (red circle), dotted vessels (black circle), micropustule (black arrow), broken hair (white arrow), and black dot (white circle)

Dermoscopic follow-up: Dermoscopic findings of tinea corporis at follow-up at 2 and 4 weeks are shown in Table II. The first dermoscopic parameter to resolve completely was micropustules, which decreased from 12.1% at baseline to 0% at 2 weeks, followed by black dots, which decreased from 17.3% at baseline to 0% at 4 weeks. Erythema, the most common dermoscopic finding, showed a slow response, decreasing from 98.3% at baseline to 76.5% at 2 weeks (P = 0.179), but reduced significantly to 17.4% at 4 weeks of treatment (P = 0.005). The frequency of other dermoscopic parameters, including dotted vessels, perifollicular scales, brown globules, peripheral peeling scales, moth-eaten scales, translucent hairs, broken hairs, black dots, and telangiectasia, significantly decreased at 2 weeks. By 4 weeks, dotted vessels, perifollicular scales, translucent hairs, brown globules, broken hairs, and telangiectasia showed a significant reduction compared to 2 weeks. However, peripheral peeling scales and moth-eaten scales did not decrease significantly at 4 weeks compared to 2 weeks (P = 0.30 and P = 0.74, respectively).

Variables	Baseline N (%)	Post treatment N (%) 2 weeks	Post treatment N (%) 4 weeks	P (Baseline vs 2 weeks)	P (2 vs 4 weeks)
Erythema	113 (98.3%)	88 (76.5%)	20 (17.4%)	0.179	0.005*
DV	80 (69.6%)	49 (42.6%)	6 (5.2%)	<0.001**	0.004*
PPS	91 (79.1%)	29 (25.2%)	3 (2.6%)	0.001**	0.30
PFS	92 (80%)	59 (51.3%)	18 (15.7%)	<0.001**	<0.001**
MES	70 (60.9%)	11 (9.6%)	1 (0.9%)	0.005*	0.74
TH	69 (60%)	64 (55.7%)	29 (25.2%)	<0.001**	<0.001**
Brown globules	96 (83.5%)	74 (64.3%)	32 (27.8%)	<0.001**	<0.001**
Broken hairs	36 (31.3%)	20 (17.4%)	6 (5.2%)	<0.001**	<0.001**
Black dots	20 (17.3%)	8 (7.0%)	0 (0%)	<0.001**	-
Micropustule	14 (12.1%)	0	0	-	-
Talengectasia	11 (9.6%)	7 (6.1%)	2 (1.7%)	<0.001**	<0.001**

*P-value <0.05 and **P-value <0.001

Abbreviations: DV= Dotted vessels, PPS= Peripheral peeling scales, PFS= Perifollicular scales, MES=Moth-eaten scales, TH= translucent hair

Table II: Dermoscopic findings of tinea corporis at follow-up in 2 weeks and 4 weeks

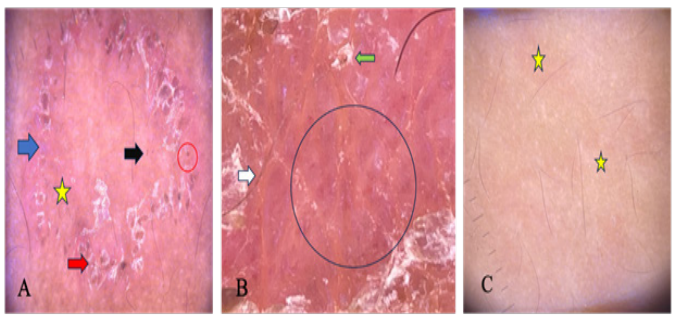

Figure 3: A & B showing pre-treatment dermoscopic features of a patient. A shows peripheral peeling scales (red arrow), moth eaten scale (blue arrow), erythema (yellow star), broken hair (black arrow), and brown globules at the periphery (red circle); B shows dotted vessels (black circle), translucent hair (white arrow) and perifollicular scale (green arrow); C showing post-treatment dermoscopic feature of the same patient.

There's a minimal patchy background erythema (yellow star) and other dermoscopic findings has subsided.

DISCUSSION

Tinea corporis is a common superficial dermatophyte infection of the glabrous skin, characterized by the appearance of the itchy, well-demarcated, oval or annular scaly patch with raised borders and central clearing giving rise to the term 'ringworm'.[5] Traditionally diagnosed through clinical examination, the condition has become increasingly challenging for physicians to identify due to partial treatments and steroid misuse. Dermoscopy can enhance diagnostic accuracy for tinea corporis by allowing in vivo examination of skin features not visible to the naked eye. However, research and case reports on the use of dermoscopy for diagnosing and monitoring tinea corporis remain limited.

Our study N=115	Bhat et al[8] N=30	Yadav et al[9] N=31	Lekkas et al[11] N=36
Erythema (98.3%)	Diffuse erythema (100%)	Erythema (100%)	Dotted vessel (100%)
Brown globules (83.5%)	Whitish scales (100%)	Dotted vessels (12.9%)	Peripheral vascular arrangement (63.6%)
Perifollicular scales (80%)	Follicular micropustules (36.7%)	Telangiectasia (12.9%)	Peripheral scles (76.5%)
Peripheral peeling scales (79.1%)	Brown spots surrounded by a white-yellowish halo (20%)	Brown spot with yellow halo (87%)	White scales (86.1%)
Dotted vessels (69.6%)	Wavy and broken hairs (13.3%)	Bent hairs (87%)	Perifollicular scale (13.9%)
Moth-eaten scales (60.9%)	Morse code-like vellus hairs (3.3%)	Translucent hairs (74.1%)	Moth eaten scles (97.2%)
Translucent hairs (60%)		Broken hairs (58%)	Outward peeling scales (97.2%)
Broken hairs (31.3%)		Morse code hair (54.8%)	Broken hairs (63.9%)
Black dots (17.3%)		Perifollicular scales (29%)	
Micropustule (12.1%)		Micropustule (19.3%)	
Talengectasia (9.6%)			

Table III: Comparison of dermoscopic features in tinea corporis

In our study, erythema was the most prevalent dermoscopic feature, observed in 98.3% of tinea corporis cases. Background erythema has been histopathologically linked to inflammation and vascular dilation in previous research.[7] The second most frequent finding in our study was brown globules, present in 83.5% of cases. These globules result from melanin deposition in the epidermis due to a post-inflammatory response.[7] While other studies have reported brown globules surrounded by a halo in tinea corporis, this halo was not observed in our study.[8-10]

Scales are a crucial indicator of dermatophytosis, reflecting hyperkeratosis. Our study identified scales as perifollicular scales (80%), peripheral peeling scales (79.1%), and moth-eaten scales (60.9%). Lekkas et al reported peripheral scales, moth-eaten scales, and outward peeling scales as strong dermoscopic predictors of tinea corporis, defining 'moth-eaten scales' as coalescing peripheral scales that form larger, multicyclic lesions.[11] Additionally, in our study, dotted vessels, which correspond to the tips of dilated vessels, were observed in 69.6% of cases.[7] This finding was seen in other studies, including those by Lekkas et al, Yadav et al and Hussain et al.[9,11,12] In our study, hair changes included translucent hairs (60%), broken hairs (31.3%), and black dots (12.1%). Translucent hairs may result from extensive fungal invasion of vellus hairs, while broken hairs, black dots, morse code-like hair and follicular micropustules are also associated with fungal parasitism.[12] Some researchers suggest that the involvement of vellus hairs could be a criterion for starting systemic treatment.[10,13-15] However, morse code-like hair, characterized by alternating white bands across the hair shaft, was not observed in our study. Micropustules, which correspond to neutrophilic abscesses in the epidermis, were present in only 12.1% of cases, consistent with findings by Yadav et al.[9]

Dermoscopic follow-up

In our study, we conducted a dermoscopic follow-up to assess the treatment response for tinea corporis. Our findings revealed that erythema took the longest to show significant improvement, requiring about 4 weeks, whereas micropustules resolved the quickest, typically within 2 weeks, followed by black dots, which cleared by 4 weeks. Hair-related changes such as translucent hairs, broken hairs, and black dots responded well to treatment, with significant improvement observed at both 2 and 4 weeks. Other dermoscopic features, including dotted vessels, brown globules, perifollicular scales, peripheral peeling scales, and moth-eaten scales, showed considerable improvement at 2 weeks, with further reduction in all these findings by 4 weeks. A similar study, which evaluated the dermoscopy in patients with tinea corporis and tinea incognito also reported the resolution of micropustules within 2 weeks, aligning with our results. Additionally, they found that erythema resolved more quickly in naïve tinea infections compared to tinea incognito. They observed that altered hair morphology features, such as translucent hairs, broken hairs, and morse code hairs, showed a favorable response by 4 weeks in both naïve tinea infections and tinea incognito.[9]

In our study, patients displaying persistent erythema, dotted vessels, and telangiectasia after 4 weeks of treatment may be attributed to prior misuse of topical steroids. Patients who continued to exhibit abnormal hair features, such as translucent and broken hairs, beyond 4 weeks likely experienced a suboptimal response to treatment. This highlights the critical role of dermoscopy in identifying such cases and suggests the need for considering extended treatment beyond 4 weeks. Thus, dermoscopy proves to be a valuable monitoring tool for evaluating treatment efficacy, as it clearly documents the regression of various dermoscopic patterns and the eventual resolution of all altered hair features by the end of therapy.

LIMITATION

Long-term follow-up could provide insights into long-term treatment outcomes and help document recurrences.

CONCLUSION

Our study underscores the significant role of dermoscopy in monitoring and evaluating the response to treatment for tinea corporis. The study highlights that dermoscopy not only aids in accurate diagnosis but also serves as a valuable tool for assessing treatment response and guiding therapeutic decisions. Persistent abnormal findings, despite treatment, emphasize the necessity for ongoing evaluation and potentially prolonged treatment to achieve complete resolution.

REFERENCES

1. Carrascal-Correa DF, Zuluaga A, González A. Species distribution of the main aetiologic agents causing skin dermatophytosis in colombian patients: a 23-year experience at a mycological reference center. Mycoses. 2020;63(5):494-9. https://doi: 10.1111/myc.13073

2. Lim SS, Shin K, Mun JH. Dermoscopy for cutaneous fungal infections: A brief review. Health Science Reports. 2022;5(1):e464. https://doi: 10.1002/hsr2.464

3. Poudyal Y, Joshi SD. Medication practice of patients with dermatophytosis. J Nepal Med Assoc. 2016;55(203):07–10. https://doi:10.31729/jnma.2830

4. Adams BB. Tinea corporis gladiatorum. Journal of the American Academy of Dermatology. 2002;47(2):286-90.https://doi: 10.1067/mjd.2002.120603

5. Leung AK, Lam JM, Leong KF, Hon KL. Tinea corporis: an updated review. DIC. 2020;9:1-12.https://doi: 10.7573/dic.2020-5-6

6. Sonthalia S, Yumeen S, Kaliyadan F. Dermoscopy Overview and Extradiagnostic Applications. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537131/

7. Ankad BS, Mukherjee SS, Nikam BP, Reshme AS, Sakhare PS, Mural PH. Dermoscopic characterization of dermatophytosis: A preliminary observation. Indian Dermatol Online J. 2020;11(2):202-07. https://doi: 10.4103/idoj.IDOJ_190_19

8. Bhat YJ, Keen A, Hassan I, Latif I, Bashir S. Can Dermoscopy Serve as a Diagnostic Tool in Dermatophytosis? A Pilot Study. Indian Dermatol Online J. 2019;10(5):530-35. https://doi: 10.4103/idoj.IDOJ_423_18

9. Yadav S, Pandhi D, Grover C, Das S. Dermoscopic Findings and Assessment of Treatment Response in Patients with Tinea Incognito: A Pilot Study. Indian Dermatol Online J. 2024;15(2):205-12. https://doi: 10.4103/idoj.idoj_264_23

10. Knöpfel N, Del Pozo J, Escudero MM, et al. Dermoscopic visualization of vellus hair involvement in tinea corporis: a criterion for systemic antifungal therapy. Pediatric Dermatol 2015;32:e226–22. https://doi: 10.1111/pde.12648

11. Lekkas D, Ioannides D, Lazaridou E, et al. Dermatoscopy of tinea corporis. J Eur Acad Dermatol Venereol. 2020;34(6):e278-e280. https://doi: 10.1111/jdv.16277

12. Hussain AA, Narkhede ND. A Study to Establish Correlation between Dermoscopic and Clinical Findings of Dermatophytosis. Indian Journal of Public Health Research & Development. 2020;11(3), 857–62. https://doi.org/10.37506/ijphrd.v11i3.1436

13. Gómez-Moyano E, Crespo-Erchiga V. Tinea of vellus hair: an indication for systemic antifungal therapy. British Journal of Dermatology. 2010;163(3):603-6. https://doi: 10.1111/j.1365-2133.2010.09811.x

14. Moyano EG, Erchiga VC, Pilar LM, et al.Correlation between dermoscopy and direct microscopy of morse code hairs in tinea incognito.J Am Acad Dermatol 2016;74:e7–8

15. Jartarkar SR, Patil A, Goldust Y, Cockerell CJ, Schwartz RA, Grabbe S, Goldust M. Pathogenesis, Immunology and Management of Dermatophytosis. J Fungi (Basel). 2021;8(1):39. https://doi: 10.3390/jof8010039

Comparison of Sputum Cytology with BronchoAlveolar Lavage Cytology in Diagnosis of Lung Cancer: A Hospital Based Study In BPKIHS

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ABSTRACT

Introduction: Lung cancer is one of the commonest cancers and its burden is increasing in developing countries as well. It has high mortality rate as most cases are diagnosed at late stages where there have very less therapeutic benefits. Early diagnosis of lung cancer can be done by cytology screening tools like Sputum and Bronchoalveolar Lavage Cytology study. **Aims**: To compare the diagnostic yield of Sputum cytology with Broncho-Alveolar Lavage cytology in diagnosing lung cancer by correlating with biopsy findings. **Methods**: This is a one-year hospital based prospective cross sectional study done at Department of Pathology, BPKIHS, Dharan. It included 34 cases subjected to Sputum and broncho-alveolar lavage cytology as well as Transbronchial biopsy. Diagnostic yield of Sputum and BAL cytology were calculated by correlating with biopsy findings. **Results:** Age of patients ranged from 29 to 84 years with near equal gender distribution. Biopsy was positive for lung cancer in 22 cases (65%). Sensitivity of Sputum and broncho-alveolar lavage cytology were calculated as 38.9 % and 68.4% respectively. Cigarette smoking showed statistically significant correlation with Lung cancer. Most common cancer detected in biopsy was squamous cell carcinoma followed by Adenocarcinoma. **Conclusion:** Sputum and Bronchoalveolar Lavage cytology study can serve as initial screening tools for suspected lung cancer cases, especially in limited resources settings. However, the final confirmation has to be done by the gold standard histopathology study.

Keywords: Biopsy, Bronchoalveolar Lavage, Carcinoma, Cytology, Sputum

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INTRODUCTION

Lung cancer is one of the commonest cancers and cause of cancer related deaths all over the world.[1] In Nepal, lung cancer is the commonest cancer among male and third most common in female population with overall incidence of 16.64%.[2] Deaths by lung cancer is largely by the carcinogenic effects of cigarette smoking.[3] Lung cancer is fatal in more than 90% of diagnosed cases because most cases are diagnosed at very late stage when the disease is incurable.[4] This dismal mortality makes early diagnosis and treatment essential for improvement in the morbidity and mortality.[5] Evidences suggest screening and early detection may improve outcome in lung cancer which can be achieved by evaluation of various cytological specimen.[3] Sputum Cytology is a simple reliable, cost effective and non-invasive procedure for diagnosis of pulmonary lesions.[6] BAL is a safe and reliable sampling method from distal airways and alveoli, which has been referred to as a 'liquid biopsy of the lung'.[7] Diagnosis made by any cytological examined hence has to be verified by the gold standard- biopsy. A diagnostic TBBx may prevent the need for an open lung biopsy.[8] Therefore, this study was carried out to see the difference in the diagnostic yield of Sputum cytology with BAL cytology in the diagnosis of lung cancer and correlating them with transbronchial biopsy.

METHODS

A Hospital based comparative cross sectional study was carried out from May 2017 to April 2018 in the Department of Pathology, BPKIHS, after obtaining ethical clearance from the institutional review board (Ref. no: 333/073/074-IRC). All patients suspected of lung malignancy undergoing cytological (Sputum and BAL) as well as histopathological diagnostic procedures were included in the study after taking informed consent. Failure to give any of the three samples were excluded from the study.

A total of 34 cases were taken for the study which was calculated based on the study done by Kumar P et al which showed the sensitivity of sputum cytology as 30%. (Kumar P et al). Both BAL as well as 3 samples of sputum were processed and stained with PAP and Giemsa stains as per the standard protocol. Biopsy specimen were processed and stained with routine H and E stain as per the standard protocols. Slides were screened and reporting done by expert pathologists.

Data were analyzed using Microsoft excel 2010 and standard statistical software SPSS 20.0.

RESULTS

Age of the patients in our study ranged from 29 to 84 years with a mean age of 57.59 ±13.28 Years. Mean age of the cancer positive patients in our study was found to be 60.5 years. We received total of 34 cases out of which 19 (55.9%) were males and 15 (44.1%) were females. 13 (76.50%) out of 19 male and Nine (69.20%) out of 15 females were biopsy positive for lung cancer. But gender as such was not significant in causation of lung cancer. (p value of 0.6).

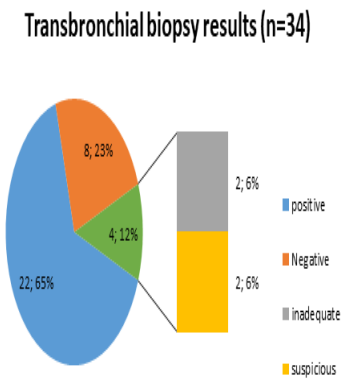

Figure 1: Biopsy Result (n=34)

Of the total 34 cases, biopsy was positive for malignancy in 22 cases (65%), negative in Eight cases (23%) and undetermined in Four cases (12%). Undetermined cases were those which were either inadequate for evaluation or suspicious for malignancy which could have either of the results.

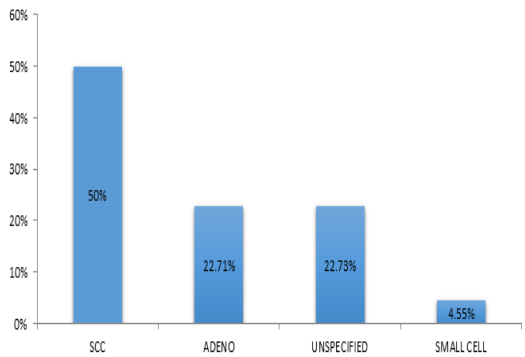

Figure 2: Type of malignancies in biopsy positive cases

11 (50%) of the biopsy positive cases were diagnosed as SCC while five (22.71%) cases were diagnosed adenocarcinoma. One case was diagnosed as small cell carcinoma and no specific cancer subtyping was possible in Five cases.

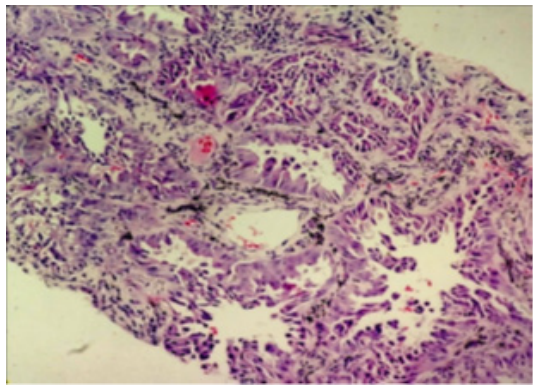

Photo1: Adenocarcinoma of lung (H &E stain, 40x)

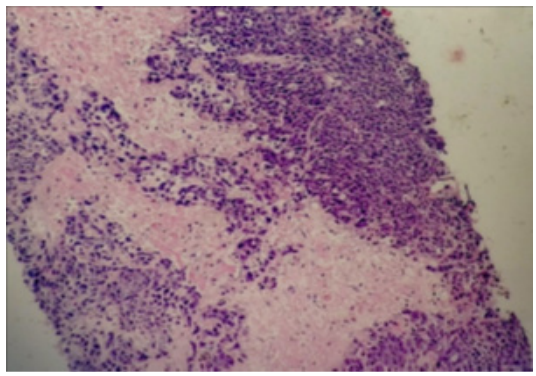

Photo 2: SCC Lung (H &E, 40x)

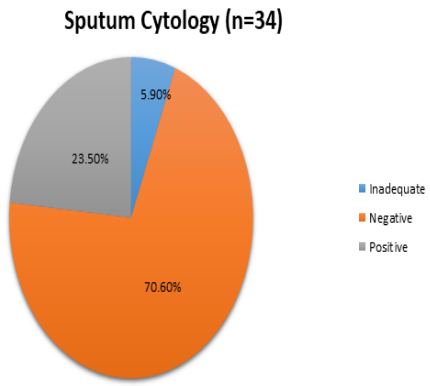

Figure 3: sputum cytology result (n=34)

Eight (23.5%) cases showed positive sputum cytology while 24 (70.6% cases) were cancer negative. Two cases (5.90%) were inadequate for evaluation. Six out of Eight sputum positive cases were diagnosed as squamous cell carcinoma while two cases were given a diagnosis of malignancy as definite type could not be ascertained by sputum cytology alone.

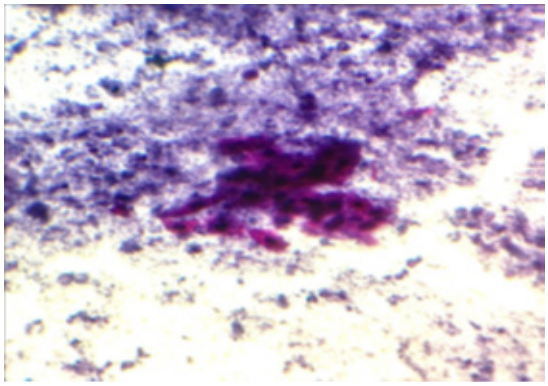

Photo 3: Squamous cell carcinoma in sputum (PAP Stain, 40x)

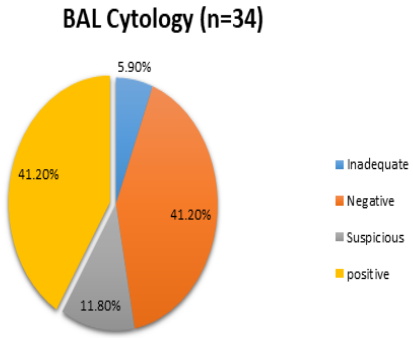

Figure 4: BAL cytology

BAL cytology was positive in 14 cases (41.20%), negative in 14 cases (41.20%), suspicious of malignancy in Four cases (11.80%) and was inadequate for evaluation in Two cases. Of the positive cases detected by BAL, three cases (21.4%) were diagnosed as adenocarcinoma while the subtype of 11 cases (78.6%) could not be identified and hence were reported as malignancy only.

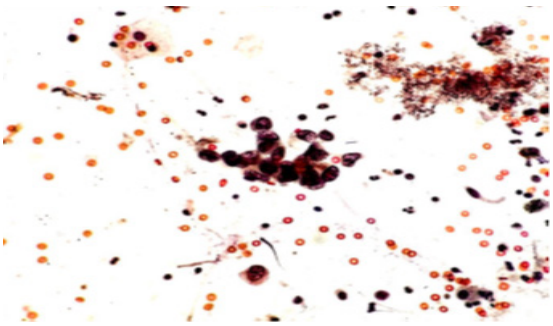

Photo 4: Adenocarcinoma in BAL cytology (PAP stain, 40x)

All the undetermined Sputum and BAL samples (inadequate and suspicious for malignancy), to which corresponding histology is either positive or negative is excluded for analysis and test results are grouped into test positive/ not-positive and test negative/ not-negative and thus sensitivity for each were calculated.

		Histopathology	
		Positive	Not positive
Sputum cytology	Positive	8	0
	Not positive	13	12
	Total	21	12

Table I: sputum sensitivity

Sensitivity of sputum cytology = (Test positive/ True positive) * 100

= 8/21 * 100

= 38.09%

		Histopathology		
		Positive	Not positive	Total
BAL cytology	Positive	13	1	14
	Not positive	6	11	17
	Total	19	12	31

Table II: Sensitivity of BAL cytology

Sensitivity of BAL cytology = (Test positive/ True positive) * 100

=13/19 * 100

= 68.4 %

Twenty four of the participants were ever smokers and 10 were never smokers. Duration of smoking varied widely from less than 10 yrs in two participants to >30 years in maximum of six patients.

The median pack years among smokers was found to be 8.

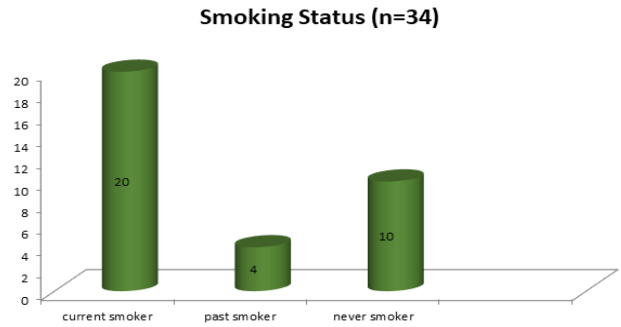

Figure 5: Smoking status among study population

Characteristic	categories	cancer		P value	Remark
		Positive	Negative		
Smoking	Never smoker	2 (25%)	6 (75%)	0.001	S *
	Ever smoker	20 (90.9%)	2 (9.1%)		
* Fisher's Exact test applied					

Table III : Association of smoking with lung cancer

Two (25%) out of Eight never smokers were lung cancer positive whereas 20 (90.90%) of the 22 ever smokers were cancer positive and the association of smoking with lung cancer was statistically significant. (P value- 0.001)

DISCUSSION

We received a total of 34 cases out of which 19 (55.9%) were males and 15 (44.1%) were females. 13 (76.50%) out of 19 male and 9 (69.20%) out of 15 females were biopsy positive for lung cancer. But gender as such was not significant in the causation of lung cancer with a p-value of 0.6. Age of the patients in our study ranged from 29 to 84 years with a mean age of 57.59 ±13.28 Years. Mean age of the cancer positive patients in our study was found to be 60.5 years and that of cancer negative patients was 53.15 years with p value of 0.2 which was statistically non-significant. A comparable study on clinicopathological evaluation of bronchogenic carcinoma by Barsky et al revealed the mean age of BAC patients as 59.2 ± 11.5 years, as compared to 64.1 ± 13.5 years for non- bronchoalveolar carcinoma.[9]

The sensitivity of sputum cytology in our study was 38.09%. Studies have shown the sensitivity of sputum cytology in diagnosing lung cancers ranged from as less as 4% to as high as 60%. comparable results were obtained from the studies done across the globe%.[3,4,10-12]

Discordent to our study, Ammanagi et al studied the value of sputum cytology in diagnosing lung cancer in which sensitivity of sputum cytology was 60%, which increased with an increase in the number of samples examined.[13]

In our study Sensitivity of BAL cytology in detecting lung cancers was found to be 68.48%. most of the studies in the past have results comparable to ours, with the sensitivity ranging from 42% to 69.6%.[3,14,15,17,18]

Among the 22 biopsy positive cases, 11(50%) cases were biopsy-proven SCC, Five (22.7%) were adenocarcinoma, one (4.5%) case of small cell carcinoma and Five cases (22.7%) were unclassified. All the cases were classified into specific subtypes based on the morphological features and some special stains. Though the current trend has suggested adenocarcinoma to be the commonest lung carcinoma, in our study Squamous cell carcinoma was the commonest one followed by adenocarcinoma.[19,20]

90% of ever smokers (current and past) had positive cancer biopsy whereas only 25% of non-smokers were cancer positive. In our study significant association is seen between smoking and lung cancer (p-value of 0.001). No of pack years of smoking is not statistically significant in our study though other studies have shown that the likelihood of getting lung carcinoma is directly proportional to the frequency and duration of smoking (pack years).[19,21,22] The non-significant result of our study might be due to the small sample size and also the history of smoking being quite common among the biopsy negative patients.

LIMITATIONS

The most important limitation of our study is a small sample size. Study on a large scale which would have better represented the study population would produce more reproducible results. Undetermined cases (inadequate for evaluation and suspicious for malignancy in biopsy) could not be included in the analysis of variables. Owing to unavailability of IHC during the study period, 2 cases had to be omitted wherein definite diagnosis of malignancy based on histopathology alone could not be made.

CONCLUSION

The overall accuracy of our sputum cytology diagnosis and BAL cytology diagnosis is similar to those reported in the literature. Few cases we missed out in our study owing to the sample inadequacy and lack of IHC in suspicious cases. Had these things been taken care of and feasible, the diagnostic yield of these cytological procedures, as well as biopsy diagnosis, would have been higher in our study.

REFERENCES

1. Malik PS, Raina V. Lung cancer: prevalent trends & emerging concepts. Indian J Med Res. 2015 Jan;141(1):5–7.
2. Piya MK, Acharya SC. Oncology in Nepal. South Asian J cancer. 2012;1(1):5–8.
3. Kumar P. Comparison of Effectiveness of Sputum Cytology With Bronchoalveolar Lavage (Bal) in the Diagnosis of Lung Cancer.International Journal of current Research 2014;6(8):8150–52.
4. Ch KM, Younus M, Rehman AU, Zafar SF, Bukhari SMH. The Importance of Sputum Cytology in the Diagnosis of Lung Cancer. 2010;16(3):198–201.
5. Shukla S, Malhotra KP, Husain N, Gupta A, Anand N. The utility of cytology in the diagnosis of adenocarcinoma lung: A tertiary care center study. J Cytol. 2015;32(3):159–64.
6. Krane JF. Koss' Diagnostic Cytology and Its Histopathologic Bases, Fifth Edition., International Journal of Gynecological Pathology. 2007.26(3) 270.
7. Wongsurakiat P, Wongbunnate S, Dejsomritrutai W, Charoenratanakul S, Tscheikuna J, Youngchaiyud P, et al. Diagnostic value of bronchoalveolar lavage and postbronchoscopic sputum cytology in peripheral lung cancer. Respirology. 1998;3(2):131–7.
8. Donato L, Tran TMH, Mihailidou E. Interventional bronchoscopy. Vol. 38, Paediatric Bronchoscopy. 2010. 64–74
9. Holmes E. Rising incidence of bronchioloalveolar lung carcinoma and its unique clinicopathologic features. Cancer. 1994 Feb 15;73(4):1163–70.
10. Agrawal R. SPUTUM CYTOLOGY IN BRONCHOGENIC CARCINOMAS. 2000;39(1):326–8.
11. Sing A, Freudenberg N, Kortsik C, Wertzel H, Klosa B, Hasse J. Comparison of the sensitivity of sputum and brush cy-

tology in the diagnosis of lung carcinomas. Acta Cytol. 1997;41(2):399–408.

12. Raab SS, Hornberger J, Raffin T. The importance of sputum cytology in the diagnosis of lung cancer: a cost-effectiveness analysis. Chest. 1997 Oct;112(4):937–45.

13. Ammanagi AS, Dombale VD, Miskin AT, Dandagi GL, Sangolli SS. Sputum cytology in suspected cases of carcinoma of lung (Sputum cytology a poor man's bronchoscopy!). Lung India. 2012 Jan;29(1):19–23.

14. Bhat N, Nazeir MJ, Bashir H, Bashir N, Farooq S, Fatima K, et al. Correlation of bronchial biopsy with bronchoalveolar lavage in lung malignancies. 2016;4(2):428–35.

15. Das SK, Das A, Saha SK, Biswas S. Diagnostic yield of broncho-alveolar lavage fluid and postbronchoscopic sputum cytology in endoscopically non-visible lung cancers. J Indian Med Assoc. 2011 Oct;109(10):730–2, 741.

16. Richa Sharma, Hemina Desai, Pankaj Malukani, R.N.Gonsai HMG. Comparison Of Bronchoalveolar Lavage Cytology And Biopsy In Lung Malignancy. Int J Curr Res Rev. 2014;6(5):43–7.

17. Binesh F, Pirdehghan A, Mirjalili MR, Samet M, Majomerd ZA, Akhavan A. Comparative assessment of the diagnostic value of transbronchial lung biopsy and bronchoalveolar lavage fluid cytology in lung cancer. Asian Pac J Cancer Prev. 2015;16(1):201–4.

18. Rennard SI. Bronchoalveolar lavage in the diagnosis of cancer. Lung. 1990 Dec;168(S1):1035–40.

19. Janssen-Heijnen MLG. Epidemiology of Lung Cancer. In: Tumors of the Chest. Springer Berlin Heidelberg; 2006. p. 3–12.

20. Lewis DR, Check DP, Caporaso NE, Travis WD, Devesa SS. US lung cancer trends by histologic type. Cancer. 2014 Sep 15;120(18):2883–92.

21. Kumar V, Abbas AK, Aster JC, editors. Robbins and Cotran pathologic basis of disease. Ninth edit. Philadelphia, PA: Elsevier/Saunders; 2015. 1391 p.

22. Boyle P, Maisonneuve P. Lung cancer and tobacco smoking. Lung Cancer 1995

ORIGINAL ARTICLE

Metronidazole With or Without Probiotics for Prevention of Recurrent Bacterial Vaginosis: A Comparative Study

Mahaseth BK[1], Shrewastwa MK[2]

ABSTRACT

Introduction: Bacterial vaginosis is one of the most common vaginal infections affecting women of reproductive and also post-menopausal age groups worldwide. It is characterized by a decrease in number of good bacteria like, lactobacilli and an overgrowth of pathological anaerobic bacteria, leading to symptoms such as abnormal foul smelling vaginal discharge. Till date metronidazole, ornidazole, tinidazole and clindamycin are the standard antibiotic treatment, at a same time recurrence rates have been found to be high. Probiotics have emerged as a potential adjunct therapy to restore and maintain a healthy vaginal microbiome, leads to reducing bacterial vaginosis recurrence. **Aims:** To evaluate the efficacy of metronidazole alone versus metronidazole added with oral probiotics in preventing bacterial vaginosis recurrence. **Methods**: A randomized comparative study was carried out at Nepalgunj Medical College Teaching Hospital from October 2022 to September 2023. Seventy-two non-pregnant women diagnosed with bacterial vaginosis were divided into two groups: Group A (metronidazole alone) and Group B (metronidazole with probiotics). Primary outcomes, including vaginal discharge, odor, vaginal pH, Nugent score, and bacterial vaginosis recurrence, were assessed at 8, 30, and 60 days post-treatment. **Results:** At the 8th day follow-up, Group B (metronidazole + probiotics) demonstrated a statistically significant reduction in abnormal vaginal discharge compared to Group A (p=0.013). By Day 60, Group B maintained superior outcomes across all measured parameters, including vaginal discharge (p=0.089), odor (p=0.230), pH (p=0.009) and Nugent scores (p<0.001). The recurrence rate of bacterial vaginosis was consistently minimum in Group B throughout the study period. **Conclusion:** The addition of probiotics to metronidazole therapy significantly prevent recurrence of bacterial vaginosis.

Keywords: Bacterial Vaginosis, Metronidazole, Probiotics

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INTRODUCTION

Bacterial vaginosis (BV) is a common vaginal infection affecting up to 30% of women of reproductive age globally. It arises from an imbalance in the vaginal microbiota, characterized by a reduction in beneficial lactobacilli and an overgrowth of anaerobic bacteria. Lactobacilli are essential for maintaining an acidic vaginal pH, which inhibits the proliferation of harmful bacteria. When lactobacilli levels decline, pathogenic anaerobes can flourish, leading to BV symptoms such as a fishy odor, abnormal discharge, and irritation.[1] Diagnosis of BV typically involves clinical criteria, such as Amsel's criteria or laboratory methods like Gram staining, with the latter considered the gold standard. Standard treatment includes antibiotics like metronidazole or clindamycin, administered orally or vaginally. However, recurrence rates remain high, with studies indicating that 50% to 80% of women experience a recurrence within a year of treatment. Factors contributing to recurrence include sexual activity, use of intrauterine devices, smoking and practices like vaginal douching.[2,3,4,5] Given the high recurrence rates and potential complications—such as increased susceptibility to sexually transmitted infections and adverse pregnancy outcomes-there is a need for improved preventive strategies.[6] Recent research has explored the use of probiotics, particularly strains like Lactobacillus crispatus, to restore the natural vaginal flora and reduce recurrence rates. Probiotics can be administered orally or vaginally and have shown promise in re-establishing a healthy microbiome. Combining probiotics with antibiotic therapy may enhance treatment efficacy and reduce the likelihood of recurrence.[7] This study aims to evaluate the effectiveness of metronidazole (500 mg) with or without the addition of oral probiotics in preventing the recurrence of bacterial vaginosis.

METHODS

This study was conducted in the Department of Obstetrics and Gynecology, Nepalgunj Medical College Teaching Hospital, Kohalpur from October 2022 to September 2023. Patients presented with complaints of vaginal discharge at the outpatient department underwent thorough clinical examinations. Vaginal samples were collected and Gram staining was performed to assess bacterial morphology. Microscopic examination, conducted with the assistance of a laboratory technician, focused on identifying clue cells—vaginal epithelial cells covered with bacteria—which are indicative of bacterial vaginosis. Additionally, the "whiff test" was performed by adding 10% potassium hydroxide to the vaginal discharge to detect a characteristic fishy odor. These assessments were conducted to fulfill Amsel's criteria[3] and to calculate the Nugent score[5] by using counts of Rhodes and cocci /high power field, both of which are standard diagnostic methods for bacterial vaginosis. After confirming the diagnosis of bacterial vaginosis through clinical examination, Amsel's criteria[3] and the Nugent scoring system[5] participants received counseling on the benefits and risks associated with metronidazole therapy, both with and without the addition of probiotics. Those who provided informed consent were subsequently enrolled in the study. Group division was performed by using the lottery method, a form of simple random sampling. In this approach, each participant was assigned a unique identifier, and these identifiers were placed into a container. The identifiers were thoroughly mixed, and then drawn at random to assign participants to one of two groups: Group A (Metronidazole alone) or Group B (Metronidazole combined with probiotics). This method ensures that each participant had an equal chance of being allocated to either group, thereby minimizing selection bias and promoting the internal validity of the study. Diagnosis of Bacterial vaginosis (BV) was confirmed on the basis of clinical examination, presence of at least three of Amsel's clinical criteria and a Nugent score >7.

Amsel's criteria include: (1) homogeneous, thin, white vaginal discharge; (2) vaginal pH > 4.5; (3) a positive "whiff" test, characterized by a fishy odor upon addition of 10% potassium hydroxide; and (4) the presence of clue cells on microscopic examination.[3] The Nugent scoring system, considered the gold standard for BV diagnosis, involves Gram staining of vaginal smears and evaluating the relative abundance of bacterial morphotypes. A score of <7 considered normal, >7 indicates BV. A score above 4 suggests an imbalance in the vaginal flora, supporting the diagnosis of BV.[5]

Inclusion Criteria: Diagnosed case of BV based on clinical examination, Amsel's criteria[3], and Nugent scoring system.[5]

Exclusion Criteria:

Diagnosed case of malignancy

Immunocompromised status

Diabetes mellitus

Planning for pregnancy in the near future

Allergy or contraindication to the study drugs

The outcomes of the study were measured at follow-up visits on days 8th, 30th and 60th, focusing on the following parameters:

• **Clinical Symptoms**: The effectiveness of the treatment was evaluated based on the resolution of clinical symptoms at each follow-up visit.

• **Recurrence Rate:** The recurrence of symptoms was documented during each follow-up to monitor the persistence or return of bacterial vaginosis.

• **Amsel's Criteria**: Diagnostic assessments were conducted using Amsel's criteria.[3]

• **Nugent Score:** Vaginal smears were analyzed using the Nugent scoring system.[5]

• These assessments were also conducted at each follow-up visit.

Sample Size Calculation:

Prevalence of BV (p) = 24.4% = 0.244. [8]

q = 1 - 0.244 = 0.756

Allowable error (L) = 10% = 0.1

Z = 1.96

Sample size (N) = $Z^2 \times p \times q / L^2 = (1.96)^2 \times 0.244 \times 0.756 / (0.1)^2 = 70.86$.

Rounding up, the required sample size was 71 participants. To facilitate equal group distribution, the total was adjusted to 72, with 36 participants in each group. Participants (N = 72) were randomly assigned to the two groups using the lottery method.

Statistical Analysis:

Data was analyzed using SPSS 26. The Student's t-test was used to compare mean symptoms pre- and post-therapy, recurrence rates by using Amsel's criteria, and Nugent scores between the two groups. A p-value < 0.05 was considered statistically significant.

RESULTS

Out of 342 participants who presented with symptoms of vaginal discharge during the study period, 88 cases were enrolled during the first visit, while 16 cases were lost to follow-up. The remaining 72 participants met the inclusion criteria and continued with follow-up, allowing for further statistical analysis. The overall prevalence of bacterial vaginosis was 25.73%, and these cases were subsequently analyzed.

Parameter	Group A				Group B				p value
Age	33.36 ± 6.79				32 ±6.02				0.336
Parity	3.31 ± 1.36				2.14 ± 1.01				0.078
Cycle	Regular		Irregular		Regular		Irregular		
	30 (83.33%)		6 (16.66%)		31 (86.11%)		5 (13.88%)		
Residence	Rural		Urban		Rural		Urban		
	26 (72.22%)		10 (27.77%)		29 (80.55%)		7 (19.44%)		
Contraceptive	None	Barrier	LARC	Permanent	None	Barrier	LARC	Permanent	
	31 (86.11%)	2 (5.55%)	2 (5.55%)	1 (2.77%)	31 (86.11%)	3 (8.34%)	1 (2.77%)	1 (2.77%)	
Education	Illiterate	Lower secondary	Upper seconday	University	Illiterate	Lower secondary	Upper secnday	university	
	31 (86.11%)	3 (8.34%)	1 (2.77%)	1 (2.77%)	28 (77.77%)	2 (5.55%)	3(8.34%)	3 (8.34%)	
Occupation	House wife		Job holder		House wife		Job holder		
	33 (91.66%)		3 (8.34%)		33 (91.66%)		3 (8.34%)		

Table I: Demographic characteristics

The table above presents the baseline characteristics of participants in both study groups. The mean age in Group A (metronidazole alone) was 33.36 years, while in Group B (metronidazole with probiotics), it was 32 years. The p-value for age comparison was 0.336, indicating no statistically significant difference. Regarding parity, Group A had a higher mean parity of 3.31 compared to 2.14 in Group B; however, this difference was not statistically significant (p = 0.078). Most participants in both groups reported regular menstrual cycles. In terms of educational attainment, Group A had a slightly lower education level compared to Group B. The majority of participants in both groups resided in rural areas. Occupationally, both groups had similar distributions, with the majority being housewives. Mean with student T-test used for data analysis.

Parameters	Group A	Group B
Vaginal discharge at time of enrollment		
Present	34	34
Absent	2	2
p Value	0.693	
On Day 8th follow up visit		
Present	13	4
Absent	23	32
p Value	0.013*	
On Day 30th follow up visit		
Present	14	5
Absent	22	31
p Value	0.016*	
On Day 60th follow up visit		
Present	11	5
Absent	25	31
p Value	0.089	
Smell at time of enrollment		
Present	36	35
Absent	0	1
p Value	0.314	
On Day 8th follow up visit		
Present	35	34
Absent	1	2
p Value	0.555	
On Day 30th follow up visit		
Present	22	18
Absent	14	18
p Value	0.343	
On Day 60th follow up visit		
Present	24	12
Absent	19	17
p Value	0.230	

Table II: Clinical examination

The table above presents the clinical outcomes observed during the study period.

Abnormal Vaginal Discharge: At enrollment, all participants exhibited abnormal vaginal discharge. By day 8, Group B (metronidazole with probiotics) demonstrated a significant reduction in abnormal discharge compared to Group A (metronidazole alone), with a p-value of 0.013. This improvement persisted through day 30 (p = 0.016) and day 60 (p = 0.089), indicating a consistent trend favoring the combination therapy, though the difference on day 60 was not statistically significant

Foul Odor of Vaginal Discharge: Initially, all participants reported a foul odor associated with their discharge. By day 8, both groups showed improvement, with Group B exhibiting a slightly greater reduction; however, this difference was not statistically significant (p = 0.555). By day 60, the distinction between the groups became more pronounced, with Group B showing better outcomes (p = 0.230), though still not reaching statistical significance. Mean with student T-test used for data analysis.

Parameters	Group A	Group B
Vaginal pH in enrolment		
<4.5	0	0
>4.5	36	36
p Value	Not applicable	
On Day 8th follow up visit		
<4.5	27	28
>4.5	9	8
p Value	0.0781	
On Day 30th follow up visit		
<4.5	23	31
>4.5	13	5
p Value	0.029*	
On Day 60th follow up visit		
<4.5	24	33
>4.5	12	3
p Value	0.009*	
Nugent's scoring[5] at time of enrollment		
<7	0	0
>7	36	36
p Value	Not applicable	
On Day 8th follow up visit		
<7	32	34
>7	4	2
p Value	0.737	
On Day 30th follow up visit		
<7	19	30
>7	17	6
p Value	0.006*	
On Day 60th follow up visit		
<7	19	2
>7	17	34
p Value	<0.001*	

Table III: Labarotory parameters

The table above presents findings from the examination of vaginal discharge, including pH measurement, the Whiff test (addition of potassium hydroxide to detect fishy odor), microscopic identification of clue cells for Amsel's criteria[3] and Gram staining for Nugent scoring.[5]

Vaginal pH: At enrollment, all participants had a vaginal pH >4.5. By the second follow-up on day 8th, both groups showed improvement, with Group B demonstrating a more significant reduction in pH (p = 0.0781), though this was not statistically significant. By day 60, Group B had a significantly lower pH compared to Group A (p = 0.009).

Whiff Test: All participants tested positive at enrollment. By day 8, Group B showed a more notable reduction in positive Whiff test results (p = 0.045), which was statistically significant. At the final follow-up on day 60, Group B continued to show better improvement, though the difference was not statistically significant (p = 0.966).

Nugent Score: Both groups had similar scores at enrollment. By day 8, Group B showed greater improvement (p = 0.737), though this was not statistically significant. However, this difference became statistically significant at the subsequent follow-ups on day 30 (p = 0.006) and day 60 (p < 0.001). Mean with student T-test used for data analysis.

DISCUSSION

The prevalence of bacterial vaginosis (BV) in the present study was found to be 25.73%, which is comparable to the findings of Ranjit E. et al[8] who reported a prevalence of 24.4%, Recine N. et al[9] also reported a prevalence of 24 %, similarly, Peebles K. et al[10] concluded a prevalence of 23% in Central Asia. Singh et al[11] reported a slightly higher prevalence of 31.5%, while Bitew A. et al[12] documented a prevalence of 39.5%, possibly due to the inclusion of pregnant women with HIV as a study population. Singh A. et al and Singh S et al reported 20% a prevalence of 20% may be due to geographical variation.[13,14] Regarding participant demographics, the mean age in Group A was 33.36 ± 6.79 years, and in Group B, it was 32 ± 6.02 years. Singh et al reported a mean age of 29.5 ± 5.5 years in their study population.[11] This slight age difference is unlikely to have significantly impacted the study outcomes, as all participants were within the reproductive age range (15–49 years), where BV is most commonly observed. Additionally, the p-value of 0.336 indicates that the age difference between groups was not statistically significant.

Regarding parity, Group A had a higher mean parity (3.31± 1.36) compared to Group B (2.14 ± 1.01). Parity is a known risk factor for bacterial vaginosis, as higher parity is associated with changes in the vaginal flora, increasing susceptibility to infections, as reported by Ajani et al, Verstraelen H et al, Thoma ME et al., and Gibbs RS et al.[15,16,17,18] However, the study design included randomization, which likely helped to balance this factor between the groups. Conversely, studies by Kenyon C et al, Schmidt RM et al and Bautista C et al[19,20,21] reported that parity does not significantly affect BV prevalence. Similarly, Peebles K et al and Bradshaw CS et al[10,22] concluded that parity differences are unlikely to meaningfully impact study outcomes, especially when groups are randomized and other risk factors such as sexual activity and hygiene are balanced. In the present study, the p-value for parity was 0.078, indicating that the difference was not statistically significant. Regarding the menstrual cycle, most participants in both groups had a regular cycle. Hormonal fluctuations during the menstrual cycle can influence vaginal pH and microbiota, potentially affecting BV recurrence. However, as menstrual cycle regularity was similar between the two groups in this study, this factor is unlikely to have biased the results, as also reported by Russo R et al.[23]

In terms of education level, Group A had a slightly lower education level compared to Group B. Education can influence health-seeking behavior, understanding of treatment importance, and awareness of preventive measures, as reported by Bitew A et al. While lower education levels may contribute to poor health outcomes in some studies, the minimal difference in education levels in the present study is unlikely to have significantly impacted the results.[12]

Most participants in both groups were from rural areas, which aligns with the study setting, where a significant portion of the population resides in rural regions. According to Vicariotto F et al, limited healthcare access in rural areas could influence BV prevalence and recurrence rates. However, since both groups had similar distributions, this factor was controlled for in the present study.[24]

Both groups exhibited similar occupational profiles, predominantly comprising housewives, reflecting Nepal's sociocultural context where many women are homemakers. Occupation can influence exposure to bacterial vaginosis (BV) risk factors, such as stress and hygiene practices, as reported by Romeo M et al.[25] However, since both groups were comparable in this regard, occupation is unlikely to have affected the study outcomes. At enrollment, all participants presented with abnormal vaginal discharge, a classical symptom of BV. This aligns with the diagnostic criteria for BV, which include the presence of thin, grayish-white, homogeneous discharge, as reported by Amsel R.et al[3] By the first follow-up visit on day 8th, Group B (metronidazole + probiotics) showed a significant reduction in abnormal discharge compared to Group A (metronidazole alone) (p = 0.013). This suggests that probiotics may enhance the efficacy of metronidazole in resolving BV symptoms by restoring the vaginal microbiome, as similarly reported by Wang Z et al, Recine N et al and Russo R et al.[7,9,23]

However, a study conducted by Hemalatha R. et al[26] did not support early improvement between these groups, possibly due to differences in probiotic strains used. By the second and third follow-up visits on day 30 and day 60, the trend of improvement continued, with Group B consistently showing better outcomes (p = 0.016 and p = 0.089, respectively). However, the difference observed at the longer follow-up (day 60) was not statistically significant compared to the earlier visit on day 30. This aligns with previous studies conducted by Wang Z JM et al, Recine N et al and Bohbo et al[7, 9, 27] which concluded that probiotics effectively maintain a healthy vaginal flora and prevent the overgrowth of pathogenic bacteria over shorter periods. However, Mastromarino P et al failed to demonstrate a significant difference in outcomes between the two groups, possibly due to variability in anaerobic bacterial strains.[28]

At enrollment, all participants presented with foul-smelling vaginal discharge—a classical symptom of bacterial vaginosis (BV)—commonly described as a "fishy odor" caused by amines produced by anaerobic bacteria, as reported by Spiegel CA et al.[4] By the first follow-up visit on day 8, both groups showed improvement, with Group B demonstrating a slightly greater reduction in odor (p = 0.555), though this difference was not statistically significant. This improvement is likely attributable to the combined effect of metronidazole, which targets anaerobic bacteria, and probiotics, which help restore the vaginal microbiome. These findings are consistent with studies by Recine N et al, Vicariotto F et al, and Anukam et al.[7,24,29] However, studies by Hemalatha R et al and Mastromarino et al[26,28] did not show significant improvement in vaginal odor, possibly due to differences in the anaerobic bacterial strains used or variations in probiotic formulations. By the second follow-up visit on day 60, the difference between the groups became more pronounced, with Group B showing better outcomes (p = 0.230); however, this result also failed to reach statistical significance.

This suggests that probiotics may have a sustained effect in preventing the recurrence of BV symptoms, including foul-smelling discharge, as reported by Recine R et al, Bohbot JM et al, and Reznichenko H et al.[9,27,30] However, Mastromarino et al[28] failed to demonstrate a similar effect, possibly due to variations in anaerobic bacterial strains within the study population and the use of different probiotic strains. At enrollment, all participants had a vaginal pH greater than 4.5, which is a diagnostic criterion for BV, as reported by Nugent et al. A high vaginal pH indicates a reduction in lactobacilli, which are essential for maintaining an acidic vaginal environment. By the first follow-up on day 8, both groups showed improvement, with Group B exhibiting a more notable reduction in pH (p = 0.0781), though this difference did not reach statistical significance.

This aligns with the role of probiotics in restoring lactobacilli and lowering vaginal pH, as similarly reported by, Recine N et al, Anukam et al, and Muñoz-Cruz MR et al.[9, 29, 31] However, studies by Hemalatha R et al and Mastromarino P et al failed to demonstrate a similar effect, possibly due to differences in the probiotic strains used for BV management.[26, 28] By the second visit on Day 60, Group B had a significantly lower pH compared to Group A (p = 0.009). This finding supports the use of probiotics as a long-term strategy to maintain a healthy vaginal pH and prevent BV recurrence, as reported by Bradshaw CS et al.[22]

At enrollment, all participants had a positive Whiff test, indicating the presence of amines and confirming the diagnosis of BV, as reported by Muñoz-Cruz MR et al.[31] By the first follow-up visit on day 8, Group B showed a more significant reduction in positive Whiff tests. This was accompanied by a reduction in vaginal pH to < 4.5, suggesting improved vaginal health. According to Nugent RP et al[5] this improvement may reflect the enhanced effectiveness of the combined treatment with metronidazole and probiotics in reducing the production of amines by anaerobic bacteria. By the second and third follow-up visits on day 30 and day 60, respectively, Group B continued to show greater improvement (p = 0.029 and p = 0.009), with these differences found to be statistically significant. These findings further support the potential role of probiotics in maintaining a healthy vaginal environment and preventing BV recurrence, as also supported by Nugent RP and Muñoz-Cruz MR et al[5,31]

At enrollment, both groups had similar Nugent scores, indicating comparable severity of BV at baseline. By the first follow-up visit on day 8, Group B showed greater improvement

in Nugent scores (p = 0.737); however, this difference was not statistically significant. This suggests that probiotics may aid in the restoration of normal vaginal flora, as reflected by the Nugent score—a microscopic assessment of vaginal bacteria—supported by Nugent RP et al.[5] By the second follow-up visit on day 60, Group B had a significantly lower Nugent score compared to Group A (p < 0.001). This finding aligns with previous studies conducted by Muñoz-Cruz MR et al[31], demonstrating that probiotics help maintain a healthy vaginal microbiome and reduce the likelihood of BV recurrence. Throughout all follow-up visits, Group B consistently showed lower recurrence rates compared to Group A.

This is a critical observation, as recurrent BV remains a major clinical challenge, with up to 50% of women experiencing recurrence within 12 months of treatment, as reported by Muñoz-Cruz MR et al.[31] The addition of probiotics to metronidazole therapy appears to reduce the risk of recurrence restoring and sustaining a healthy vaginal microbiome, as supported by Bradshaw CS et al.[22]

Clinical Implications:

The results of this study suggest that probiotics should be considered as an adjunct to metronidazole therapy in the prevention of recurrent BV. Probiotics help restore the vaginal microbiome, reduce symptoms, and prevent recurrence, potentially reducing the need for repeated antibiotic courses. This approach may be particularly beneficial in low-resource settings, where access to healthcare is limited, and recurrent BV is a significant burden.

LIMITATIONS

The study had a relatively small sample size (72 participants), which may limit the generalizability of the findings. The follow-up period was limited to 60 days and longer-term studies are needed to assess the sustained benefits of probiotics in preventing BV recurrence.

CONCLUSION

The addition of probiotics to metronidazole significantly prevented the recurrence of bacterial vaginosis, with improvements observed in abnormal vaginal discharge, foul odor, vaginal pH, and Nugent scores. Group B (metronidazole + probiotics) consistently showed a lower recurrence rate.

REFERENCES

1. Bradshaw CS, Morton AN, Hocking J, Garland SM, Morris MB, Moss LM, et al. High recurrence rates of bacterial vaginosis over the course of 12 months after oral metronidazole therapy and factors associated with recurrence. J Infect Dis. 2006;193(11):1478–86.

2. Centers for Disease Control and Prevention. Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Available from: https://www.cdc.gov/std/bv/stats.htm. Published 2021. p. 83–7.

3. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis: diagnostic criteria and microbial and epidemiologic associations. Am J Med. 1983; 74(1):14–22.

4. Spiegel CA. Bacterial vaginosis. Clin Microbiol Rev. 1991;4(4):485–502

5. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. J Clin Microbiol. 1991; 29(2):297–301.

6. Brotman RM, Shardell M, Gajer P, Buck GA, Zhang Y, Ravel J. Bacterial vaginosis and the risk of HIV acquisition. J Infect Dis. 2010; 202 (12):1723–33.

7. Wang Z, He Y, Zheng J. Probiotics for the treatment of bacterial vaginosis: a meta-analysis. Int J Environ Res Public Health. 2019;16 (1):13.

8. Ranjit E, Raghubanshi B R, Maskey S, and Parajuli P prevalence of Bacterial Vaginosis and Its Association with Risk Factors among Nonpregnant Women: A Hospital Based Study. International Journal of Microbiology 2018:1-9

9. Recine N, Palma E, Domenici L, Giorgini M, Imperiale L, Sassu C, et al. Restoring vaginal microbiota: biological control of bacterial vaginosis. A prospective case–control study using Lactobacillus rhamnosus BMX 54 as adjuvant treatment against bacterial vaginosis. Arch Gynecol Obstet. 2016; 293(1):101–7.

10. Peebles K, Velloza J, Balkus JE, McClelland RS, Barnabas RV. High global burden and costs of bacterial vaginosis: a systematic review and meta-analysis. Sex Transm Dis. 2019; 46(5):304–11.

11. Singh A, Kanti V, Dayal S, Shukla SK, Mishra N. Prevalence and risk factors of bacterial vaginosis among women of reproductive age attending rural tertiary care institute of western Uttar Pradesh. J Evol Med Dent Sci. 2016;5(43):2695–701.

12. Bitew A, Abebaw Y, Bekele D, Mihret A. Prevalence of bacterial vaginosis and associated risk factors among women complaining of genital tract infection. Int J Microbiol. 2017; 2017:1–8.

13. Singh A, Agarwal J, Gupta V, Ghosh S. Prevalence of bacterial vaginosis and its associated risk factors among women attending a tertiary care hospital in India. Int J Infect Dis. 2011; 15(10):732–6.

14. Singh S, Saha R, Suneja A, Das S, Singh NP. Vaginitis in women of reproductive age group: a hospital-based study from North India. EJMS. 2020;5 (2):44–7.

15. Ajani G, Oduyebo O, Haruna M, Elikwu C. Nugent scores of pregnant women in a tertiary institution in Nigeria. Adv Microbiol. 2012; 2:531–6.

16. Verstraelen H, Verhelst R, Claeys G, Verschraegen G, Simaey LV, Ganck CD, et al. Comparison between Gram stain and culture for the characterization of vaginal microflora: definition of a distinct grade that resembles grade I microflora and revised categorization of grade I microflora. BMC Microbiol. 2005;5:61.

17. Gibbs RS, Schrag S, Schuchat A. Perinatal infections due to Group B streptococci. Obstet Gynecol. 2004;104(5):1062–76.

18. Thoma ME, Klebanoff MA, Rovner AJ, Nansel TR, Neggers Y, Andrews WW, et al. Bacterial vaginosis is associated with variation in dietary indices. J Nutr. 2011;141(9):1698–704.

19. Kenyon C, Colebunders R, Crucitti T. The global epidemiology of bacterial vaginosis: a systematic review. Am J Obstet Gynecol. 2013;209(6):505–23.

20. Schmidt RM, Gravitt PE, Maza M, McKinney W, Rojas L, Velazquez R. Equivocal effects of female hormonal contraception on the risk of bacterial vaginosis. J Sex Transm Dis. 2012;39(8):608–12.

21. Bautista CT, Wurapa E, Sateren WB, Panganiban R, Tomasi M. Prevalence and risk factors for bacterial vaginosis in a cohort of HIV-infected and HIV-uninfected women in Zimbabwe. Sex Transm Dis. 2016;43(3):166–72.

22. Bradshaw CS, Sobel JD. Current treatment of bacterial vaginosis—limitations and need for innovation. J Infect Dis. 2016 Aug 15;214(1):14–20.

23. Russo R, Karadja E, De Seta F. Evidence-based mixture containing Lactobacillus strains and lactoferrin to prevent recurrent bacterial vaginosis: a double blind, placebo controlled, randomised clinical trial. Benef Microbes. 2019;10(1):19–26.

24. Vicariotto F, Mogna L, Del Piano M. Effectiveness of the two microorganisms Lactobacillus fermentum LF15 and Lactobacillus plantarum LP01, formulated in slow-release vaginal tablets, in women affected by bacterial vaginosis: a pilot study. J Clin Gastroenterol. 2014;48(suppl 1):S106–12.

25. Romeo M, D'Urso F, Ciccarese G, Di Gaudio F, Broccolo F. Exploring oral and vaginal probiotic solutions for women's health from puberty to menopause: a narrative review. Microorganisms. 2024;12(7):1601–14.

26. Hemalatha R, Mastromarino P, Ramlaxmi BA, Balakrishna NV, Sesikiran B. Effectiveness of vaginal tablets containing lactobacilli versus pH tablets on vaginal health and inflammatory cytokines: a randomized, double-blind study. Eur J Clin Microbiol Infect Dis. 2012;31(11):3097–105.

27. Bohbot JM, Darai E, Bretelle F, Brami G, Daniel C, Cardo JM. Efficacy and safety of vaginally administered lyophilized Lactobacillus crispatus IP 174178 in the prevention of bacterial vaginosis recurrence. J Gynecol Obstet Hum Reprod. 2018;47(2):81–6.

28. Mastromarino P, Hemalatha R, Barbonetti A, Cinque B, Cifone MG, Tammaro F, et al. Biological control of vaginosis to improve reproductive health. Indian J Med Res. 2014;140:91–7.

29. nukam KC, Osazuwa EO, Ahonkhai I, Ngwu M, Osemene G, Bruce AW, et al. Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14: randomized, double-blind, placebo controlled trial. Microbes Infect. 2006;8(6):1450–4.

30. Reznichenko H, Henyk N, Maliuk V, Khyzhnyak T, Tynna Y, Filipiuk I, et al. Oral intake of lactobacilli can be helpful in symptomatic bacterial vaginosis: a randomized clinical study. J Low Genit Tract Dis. 2020;24(3):284–9.

31. Muñoz-Cruz MR, Jennifer TC, Lylah D. Comparison of the efficacy of metronidazole and metronidazole plus probiotics capsule in the treatment of bacterial vaginosis among non-pregnant patients seen at the outpatient department of a tertiary hospital: a single blind randomized controlled trial. PJOG. 2017;41(3):1–10.

Comparative Analysis of Prone vs Supine Position in PCNL: A Hospital Based Prospective Study

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ABSTRACT

Introduction: Percutaneous nephrolithotomy is a standard minimally invasive procedure for managing large or complex renal calculi. While the traditional prone position is commonly used, the supine position has gained attention for its potential benefits in surgical access and outcome. **Aims: T**o compare the intraoperative and postoperative outcomes of prone versus supine percutaneous nephrolithotomy. **Methods:** A prospective hospital-based study was conducted at Nobel Medical College, Biratnagar, from February 2024 to January 2025. A total of 60 patients with renal stones undergoing percutaneous nephrolothotomy were enrolled and divided into two groups: Group A (prone position) and Group B (supine position), each with 30 patients. Parameters such as operative time (minutes), blood loss (g/dL), stone clearance rate (%), and postoperative complications were recorded and analyzed using SPSS version 16. **Results:** The mean operative time was shorter in the supine group (80 ± 12 minutes) compared to the prone group (95 ± 15 minutes). Blood loss was lower in the supine group, with fewer patients requiring transfusion. Stone clearance was slightly higher in the prone group (90%) versus the supine group (80%). Postoperative complications, including fever and pain, were comparable between the groups, with no significant differences observed. **Conclusion:** Both prone and supine percutaneous nephrolithotomy positions are safe and effective. However, the supine position demonstrated advantages in operative time and reduced blood loss, making it a favorable option in selected cases.

***Keywords**:* Comparative Analysis, Operative Time, Prone percutaneous nephrolithotomy, Stone Free Rate, Supine percutaneous nephrolithotomy

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INTRODUCTION

Kidney stones (renal calculi) are a prevalent urological condition, affecting approximately 12% of the global population, posing significant health challenges. Prevalence varies geographically, with rates of 1-5% in Asia, 7-13% in North America, and 5-9% in Europe, driven by differences in climate, diet, and socioeconomic factors.[1] In South Asia, hot climates, low fluid intake, and oxalate-rich diets exacerbate stone formation. Untreated stones can cause severe complications, including urinary obstruction, infections, chronic kidney disease, ureteral strictures, and recurrence. Percutaneous Nephrolithotomy (PCNL) is the gold standard for large or complex stones, involving a percutaneous tract into the kidney under fluoroscopy or ultrasound guidance. A nephroscope fragments and extracts stones using ultrasonic, pneumatic, or laser lithotripsy. Traditionally performed in the prone position, PCNL provides optimal access to the renal collecting system, high stone-free rates, and low morbidity. However, prone positioning presents challenges for obese patients or those with cardiopulmonary issues, requiring repositioning for ureteric catheter placement and anesthesia, increasing procedural complexity and risks.[2] In 1987, Gabriel Valdivia introduced supine PCNL, which reduces operative time, improves airway access for anesthesiologists, and enhances surgeon ergonomics. It enables simultaneous antegrade and retrograde access, minimizing positioning-related complications like nerve compression and radiation exposure.[3] However, concerns remain about potential risks of visceral or vascular injuries in complex cases.[2] Despite growing adoption, debate persists over supine PCNL's superiority compared to the prone approach. This prospective study analyzes clinical data to compare prone and supine PCNL, assessing advantages, limitations, and challenges to guide evidence-based technique selection in modern urology.

METHODS

This is a prospective simple randomized comparative study conducted at Department of Urology, Nobel Medical College, Biratnagar, Nepal over a period of one year from February 2024 to January 2025 following ethical approval from the Institutional Review Board of our institution. This comparative study consisted of 60 patients divided into two equal groups. 30 patients who underwent traditional prone PCNL and 30 patients who underwent supine PCNL during the study period were randomly assigned in the study as prone or supine groups. The inclusion criteria consisted of patients of both sexes, aged 18 years or older, undergoing PCNL for single renal stones measuring between 15 and 25 mm, with a radiologically confirmed diagnosis of renal calculi during the study period. Pediatric age group patients (<18 years), patients with active urinary tract infections, bleeding disorders, and complex anatomy like horseshoe kidney, pelvic kidney were excluded from the study. A prophylactic dose of intravenous Piperacillin-Tazobactam (4.5 g) was administered 30 minutes prior to the induction of anesthesia. Both prone and supine PCNLs were conducted under spinal anesthesia. For Prone PCNL following anesthesia, patients were initially placed in the lithotomy position. Cystoscopy was performed to insert a 6 Fr open-ended straight-tip ureteral catheter (Indovasive) into the ipsilateral pelvicalyceal system under fluoroscopic guidance. A retrograde pyelogram was performed, followed by calyceal selection and puncture under fluoroscopic guidance using a two-part needle. A 0.035" Terumo guidewire was then advanced into the collecting system. The choice of calyx and number of punctures were based on the size and location of the renal calculi. Tract dilation was performed using a screw fascial dilator, followed by placement of an Amplatz sheath of 18 Fr. Nephroscopy was conducted using a 12 Fr (Karl Storz) rigid nephroscope.

In the Supine PCNL group, patients were positioned in the modified Valdivia position. Cystoscopy and urethral catheterization was performed as prone PCNL, followed by calyceal selection. Puncture done by same as supine position using two path needle. The guidewire was then advanced into the upper ureter to maintain tract access. Tract dilation was performed using a screw fascial dilator, followed by placement of an Amplatz sheath of 18 Fr. Nephroscopy was conducted using a 12 Fr (Karl Storz) rigid nephroscope. Stones were visualized and fragmented using a pneumatic lithotripter (Nidhi) in both cases. Finally, the stone fragments were extracted using grasping forceps or flushed out with an irrigation pump. Operative time was defined as the duration from ureteral catheterization to the completion of the procedure. On the first postoperative day, the Foley catheter was removed. If a nephrostomy tube had been placed, it was typically removed on the second postoperative day. Patients who were stable—afebrile, comfortable, and with a dry nephrostomy site (for patients who underwent standard PCNL) were discharged on the same day as nephrostomy removal. Double-J (DJ) stents were removed after a four-week interval. A stone-free status was defined as the absence of residual stones on X-ray KUB or ultrasonography (USG) at the one-month follow-up. Residual fragments measuring ≤4 mm and deemed non-obstructive on imaging were considered clinically insignificant. Patients with significant residual stones were scheduled for either Retrograde Intrarenal Surgery (RIRS) or a second-stage PCNL. Postoperative complications were categorized using the Modified Clavien-Dindo Classification System.[4] Collected data included patient demographics, stone-free rate, stone volume, operative time, access time, irrigation volume, and the drop in hemoglobin levels pre- and postoperatively.

SPSS software package (versions 16.0) was used for all statistical analyses. The results were expressed as the mean ± standard deviation and range. Fisher's exact test and student's T test were applied to find out the significant differences between the two groups. p value < 0.05 was considered statistically significant.

RESULTS

In this study, a total of 60 patients undergoing percutaneous nephrolithotomy (PCNL) were equally divided into two groups: prone (n = 30) and supine (n = 30) positions. The demographic and baseline characteristics were comparable between the two groups. The mean age of patients in the prone group was 47.3 ± 12.5 years, while in the supine group it was 49.1 ± 11.8 years (p = 0.52). The proportion of male patients was 70% in the prone group and 66.7% in the supine group (p = 0.78). The mean body mass index (BMI) was 26.4 ± 3.2 kg/m² in the prone group and 25.9 ± 3.6 kg/m² in the supine group (p = 0.47). The average stone size was similar between the two groups, measuring 22.1 ± 6.3 mm in the prone group and 21.8 ± 5.9 mm in the supine group (p = 0.83). Stone laterality was also comparable, with right/left distribution of 17/13 in the prone group and 16/14 in the supine group (p = 0.79). The prevalence of diabetes mellitus was 20% in the prone group and 16.7% in the supine group (p = 0.73), while hypertension was observed in 23.3% and 26.7% of patients, respectively (p = 0.77). The distribution of ASA (American Society of Anesthesiologists) scores (I/II/III) was 10/15/5 in the prone group and 9/16/5 in the supine group (p = 0.96). Previous history of renal surgery was noted in 13.3% of prone and 10% of supine patients (p = 0.68). These findings indicate no statistically significant differences in demographic or clinical baseline characteristics between the two groups (Table I).

Demographic Parameter	Prone PCNL (n=30)	Supine PCNL (n=30)	p-value
Age (years, mean ± SD)	47.3 ± 12.5	49.1 ± 11.8	0.52
Male (%)	21 (70%)	20 (66.7%)	0.78
BMI (kg/m², mean ± SD)	26.4 ± 3.2	25.9 ± 3.6	0.47
Stone size (mm, mean ± SD)	22.1 ± 6.3	21.8 ± 5.9	0.83
Laterality (Right/Left)	17/13	16/14	0.79
Diabetes Mellitus (%)	6 (20%)	5 (16.7%)	0.73

Hypertension (%)	7 (23.3%)	8 (26.7%)	0.77
ASA Score (I/II/III)	10/15/5	9/16/5	0.96
Previous Renal Surgery (%)	4 (13.3%)	3 (10%)	0.68

Table I: Comparison of Demographic and Baseline Characteristics Between Prone and Supine PCNL Groups

In terms of surgical outcomes, the stone-free rate was higher in the prone PCNL group (90%) compared to the supine group (80%), although the difference was not statistically significant (p = 0.3). Blood transfusions were required in 10% of patients in the prone group and 3.3% in the supine group (p = 0.3). Postoperative complications were observed in 16.7% of patients undergoing prone PCNL and in 10% of those undergoing supine PCNL, with no significant difference between the groups (p = 0.44). These findings suggest comparable surgical efficacy and safety profiles between the two patient positions (Table II).

Variable	Prone PCNL n (%)	Prone PCNL n (%)	p-value
Stone Free Rate	27 (90%)	24 (80%)	0.3
Transfusion	3 (10%)	1 (3.3%)	0.3
Complications	5 (16.7%)	3 (10%)	0.44

Table II: Comparison of Surgical Outcomes between Prone and Supine PCNL Groups

The mean operative time was significantly longer in the prone group (95 ± 15 minutes) compared to the supine group (80 ± 12 minutes), with a statistically significant difference (p = 0.001). The mean hemoglobin (Hb) drop was also greater in the prone group (1.8 ± 0.6 g/dL) than in the supine group (1.4 ± 0.5 g/dL), showing a significant difference (p = 0.010). Additionally, the average duration of hospital stay was slightly longer in the prone group (3.5 ± 1.0 days) compared to the supine group (3.0 ± 0.8 days), which was statistically significant (p = 0.040) (Table III).

Variable	Prone n (%)	Supine n (%)	p-value
Operative Time (minutes)	95 ± 15	80 ± 12	0.001
HB Drop (g/dL)	1.8 ± 0.6	1.4 ± 0.5	0.010
Hospital Stay (days)	3.5 ± 1.0	3.0 ± 0.8	0.040

Table III: Comparison of Operative and Postoperative Parameters between Prone and Supine PCNL Groups

DISCUSSION

In the present study, the stone-free rate (SFR) was higher in the prone percutaneous nephrolithotomy (PCNL) group (90%) compared to the supine group (80%), although the difference was not statistically significant (p = 0.3). This finding is consistent with the results reported by Kumar et al., who observed SFRs of 88.6% and 81.4% in the prone and supine groups, respectively, without statistical significance.[5] Similarly, a 2024 propensity score-matched analysis by Choi et al. reported SFRs of 74.3% for supine and 65.7% for prone PCNL (p = 0.356).[6] Sofer et al also demonstrated comparable stone clearance rates between the two positions.[7] Conversely, Shao and Chang, in their meta-analysis, found no significant difference in SFR between the lateral decubitus and prone positions.[8] Notably, Valdivia-Uria et al, who first introduced the supine PCNL technique, reported favorable outcomes with supine PCNL, particularly emphasizing ergonomic advantages and improved access to lower pole stones.[9]

A statistically significant difference in operative time was observed, with the supine group demonstrating a shorter mean duration (80 ± 12 minutes) compared to the prone group (95 ± 15 minutes, p = 0.001). This aligns with the findings from the CROES PCNL Global Study by de la Rosette et al, which analyzed over 5,800 procedures and concluded that supine PCNL is generally associated with reduced operative time due to easier patient positioning and the feasibility of simultaneous retrograde ureteroscopy.[10] Micali et al also reported reduced operative times in supine PCNL, attributing this to better anesthetic control and the avoidance of intraoperative repositioning.[11] Chapagain et al reported operative times of 44.63 ± 12.44 minutes for supine and 53.02 ± 12.67 minutes for prone groups, with statistical significance.[12] Miah Md et al found a significantly shorter operative time in the supine group (74.67 ± 11.94 minutes) compared to the prone group (90.33 ± 8.70 minutes).13 Similarly, Paudyal et al reported a mean operative time of 76.63 ± 12.42 minutes in the supine group versus 90.02 ± 12.67 minutes in the prone group, with a mean difference of 16 minutes.[14] Choi et al also found operative times of 85.5 ± 25.2 minutes for supine and 96.4 ± 25.8 minutes for prone PCNL (p = 0.012).[6] A 2024 randomized trial by Kara et al further confirmed shorter operative times and hospital stays for the supine approach.[15] Kannan et al. similarly reported a significant reduction in operative time with supine PCNL (p < 0.001).[16]

Postoperative complications were slightly higher in the prone group (16.7%) compared to the supine group (10%), though this difference was not statistically significant (p = 0.44). Paudyal et al reported overall complication rates of 15.62% in the supine group and 25% in the prone group.[14] According to Miah Md et al, both blood transfusion requirements and complication rates were slightly higher in the supine group, but these differences were not statistically significant.[13] Chapagain et al observed similar rates of postoperative fever and septic complications in both groups.[13] These results are corroborated by a meta-analysis conducted by Zhang et al, which found no significant difference in overall complication rates between the supine and prone positions.[17] Kannan et al also noted slightly higher early and late complication rates, such as postoperative fever or hematuria, in the supine group.[16] Choi et al reported overall complication rates of 8.6% in the supine group and 4.3% in the prone group (p = 0.301).[6]

In our study, the mean hemoglobin drop was significantly lower in the supine group (1.4 ± 0.5 g/dL) compared to the prone group (1.8 ± 0.6 g/dL, p = 0.010), suggesting reduced intraoperative blood loss. This aligns with findings from the meta-analysis by Shao and Chang.[8] De Sio et al reported complication rates of 20.5% for supine and 13.9% for prone PCNL[18] while Falahatkar et al observed rates of 27.5% for supine and 30% for prone PCNL.[19] In our study, blood transfusion rates were higher in the prone group (10% vs. 3.3%), although not statistically significant (p = 0.3). This observation is in line with Tay et al, who reported lower transfusion rates in the supine group, attributing this to improved renal access and reduced parenchymal trauma.[20] Liu L reported transfusion rates of 27.6% in the supine group and 18.2% in the prone group 2 while Mak et al found that patients in the prone group required more transfusions than those in the supine group (27.5% vs. 7.5%).[21] Miah Md et al, however, reported nearly identical transfusion rates between the two groups (20.0% in prone and 16.7% in supine; p = 1.000).[13]

The mean hospital stay was also shorter in the supine group (3.0 ± 0.8 days) compared to the prone group (3.5 ± 1.0 days, p = 0.040). Manohar et al similarly reported shorter recovery times and earlier ambulation with the supine approach.[22] This is supported by Kara et al, who found reduced hospital stays in supine PCNL patients.[15] Paudyal et al found significantly shorter hospital stays in the supine group (2.40 ± 0.74 days) compared to the prone group (3.20 ± 0.92 days, p < 0.001).[14] However, Mulay et al reported no significant difference in hospital stay between supine (2.76 days) and prone (2.64 days) PCNL (p = 0.44).[23] Miah Md et al reported a significantly longer hospital stay in the prone group (3.10 ± 0.61 days) compared to the supine group (2.30 ± 0.47 days).[13]

Taken together, our findings support the growing body of evidence that while both prone and supine PCNL are effective and safe, the supine position may offer certain peri-operative advantages such as reduced operative time, less blood loss, and quicker recovery. Nevertheless, the choice of position should remain individualized, based on patient anatomy, stone characteristics, and the surgeon's expertise.

LIMITATIONS

This study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other settings with different patient populations or surgical expertise. The non-randomized design, limited follow-up, and the use of X-ray KUB instead of computed tomography (CT) scan for stone clearance evaluation due to financial constraints and radiation exposure may potentially affecting accuracy of the findings.

CONCLUSION

Both prone and supine positions are effective and comparable for performing percutaneous nephrolithotomy. The prone position demonstrated a slightly higher stone clearance rate, whereas the supine position was associated with shorter operative time and reduced blood loss. Therefore, the selection of patient positioning should be individualized, taking into account anatomical considerations, surgeon expertise, and institutional capabilities.

REFERENCES

1. Sorokin I, Mamoulakis C, Miyazawa K, et al. Epidemiology of stone disease across the world. World J Urol. 2017;35(9):1301–20. doi:10.1007/s00345-017-2008-6

2. Liu L, Zheng S, Xu Y, Wei Q. Systematic review and meta-analysis of percutaneous nephrolithotomy for patients in the supine versus prone position. J Endourol. 2010;24(12): 1941-46. doi:10.1089/end.2010.0292

3. Hoznek A, Rode J, Ouzaid I, Faraj B, Kimuli M, De la Taille A, et al. Modified supine percutaneous nephrolithotomy for large kidney and ureteral stones: technique and results. Eur Urol. 2012;61(1): 164-70. doi:10.1016/j.eururo.2011.09.007

4. Tefekli A, Karadag MA, Tepeler K, Sari E, Berberoglu Y, Baykal M, et al. Classification of percutaneous nephrolithotomy complications using the modified Clavien grading system: looking for a standard. Eur Urol. 2008;53(1):184-90. doi:10.1016/j.eururo.2007.06.039

5. Kumar S, Joshi M, Maurya VK, Singh M, Sankhwar SN, Singh V. A prospective randomized study comparing prone and modified supine percutaneous nephrolithotomy. J Endourol. 2015;29(8):865-69. doi:10.1089/end.2014.0807

6. Babaoff R, Creiderman G, Darawsha AE, Ehrlich Y, Somani B, Lifshitz DA. Propensity score-matched analysis of perioperative outcomes of supine versus prone percutaneous nephrolithotomy. J Clin Med. 2024;13(9):2492. doi:10.3390/jcm13092492

7. Sofer M, Giusti G, Proietti S, Abdelrahim AF, Peschel R, de la Rosette J. Prone versus supine percutaneous nephrolithotomy: what is the evidence? CurrUrol Rep. 2016;17(6):50. doi:10.1007/s11934-016-0601-5

8. Shao C, Chang Y. A meta-analysis of the lateral decubitus position and prone position percutaneous nephrolithotomy. BMC Urol. 2024;24:202. doi:10.1186/s12894-024-01583-9

9. Valdivia JG, Scarpa RM, Duvdevani M, Gross AJ, Nadler R, Nutahara K, et al. Supine versus prone position during percutaneous nephrolithotomy: a report from the Clinical Research Office of the Endourological Society (CROES) Percutaneous Nephrolithotomy Global Study. J Endourol. 2011;25(10):1619-25. doi:10.1089/end.2010.0731

10. de la Rosette JJ, Assimos D, Desai M, Gutierrez J, Lingeman J, Scarpa R, et al. The Clinical Research Office of the Endourological Society Percutaneous Nephrolithotomy Global Study: indications, complications, and outcomes in 5803 patients. J Endourol. 2011;25(1):11–7. doi:10.1089/end.2010.0424

11. Micali S, De Stefani S, Sighinolfi MC, Grande M, Cicero C, Bianchi G. Modified supine versus prone position in percutaneous nephrolithotomy for large renal stones: a prospective randomized study. Urol Int. 2014;92(3):331-35. doi:10.1159/000356030

12. Chapagain R, et al. Outcomes of PCNL in prone and supine positions: experience from a tertiary center in Nepal. J Nepal

Health Res Counc. 2022;20(3):456-60. doi:10.33314/jnhrc.v20i3.4007

13. Miah Md, Alam Md, Islam K, Chowdhury A, Chowhury Md, Alam Md. Comparative study between supine position and prone position in PCNL. Bangladesh J Urol. 2022;24(2):200-4. doi:10.3329/bju.v24i2.59495

14. Paudyal P, et al. Comparative study of prone versus supine percutaneous nephrolithotomy: a single center experience. JNMA J Nepal Med Assoc. 2021;59(239):45–50. doi:10.31729/jnma.5542

15. Kara N, et al. Comparison of supine–prone percutaneous nephrolithotomy methods in the treatment of kidney stones in pediatric patients: prospective randomized study. Urolithiasis. 2024;52(1):73.doi:10.1007/s00240-024-01543-w

16. Kannan P, et al. Comparative evaluation of complications in prone versus supine PCNL: a retrospective study. Urol Ann. 2023;15(2):145-50. doi:10.4103/UA.UA_191_22

17. Zhang X, Xia L, Xu T, Wang X, Zhang Y. Prone versus supine percutaneous nephrolithotomy: a meta-analysis of randomized controlled trials. Urolithiasis. 2014;42(1):1–7. doi:10.1007/s00240-013-0622-3

18. De Sio M, et al. Modified supine versus prone position in percutaneous nephrolithotomy for renal stones. Urol Int. 2008;80(4):317-22. doi:10.1159/000127332

19. Falahatkar S, et al. Complete supine percutaneous nephrolithotripsy comparison with the prone standard technique. J Endourol. 2008;22(11):2513–17. doi:10.1089/end.2008.0053

20. Tay YK, Gupta M. Supine percutaneous nephrolithotomy: impact of patient position on outcomes. Indian J Urol. 2019;35(1):28–33. doi:10.4103/iju.IJU_226_18

21. Mak SK, Smith A, Patel U, et al. Supine versus prone percutaneous nephrolithotomy: a systematic review and meta-analysis. Arab J Urol. 2016;14(2):101–7. doi:10.1016/j.aju.2016.01.005

22. Manohar T, Jain P, Desai M. Supine PCNL: a prospective study of a single-center experience. Indian J Urol. 2010;26(1):20–4. doi:10.4103/0970-1591.60436

23. Mulay A, et al. Supine versus prone percutaneous nephrolithotomy for renal calculi: our experience. Curr Urol. 2022;16(1):25–9. doi:10.1159/000521279

ORIGINAL ARTICLE

Risk Factors for Meconium Aspiration Syndrome among the Babies Born Through Meconium-Stained Amniotic Fluid

Gupta MM, KC Rajesh, Sah SN

ABSTRACT

Introduction: Meconium aspiration syndrome occurs as complications in babies born through meconium-stained amniotic fluid. It presents as early onset respiratory distress mainly seen in the term and near-term infants due to the poor compliance of lungs and hypoxia which may be mild to severe. Acute or chronic hypoxia and/or infection can result in the passage of meconium in utero. Meconium aspiration before or during birth can obstruct airways, interfere with gas exchange, cause respiratory distress. The common risk factors include postdated pregnancy, Hypertensive disease of pregnancy, small for gestational age (SGA), gestational diabetes and maternal drug abuse. **Aims:** To study the risk factors for meconium aspiration syndrome, and the complications in the neonates born through meconium stained fluid. **Methods:** TA hospital based cross-sectional study was conducted in the department of pediatrics involving term and post-term inborn neonates born through meconium stained amniotic fluid at Nepalgunj Medical College from November 2024 to May 2025. **Results:** Total 300 babies were delivered with meconium stained amniotic fluid, among which 40 (13.4%) babies develop meconium aspiration syndrome. Among maternal risk factors for meconium aspiration syndrome premature rupture of membrane was most common and statistically significant, which was seen in 15 (37.5%) cases. Fetal risk factors were non-vigorous baby at birth, need of resuscitation at birth (70%), hypoxic ischemic encephalopathy (30%) and they showed statistically significance. Babies born through meconium-stained amniotic fluid showed respiratory distress as the main complication accounting for 57.5%, followed by sepsis (30%). Among babies who developed meconium aspiration syndrome 35 (87.5%) improved and were discharged, remaining 5 (12.5%) showed no improvement. **Conclusion:** Maternal risk factors for meconium aspiration syndrome were premature rupture of membrane, prolonged labor, mode of delivery. Non vigorous baby at birth, need of resuscitation were major risk factors. Respiratory distress was the main complication seen in babies born through meconium-stained amniotic fluid.

Keywords: Meconium stained amniotic fluid, Meconium aspiration syndrome respiratory distress syndrome

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INTRODUCTION

Meconium aspiration syndrome (MAS) is a serious condition that occurs in a new born when they inhale a mixture of meconium and amniotic fluid into the lungs around the time of delivery. Meconium aspiration syndrome (MAS) is a term used for the respiratory distress occurring in newborn infants born to pregnancies complicated by meconium-stained amniotic fluid1. It is mainly seen in the term and near-term infants and presenting with early onset respiratory distress due to the poor compliance of lungs and hypoxia, radiologically presenting as opacities in lung fields and hyperinflammation.[2] The common risk factors include postdated pregnancy, Hypertensive disease of pregnancy, small for gestational age (SGA), gestational diabetes and maternal drug abuse.[24] Persistent pulmonary hypertension of newborn is severe complication of baby with MAS It is a sign of fetal distress and needs immediate evaluation and management. The degree of severity of MAS has been described as Mild MAS is defined as disease requiring<40% oxygen for<48hours. Moderate MAS is defined as disease requiring >40% oxygen for >48 hours without air leak and Severe MAS is defined as disease requiring assisted ventilation for >48 hours often associated with persistent pulmonary hypertension.[23] MAS is defined by the following criteria:[22]

- Respiratory distress (tachypnea, grunting and/or retractions);
- Requirement for supplemental oxygen to maintain hemoglobin oxygen saturation >92%;

• Requirement for supplemental oxygen beginning prior to 2 hours of life, and lasting at least 12 hrs;

• Absence of congenital anomalies of the airway or heart.

This study was done with the aim of finding the risk factors for meconium aspiration syndrome among babies born through meconium stained amniotic fluid (MSAF).

METHODS

This study was hospital based cross-sectional study, conducted in Department of Pediatrics, Nepalgunj Medical College Teaching Hospital, Nepal, done from November 2024 - May 2025. All inborn neonates (term and post term- 37 weeks- 42 weeks) born through meconium-stained amniotic fluid (MSAF) during the study period were taken for study. Preterm babies, gross life threatening any congenital anomalies, out born babies were excluded from study. Convenient sampling technique was used. Written informed consent was taken in local language. Ethical clearance was obtained from institutional review committee (NGMC) before starting the study. Detailed demographic and clinical profile were taken for those who fell in the inclusion criteria. Detailed examinations were done and findings were recorded. A detailed maternal history was elicited to find out the possible risk factors in the development of MAS in babies born through MSAF, like PROM, pregnancy induced-hypertension, smoking, gestational diabetes, oligohydramnios, prolonged labor, thyroid diseases, heart diseases. Natal history was taken to find out the mode of delivery and interventions, if any for instrumental delivery. Similarly fetal risk factors for MAS like weight of baby, sex, need for resuscitation, development of HIE, DOWNE'S score were recorded. DOWNE'S score looked for cyanosis, retraction, expiratory grunt, air entry, respiratory rate. The scores given as 0,1,2 if present, score > 4 indicates respiratory distress. Other complications developed in babies with MSAF were recorded.

Statistical Analysis

After completion of data collection, the questionnaires were checked for completeness and the filled format was handled with great care, stored, and coded for further analysis. All data were recorded and analyzed in Statistical package for social science (SPSS) version22, entered in Microsoft excel 2007. For inferential statistics: association between the risk factors and MAS was calculated, where $p<0.05$ was taken significant by using the chi- square test. Data analysis was done by descriptive statistics as mean, SD, median, range and percentage. Comparison was done by applying Chi-square test. Significance was assessed at 5% level of significance ($p<0.05$). Microsoft word and excel were used to generate graphs, tables, and master charts.

RESULTS

Out of two thousand three hundred and ten (2310) deliveries during the six months study period, three hundred (300) were delivered with meconium stained amniotic fluid (13%). Out of 300 MSAF babies, 40(13.4%) babies developed MAS. The following data were observed and analyzed. The major maternal risk factors for MAS were PROM, prolonged labour, mode of delivery and other risk factors are mentioned in table I.

Risk factors	Number	Percentage (%)
PROM	45	15
>1 Risk factors	26	8.7
Hypertension	19	6.3
Diabetes	15	5
Oligohydramnios	10	3.3
Prolonged Labour	8	2.6
Anemia during pregnancy	3	1
CVS Disease	2	0.6
None	155	51.6

CVS: Cardiovascular system

Table I: Maternal risk factors for MAS

Variables (Risk factors)	Category	MAS	Percentage %	P value
Age group (years)	<20	7	17.5	>0.005
	21-30	31	77.5	
	>30	2	5	
Parity	Primigravida	30	75	>0.005
	Multigravida	10	25	
Gestational age (weeks)	37-40	13	32.5	>0.005
	40^{+1} – 42	22	55	
	>42	5	12.5	
Mode of delivery	VD	19	47.5	<0.005
	LSCS	16	40	
	Instrumental	5	12.5	
Maternal illness				
Diabetes	Present	2	5	>0.005
	Absent	38	95	
Hypertension	Present	5	12.5	>0.005
	Absent	35	87.5	
Anemia	Present	1	2.5	>0.005
	Absent	39	97.5	
Heart disease	Present	1	2.5	>0.005
	Absent	39	97.5	
Oligohydramnios	Present	6	15	>0.005
	Absent	34	85	
PROM	Present	15	37.5	<0.005
	Absent	25	62.5	
Prolonged labour	Present	4	10	<0.005
	Absent	36	90	

PROM- Premature rupture of membrane, CVS-Cardiovascular system,<0.005= statistically significant

Table II: Association of maternal risk factors with MAS

When the maternal risk factors were compared with babies having MAS, it was found that mode of delivery, PROM, and prolonged labour were statistically significant (<0.005) other risk factors were not found to be statistically significant (Table-II)

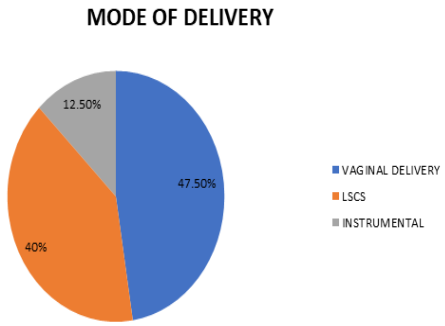

Figure1: Mode of delivery (N-40)

Out of the 40 babies with MAS, 47.5% of babies were born through Vaginal delivery (Figure-1)

Risk factors	Category	MAS	Percentage %	p-value
Weight(kg)	<2.5	8	20	>0.005
	>2.5	32	80	
Sex	Male	28	70	>0.005
	Female	12	30	
Fetaldistress				
Tachycardia	Present	0	0	>0.005
	Absent	40	100	
Bradycardia	Present	2	5	>0.005
	Absent	38	95	
Decreased movement	Present	2	5	>0.005
	Absent	38	95	
Resuscitation	Present	28	70	<0.005
	Absent	12	30	
Downe'sscore	≤4	20	50	<0.005
	>4	8	20	
	None	12	30	
HIE	Present	12	30	<0.005
	Absent	28	70	

HIE- Hypoxic ischemic encephalopathy, <0.005= statistically significant

Table III: Association of fetal risk factors with MAS

Fetal risk factors like condition of the baby at birth, need of resuscitation, DOWNE'S score, development of HIE were statistically significant (<0.005). Fetal weight, sex, fetal tachycardia, fetal bradycardia and decreased movements were statistically not significant. (Table III)

Complications: MSAF babies who developed MAS (40) were associated with development of complications which included respiratory distress as the main complication accounting for 57.5 % and pneumonia in 5% followed by sepsis (30%), hypoxic ischemic encephalopathy (25%), and meningitis (10%). 10% of babies with MAS did not develop any complications. (Figure 2)

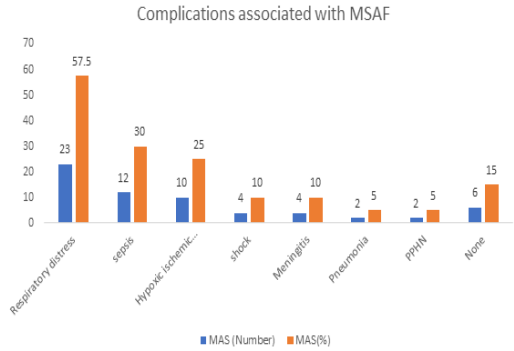

Figure 2: Complications babies born with MSAF

Outcomes of babies: All babies born with meconium stained amniotic fluid, but didn't develop MAS, were healthy and discharged. Among 40 babies who developed MAS, 5 (12.5%) showed no improvement, so 3 went in left against medical advice and 2 of them expired. However, 35(87.5%) improved and were discharged.

DISCUSSION

Out of 300 MSAF babies, 40 (13.4%) babies developed MAS. This was similar to the result of study conducted by Gauchan E et al where MSAF was seen in 13.4% and MAS developed in 1.13% of total deliveries; 8.4% of babies born through meconium-stained liquor.[4] The study done by Bhat R Y showed MAS occurred in 11.3% of babies born through MSAF5 while in other studies it varied from 1% to 38.5%.[6-10]

In our study, postdated pregnancy was seen in 156 (52%) out of the MSAF but was statistically not significant. Overall, the percentage of MAS in term babies was (12.9%), but postdated and post-term groups when combined showed higher frequency of MAS (17%).

In Gauchan E et al study, postdatism was seen in 36 (46.2%) cases but this was statistically not significant, similar finding was seen in our study in which MAS was seen with the increasing gestational age, but no association was seen between the gestational age and development of MAS.[4] Greenwood C et al also found meconium passage is more common with increasing gestationage.[11] In our study, maternal age and parity of mothers were statistically not significant, no association was present between development of MAS and age, parity of the mother which was similar to other studies.[12,14] A similar study conducted by Sundaram R et al showed no association between maternal age, gestational age, parity with MAS.[13] In our study association between mode of delivery and MAS was statistically significant, MAS was more common in babies delivered via vaginal delivery. Some studies have shown MAS to be more common in babies born through vaginal route.[14] In the study done by Raju V et al[16], majority of MSAF babies were

delivered through cesarean section similar to the study done by of Gupta V et al.[10] In our study, out of 40 MAS cases, 28 (14.8%) were males and 12 (10.8%) female. Gender was not found to be statistically significant risk factor for MAS In a study by Milind B et al, male were more in numbers than females and the male to female ratio was 1.93:1.[17] In study by Rajput S S et al high prevalence of MSAF was seen in male neonates with an incidence of 65.2%.[18] In our study, PROM (50%) and prolonged labor (50%) was found to be significant. Naveen et al found prolonged labour to be a significant risk factor for meconium-stained amniotic fluid.[19] A similar study by Gurubacharya S M et al, PROM was a significant risk for the development of MAS.[20]

In our study various fetal risk factors were significantly associated with MSAF i.e., non-vigorous babies at the time of birth, mode of resuscitation, low APGAR score at 1 & 5min, DOWNE'S score and HIE. Twenty percent (20%) of babies with MSAF had low Apgar scores in the study done by Mundraetal.[21] In a similar study conducted by Gurubacharya S M et al, found APGAR score at 1,5 minute and requirement of resuscitation as significant factors contributing to increased incidence of MAS.[20] In our study 5 (12.5%) babies did not show improvement and 2 (0.6%) expired which was similar to study done by Gupta V et al.[10]

CONCLUSION

Babies born with MSAF developing MAS had both maternal and fetal risk factors. Major maternal risk factor were premature rupture of membrane, prolonged labour, mode of delivery, major fetal risk factors were non vigorous baby at birth, need of resuscitation were significant risk factors. Most of babies developed respiratory distress as main complication.

REFRENCES

1. Vain NE, Batton DG. Meconium "aspiration"(or respiratory distress associated with meconium-stained amniotic fluid?). In: Semin Fetal Neonatal Med . Elsevier; 2017. p. 214–9.
2. Wiedemann J R, Saugstad A M, Barnes-Powell L, Duran K. Meconium aspiration syndrome. Neonatal Netw . 2008;27(2):81–7.
3. van Ierland Y, de Beaufort AJ. Why does meconium cause meconium aspiration syndrome? Current concepts of MAS pathophysiology. Early Hum Dev. 2009;85(10):617–20.
4. Gauchan E, Basnet S, Malla T. Meconium Aspiration Syndrome and Neonatal Outcome: A Prospective Study. Am J Public Health Res. 2015;3(5A):48–52.
5. Bhat R Y, Rao A. Meconium-stained amniotic fluid and meconium aspiration syndrome: a prospective study. Ann Trop Paediatr . 2008;28(3):199–203.
6. Mulivor R A, Mennuti M T, Harris H. Origin of the alkaline phosphatases in amniotic fluid. Am J Obstet Gynecol ,1979 Sep 1;135(1):77-81.
7. Richey S D, Ramin S Z, Bawdon R E, R .oberts S W, Dax J, Roberts J, et al. Markers of acute and chronic asphyxia in infants with meconium-stained amniotic fluid. Am J Obstet Gynecol . 1995;172(4 Pt 1):1212–5.
8. Bhaskar S H, Karthikeyan G, Bhat B V, Bhatia B D. Antenatal risk factors and neonatal outcome in meconium aspiration syndrome. Indian J Matern Child Health. 1997;8(1):9–12.
9. Tran S H, Caughey, Musci TJ. Meconium-stained amniotic fluid is associated with puerperal infections. Am J Obstet Gynecol . 2003;189(3):746–50.
10. Gupta V, Bhatia B D, Mishra O P. Meconium stained amniotic fluid: antenatal, intrapartum and neonatal attributes. Indian Pediatr . 1996;33(4):293–7.
11. Greenwood C, Lalchandani S, MacQuillan K, Sheil O, Murphy J, Impey L. Meconium passed in labor: How reassuring is clear amniotic fluid? Obstet Gynecol 2003;102(1):89–93.
12. Fischer C, Rybakowski C, Ferdynus C, Sagot P, Gouyon J B. A Population-Based Study of Meconium Aspiration Syndrome in Neonates Born between 37 and 43 Weeks of Gestation. Int J Pediatr . 2012;2012:1–7.
13. Sundaram R, Murugesan A. Risk factors for meconium stained amniotic fluid and its implications. Int J Reprod Contracept Obstet Gynecol . 2016;5(8):2503–6.
14. Khazardoost S, Hantoushzadeh S, Khooshideh M, Borna S. Risk factors for meconium aspiration in meconium stained amniotic fluid. J Obstet Gynaecol. 2007;27(6):577–9.
15. Meydanli M M, Dilbaz B, Çalişkan E, Dilbaz S, Haberal A. Risk factors for meconium aspiration syndrome in infants born through thick meconium. Int J Gynaecol Obstet . 2001;72(1):9–15.
16. Raju V, Narayani D M, Vindyarani W K. Immediate clinical outcome of newborns with meconium stained amniotic fluid. Int J Contemp Pediatr . 2018;5(5):1824–7.
17. Kamble M B, Jain P. Meconium aspiration syndrome: clinical profile, risk factors and outcome in central India. Int J Contemp Pediatr. 2019;6(1):144–9.
18. Rajput S S, Verma Y S, Yadav D. Study of Risk Factors and Outcome in Neonates Born with Meconium Stained Liquor . Sch J App Med Sci. 2016;4(9E):3548–52.
19. Sundaram R, Murugesan A. Risk factors for meconium stained amniotic fluid and its implications. Int J Reprod Contracept Obstet Gynecol. 2016;5(8):2503–6.
20. Gurubacharya S M, Rajbhandari S, Gurung R, Rai A, Mishra M, Sharma K R, et al. Risk Factors and Outcome of Neonates Born through Meconium Stained Amniotic Fluid in a Tertiary Hospital of Nepal. J Nepal Paediatr Soc. 2015;35(1):44–8.
21. Mundhra R, Agarwal M. Fetal Outcome in Meconium Stained Deliveries. J Clin Diagn Res. 2013;7(12):2874–6.
22. Olicker A L, Raffay T M, Ryan R M. Neonatal Respiratory Distress Secondary to Meconium Aspiration Syndrome. Children (Basel) . 2021;8(3):246
23. Monfredini C, Cavallin F, Villani P E, Paterlini G, Allais B, Trevisanuto D. Meconium Aspiration Syndrome: A Narrative Review. Children (Basel). 2021;8(3):230
24. Curtis PD, Matthews TG, Clarke TA. Neonatal seizures: McIntosh N, Helm P. Smyth R. Meconium Aspiration Syndrome, The Newborn In: Forfar and Arneils textbook of pediatrics. 6th. ed. 2004:185-186.

ORIGINAL ARTICLE

Thyroid Dysfunction in Individuals with Type 2 Diabetes Mellitus and Its Relationship with Diabetic Nephropathy: A Hospital Based Cross-Sectional Study

Shrewastwa MK[1], Mahat AK[2], BK SK[3], Sah B[1], Karn SL[4]

ABSTRACT

Introduction: People diagnosed with type 2 diabetes mellitus have a heightened susceptibility to thyroid-related issues. For these individuals, hypothyroidism can exacerbate microvascular complications like diabetic nephropathy, and the combination of diabetes and hypothyroidism significantly elevates the risk of cardiovascular problems. Conducting screenings for thyroid dysfunction in type 2 diabetic patients allows for the early identification and management of hypothyroidism. **Aims:** To evaluate how common thyroid dysfunction is among those with type 2 diabetes and to explore the possible relationship between thyroid issues and complications associated with diabetes like diabetic nephropathy. **Methods:** This study was a cross-sectional analysis conducted at the Department of biochemistry with collaboration to medicine of Nepalgunj medical college & teaching hospital, kohalpur, from June 2024 to May 2025. It included 400 outpatients with type 2 diabetes mellitus who had no previous history of thyroid disorders, chronic liver disease, or acute illnesses. All participants were evaluated for diabetic complications, such as nephropathy. Furthermore, thyroid function tests were performed on all participants using the chemiluminescence immunoassay technique. **Results:** The prevalence of thyroid dysfunction among individuals with type 2 diabetes mellitus was identified to be 34.5%. Hypothyroidism was identified in 28% of the participants, whereas 6.5% were diagnosed with hyperthyroidism. The occurrence of thyroid dysfunction was notably higher in women compared to men. Additionally, a significant relationship was established between thyroid dysfunction and diabetic complications, specifically nephropathy, within the study group ($P<0.05$). **Conclusion:** There is a statistically significant relationship between thyroid dysfunction and diabetic nephropathy, indicating that individuals with diabetes who also have thyroid dysfunction are at a higher risk of developing nephropathy.

***Keywords*:** Nephropathy, thyroid dysfunction, type 2 diabetes mellitus & Neuropathy

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INTRODUCTION

Patients with type 2 diabetes mellitus (T2DM) are more prone to developing thyroid disorders[1], particularly hypothyroidism, due to underlying insulin resistance. This coexisting condition can worsen diabetes-related complications, such as dyslipidemia, hypertension and cardiovascular diseases.[2] Timely detection and management of thyroid dysfunction in diabetic patients is essential to prevent the progression of diabetic related complications.[3] Screening for hypothyroidism is simple, requiring only a blood test, and can be routinely carried out in primary care settings. Early diagnosis and treatment may help stabilize blood glucose and lipid levels, improving overall outcomes. Subclinical hypothyroidism has been linked to an increased risk of diabetic nephropathy and cardiovascular problems in T2DM patients.[4,5] Furthermore, the coexistence of hypothyroidism and diabetes can exacerbate microvascular complications, including retinopathy and neuropathy, primarily due to lipid metabolism disturbances.[6] Recent studies have identified varying prevalence rates of diabetic

nephropathy, such as 13% in one study population[7], 16.6% in Enugu (Nigeria)[8] and 72.6% in Benin (Nigeria).[9] Interestingly, one of these studies found a significant association between thyroid dysfunction and diabetic nephropathy[7]; supporting previous findings that hypothyroidism may be a contributing risk factor.[10] Despite global research efforts, there remains a gap in data specific to Nepal, particularly in the mid-western region. To address this, the current study aims to assess the prevalence of thyroid dysfunction among T2DM patients in mid-western Nepal and explore its relationship with diabetic complications, especially nephropathy. This research seeks to provide localized insight that could support early intervention strategies in this population.

METHODS

This Hospital based cross-sectional study was carried out among patients with type 2 diabetes mellitus who visited the biochemistry laboratory at the Biochemistry Department of Nepalgunj Medical College and Teaching Hospital, located in Kohalpur, Banke, from June 2024 to May 2025. The research received approval from the Institutional Review Committee (IRC Ref. No. 10/081-082).

The minimum sample size was estimated at 358 participants, derived from the previously documented prevalence of thyroid dysfunction in diabetic patients, which was 36.84%.[11] This calculation was done with a desired absolute precision of 5% and a significance level of 5%. A convenience sampling approach was adopted to select diabetic patients from the outpatient department of medicine. Patients were excluded from the study if they had acute illness, chronic liver disease,a history of other diseases, hyperlipidemia, were pregnant, had hypertension, were undergoing corticosteroid treatment, or were on medications that could affect thyroid function. Diabetes mellitus diagnoses adhered to the criteria established by the American Diabetes Association (ADA).[12]

Data collected from each patient included demographic details (age and sex), anthropometric measurements (height, weight, BMI), as well as blood pressure readings (systolic and diastolic), duration of diabetes, family history of diabetes and thyroid conditions, and lifestyle factors such as alcohol use and smoking habits. Body Mass Index (BMI) was calculated by dividing weight (in kg) by the square of height (in meters). Participants with a BMI between 25 and 29.9 kg/m² were categorized as overweight, while those exceeding 30 kg/m² were classified as obese. Blood pressure was recorded using a digital sphygmomanometer, with values above 140/90 mm Hg indicating hypertension. A venous blood sample of 5 mL was collected from each participant following an overnight fast for biochemical evaluation. Analysis of fasting serum samples included measuring serum thyroid stimulating hormone (TSH), free triiodothyronine (free T3), and free thyroxine (free T4) via chemiluminescent immunoassay technology (using ADVIA Centaur XP from Siemens Healthcare Global, USA). The normal reference ranges for TSH, free T3, and free T4 were established as 0.35-4.5 mIU/L, 2.3- 4.2 pg/mL, and 0.89-1.76 ng/dL, respectively. Subclinical hypothyroidism was defined as TSH levels between 5-10 mIU/L with normal free T3 and T4, whereas overt hypothyroidism was indicated by TSH levels above 10 mIU/L accompanied by low free T3 and T4. Subclinical hyperthyroidism was characterized by low TSH with normal free T3 and T4, while overt hyperthyroidism was identified by low TSH and elevated free T4 levels. Blood glucose levels were assessed in the laboratory using the glucose oxidase-peroxidase method, whereas, 2 mL of EDTA blood sample was taken for estimation of glycosylated hemoglobin (HbA1c)level in blood through high-performance liquid chromatography (Bio Rad Laboratories, USA).

Diabetic nephropathy was diagnosed based on measurement of estimated globular filtration rate (eGFR) and the presence of albuminuria, with microalbuminuria defined as urinary albumin excretion between 30 and 300 mg/day, and macroalbuminuria as excretion exceeding 300 mg/day. Microalbuminuria levels were evaluated using the nephelometry technique (Mispa i3) at the biochemistry laboratory.The 2009 CKD-EPI creatinine equation for estimating glomerular filtration rate (GFR) is:

eGFR = 141 × min (Scr/k, 1)a × max(Scr/k, 1)-1.209 × 0.993Age × 1.018 [if female] × 1.159 [if Black].

Where,

- eGFR: Estimated GFR in mL/min/1.73 m².
- Scr: Serum creatinine level in mg/dL.
- k: A constant that varies based on sex (0.7 for females, 0.9 for males).
- a: A constant that varies based on sex (-0.329 for females, -0.411 for males).
- Min(Sc/k, 1): The minimum value between (Sc/k) and 1.
- Max(Scr/k, 1): The maximum value between (Scr/k) and 1.
- Age: Patient's age in years.
- 1.018: A modifier applied if the patient is female.

1.159: A modifier applied if the patient is Black

Statistical analysis:

Continuous variables, including age, duration of diabetes, BMI, and HbA1c, were reported as means with standard deviations (SD). Categorical variables, such as the prevalence of thyroid dysfunction, hypertension, obesity, and diabetic complications, were expressed as percentages and analyzed using the Chi-square test (χ^2). All statistical analyses were performed at a 5% significance level, with p-values lower than 0.05 considered statistically significant.

RESULTS

The study involved a total of 400 participants, with their primary characteristics summarized in Table I. On average, the individuals had been living with diabetes for 14.3 years

(±6.75), and their mean glycosylated hemoglobin (HbA1c) level was recorded at 9.64% (±2.01). The research indicated that 34.5% of the participants (138 individuals) experienced thyroid dysfunction. Figure 1 illustrates the results of the thyroid function tests, revealing that the majority of participants (65.5%) had normal levels of TSH, free T3, and free T4. Subclinical hypothyroidism and overt hypothyroidism were found in 16% and 12% of participants, respectively, while subclinical hyperthyroidism and overt hyperthyroidism were present in 3.5% and 3% of individuals respectively.

Table II presents detailed information regarding participant demographics, including age, family history of diabetes, duration of diabetes, glycemic control, and gender distribution. The largest proportion of diabetic patients was found in the 41 to 70-year age range. Additionally, the table outlines the prevalence of thyroid dysfunction in relation to various factors, showing that women exhibited a higher incidence of both hypothyroidism and hyperthyroidism compared to men. Hypothyroidism was particularly prevalent among those with diabetes for longer than five years, whereas hyperthyroidism was more frequently observed in individuals with diabetes for more than ten years. The analysis revealed statistically significant relationship between thyroid dysfunction and several factors: age ($p<0.001$), gender ($p<0.001$), duration of diabetes ($p<0.001$), family history of diabetes ($p<0.001$), and glycemic control ($p<0.001$). Furthermore, Table II indicates a statistically significant relationship between thyroid dysfunction and diabetic complications, particularly diabetic nephropathy ($p<0.05$), within the population of participants with Type 2 diabetes.

Characteristics		Mean±SD/n (%)
Age(years)		55.07±13.08
Gender	Female	229 (57.20 %)
	Male	171 (42.80 %)
Duration of Diabetes mellitus (years)		14.30±6.75
Body mass index (BMI) (kg/m^2)		27.79 ± 3.16
Fasting blood glucose (FBG) (mg/dl)		182.41±74.96
Postprandial Blood glucose (PPBG) (mg/dl)		293.79± 104.89
Glycated hemoglobin(HbA1c) %		9.64±2.01
Total no. of people with thyroid dysfunction		138 (34.50%)
Thyroid function test	FT3(pg/ml)	2.90±0.88
	FT4(ng/dl)	1.17±0.34
	TSH(µIU/ml)	7.92±7.71
Family history of DM	Yes	175 (43.80%)
	No	225 (56.20%)
History of alcoholism	Yes	207 (51.80%)
	No	193 (48.20%)
History of smoking	Yes	165 (41.20%)
	No	235 (58.80 %)

Table I: Demographic and clinical characteristics of study population (n=400)

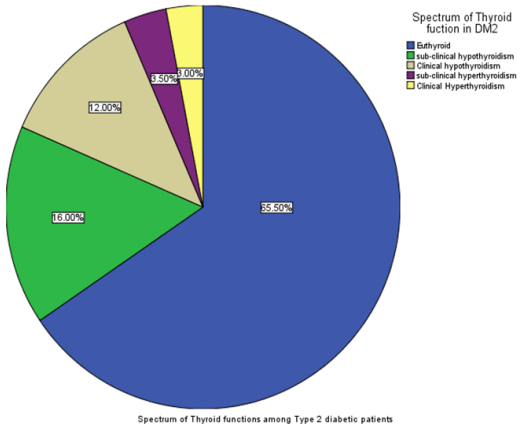

Figure1: Spectrum of Thyroid functions among Type 2 diabetic patients

Thyroid function Characteristics		Spectrum of thyroid function (N=400) Euthyroid (n=262, 65.5%)	Hyper-thyroidism (n=26, 6.50%)	Hypo-thyroidism (n=112, 28.0%)	P-value
Age group (years)	21-30	16 (6.10 %)	0	0	
	31-40	40 (15.30%)	0	4 (3.60 %)	
	41-50	61 (23.30%)	0	23 (20.50)	
	51-60	83 (31.70%)	12 (46.20%)	57 (50.90%)	

Age group (years)	61-70	21 (8.0%)	8 (30.80%)	23 (20.50%)	<0.001
	71-80	35 (13.40)	0	5 (4.50%)	
	>80	6	6 (23.10%)	0	
Gender	Female	127 (48.5%)	15 (57.7 %)	87 (77.7%)	<0.001
	Male	135 (51.5%)	11 (42.3%)	25 (22.3 %)	
Family history of DM	Yes	87 (33.20%)	11 (42.30)	77 (68.80%)	<0.001
	No	175 (66.8 %)	15 (57.7%)	35 (31.20%)	
Duration of diabetes years	< 1	18 (6.90%)	0	7 (6.9%)	<0.001
	1-5	60 (22.90)	0	12 (10.70%)	
	5-10	63 (24%)	12 (46.20%)	49 (43.8%)	
	>10	121 (46.2%)	14 (53.80%)	44 (39.3%)	
(HbA1c %)	6.5-7.0	24 (9.20)	0	0	<0.001
	7.10-8.0	56 (21.40)	0	8 (7.10%)	
	8.1-9.0	48 (18.30)	6 (23.1%)	28 (25 %)	
	>9	134 (51.1%)	20 (76.9%)	76 (67.9%)	
Nephropathy	Yes	31 (11.8%)	16 (61.6%)	37 (33%)	<0.001
	No	231 (88.2%)	10 (38.5%)	75 (67%)	

Table II: Relationship of Thyroid dysfunction with age, gender, duration of diabetes, glycemic status, Diabetic nephropathy and family history of thyroid disease in study participants (n=400)

DISCUSSION

The coexistence of diabetes mellitus (DM) and thyroid disorders is a well-recognized phenomenon. Both of these are among the most prevalent endocrine conditions encountered in clinical practice. Insulin resistance, a common feature in T2DM patients, is significantly implicated in the development of thyroid dysfunction. This dysfunction may manifest as hypothyroidism or hyperthyroidism, with subclinical hypothyroidism also prevalent among diabetic patients, potentially leading to complications such as retinopathy, neuropathy, and cardiovascular disease.[13] Our findings revealed a prevalence of thyroid dysfunction in 34.5% of T2DM patients, which is notably higher than the prevalence rates reported in several other studies (ranging from 23.6% to 37%).[11,14,15,16,17,18] This variation may be attributed to regional disparities in ethnicity and dietary practices.[19,20] Among the thyroid disorders identified, subclinical hypothyroidism was the most common at 16%, followed by clinical hypothyroidism (12%), clinical hyperthyroidism (3%), and subclinical hyperthyroidism (3.5%). These results are consistent with studies conducted in Nepal, India, and Bangladesh[11, 14,18,21,22], indicating the necessity for routine screening of T2DM patients for concurrent thyroid dysfunction, given its significant impact on glycemic control and overall diabetes management.[23]

Our study found significant statistical relationship between thyroid dysfunction and factors such as age (p<0.001), gender (p<0.001), duration of diabetes (p<0.001), family history of diabetes (p<0.001), and glycemic control (p<0.001). According to Ogbonna et al, females with T2DM have a 3.8 times greater risk of developing thyroid dysfunction compared to males.[7] This is believed to be due to the influence of estrogen on thyroid follicular cells and thyroxine-binding globulin (TBG).[24] Our study supports this finding, as the significant relationship of thyroid disorders was higher among diabetic females (P < 0.001) as compared to male, which is consistent with previous research.[7,14, 15, 25] Bassyouni et al (2010) reported a higher prevalence of thyroid dysfunction in older individuals with type 2 diabetes. Similarly, our study found an increase in thyroid dysfunction with age up to 70 years, after which it decreased, a pattern that aligns with the findings of Sahu Sulagna et al in their research.[26]

Elevated HbA1c levels, indicative of poor blood sugar control, have been strongly linked to the development of chronic complications in diabetes mellitus (DM).[27,28] This study found a significant relationship between thyroid dysfunction and glycemic control. Specifically, individuals with type 2 DM and higher HbA1c levels were more prone to thyroid dysfunction compared to those maintaining good glycemic control (HbA1c < 7.0%). This pattern is consistent with findings from Ogbonna SU and Ezeani IU.[7] The potential cause may lie in the detrimental effects of prolonged hyperglycemia on the hypothalamo-pituitary axis, which can disrupt or eliminate the nocturnal peak of thyroid-stimulating hormone (TSH).[29] Previous researches have also categorized both clinical and subclinical hypothyroidism as insulin-resistant conditions. For instance, Bazrafshan et al[30] identified a significant correlation between HbA1c and TSH levels, aligning with our study's results. Similarly, Ardekani et al[31] observed that HbA1c levels were significantly elevated in diabetic patients with thyroid disorders, which corresponds with our findings. Chronic hyperglycemia further inhibits the conversion of thyroxine (T4) to triiodothyronine (T3) by reducing the activity of thyroxine deiodinase.[23] Schlienger et al[32] also reported that poor glycemic

control (with HbA1c levels ≥ 12%) is associated with a condition known as "low T3 syndrome," resulting from impaired T4 to T3 conversion. This study identified a significant relationship between thyroid dysfunction and the duration of diabetes. This finding aligns with the research by Ogbonna SU and Ezeani IU.[7] It suggests that a longer duration of diabetes could increase the risk of developing thyroid dysfunction, potentially due to the adverse effects of prolonged hyperglycemia, which impairs the conversion of T4 to T3, contributing to thyroid dysfunction. This observation is consistent with the results of Telwani et al[33], who reported a higher prevalence of thyroid disorders in individuals with diabetes lasting five years or more, compared to those with a shorter duration (75.9% vs. 24.1%). However, a study by Diez et al found no significant link between the presence of thyroid dysfunction and the duration of diabetes. [34]

In addition to insulin resistance, autoimmunity can also play a role in the development of thyroid dysfunction in type 2 diabetes mellitus. A study by Radaideh AR et al[35] revealed that 12.5% of diabetic patients had thyroid disease, with 8.3% of those with thyroid dysfunction testing positive for antibodies against thyroid peroxidase. This suggests that screening for asymptomatic thyroid dysfunction may be valuable in identifying thyroid disease in diabetic patients.

Hypothyroidism is believed to be linked to an increased risk of nephropathy and cardiovascular disease in diabetic patients. This was demonstrated in a study by Chen HS et al[4], which found that subclinical hypothyroidism was a risk factor for both nephropathy and cardiovascular disease in type 2 diabetes patients. Our studies showed significant relationship between thyroid dysfunction and nephropathy in Type 2 diabetic patients. In this study, 21% of patients with type 2 diabetes mellitus (DM) were found to have diabetic nephropathy. This is higher than the 16.6% prevalence reported by Ulasi et al in Enugu, Nigeria [8] and the 13% observed by Ogbonna and Ezeani in Nigeria[7], but significantly lowers than the 72.6% prevalence reported by Onovughakpo-Sakpa et al in Benin, Nigeria.[9] This study found a significant relationship between diabetic nephropathy and thyroid dysfunction ($p<0.05$), indicating that patients with diabetic nephropathy are more likely to experience thyroid dysfunction compared to those without nephropathy. This result aligns with the findings of several other studies[4,36,37] but contrasts with the various studies[18,38] which found no such association between diabetic nephropathy and thyroid dysfunction in type 2 diabetes patients. Thyroid dysfunction is frequently observed in patients with type 2 diabetes, especially among those with long-duration diabetes, poor blood sugar control, older age, and women. Effectively managing thyroid dysfunction in these patients may help reduce overall morbidity and prevent the worsening of diabetic complications, such as nephropathy.

LIMITATIONS

This study does not explore the underlying mechanisms linking thyroid dysfunction to nephropathy, such as the potential roles of inflammation or oxidative stress, which may limit the understanding of the pathophysiological connection between these conditions.

CONCLUSION

In this study, the prevalence of thyroid dysfunction among patients with type 2 diabetes mellitus was 34.5%, with hypothyroidism occurring more frequently than hyperthyroidism. A significant correlation was observed between thyroid dysfunction and the presence of diabetic complications, particularly nephropathy, in the study population.

REFERENCES

1. Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: A retrospective study. Indian J Endocrinol Metab 2012; 16: S334 5.
2. Donckier JE. Endocrine diseases and diabetes. In: Pickup JC, Williams G, editors. Textbook of Diabetes Mellitus. Chicester, U.K.: Blackwell Publishing Company; 2003. p. 21 7.
3. Ghazali SM, Abbiyesuku FM. Thyroid dysfunction in type 2 diabetics seen at the University College Hospital, Ibadan, Nigeria. Niger J Physiol Sci 2010; 25:173 9.
4. Chen HS, Wu TE, Jap TS, Lu RA, Wang ML, Chen RL, et al. Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in type 2 diabetic patients. Diabet Med 2007; 24:1336 44.
5. Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, et al. Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. Arch Intern Med 2005; 165:2467 72.
6. Perros P, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: Value of annual screening. Diabet Med 1995; 12:622 7.
7. Ogbonna SU, Ezeani IU. Risk Factors of Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus. Front. Endocrinol. (2019) 10:440. doi: 10.3389/fendo.2019.00440.
8. Ulasi II, Ijeoma CK. The prevalence of diabetic nephropathy in Nigerian patients with end-stage renal disease. J Cou Med. (1998) 3:40–2
9. Onovughakpo-Sakpa OE, Onyeneke EC, Olumese EF. Incidence of diabetic nephropathy in Southern Nigeria. J Med Sci. (2009) 9:264–9
10. Oputa RN, Chinenye S. Diabetes mellitus: a global epidemic with potential solutions. Afr J Diabet Med. (2012) 20:2033–5.
11. Kandel L, Shakya YL, Yadav M, ShahNA, Gupta S. Prevalence of Thyroid Dysfunction among Patients with Type II diabetes Mellitus in Tertiary Care Center: A Cross-sectional Descriptive Study. J Nepal Med Assoc 2024; 62(278):691-6.
12. Diabetes Diagnosis & Tests | ADA. Accessed March 23, 2025. https://diabetes.org/about-diabetes/diagnosis

13. Wang C. The relationship between type 2 diabetes mellitus and related thyroid diseases. J Diabetes Res 2013; 2013:390534.

14. Asuti S, Purad S, Hosamani P. Pattern of Thyroid Dysfunction in Type II Diabetes Mellitus Patients in a Tertiary Care Center: A Cross-Sectional Study. J Med Sci Health 2023; 9(2):204-210.

15. Elgazar EH, Esheba NE, Shalaby SA, Mohamed WF. Thyroid dysfunction prevalence and relation to glycemic control in patients with type 2 diabetes mellitus. Diabetes Metab Syndr 2019; 13:2513 7.

16. Bjoro T, Holmen J, Kruger O, Midthjell K, Hunstad K, Schreiner T, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord Trondelag (HUNT). Eur J Endocrinol 2000; 143:639 47.

17. Naz N, Rizvi SK, Sadiq Z. Assessment of thyroid hormone levels and thyroid disorders: A case study from Gujranwala, Pakistan. Pak J Pharm Sci 2017; 30:1245 9.

18. Mehalingam V, Sahoo J, Bobby Z, Vinod KV. Thyroid dysfunction in patients with type 2 diabetes mellitus and its association with diabetic complications. J Family Med Prim Care 2020; 9:4277-81.

19. Jugati A, Biradar MS. Thyroid dysfunction in patients with Type 2 diabetes mellitus in a tertiary care centre of North Karnataka. Med Innov2018; 7:28 30.

20. Kamrul Hasan A, Akter F, Selim S, Asaduzzaman M, Rahman M, Chanda P, et al. Thyroid function and autoantibody status in Bangladeshi patients with type 2 diabetes mellitus. Thyroid Res Pract2018; 15:132.

21. Elmenshawi IM, Alotaibi SS, Alazmi AS, Alazmi AM, Alruwaili FR, Alazmi MM, et al. Prevalence of thyroid dysfunction in diabetic patients. J DiabetesMetabDisord Control2017; 4:55 60.

22. Hollowell J, Staehling N, Flanders W, Hannon W, Gunter E, Spencer C, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National health and nutrition examination survey (NHANES III). J Clin EndocrinolMetab 2002; 87:489 99.

23. Hage M, Zantout M, Azar S. Thyroid disorders and diabetes mellitus. J Thyroid Res2011; 2011:1 7.

24. Aljabri KS, Bokhari SA, Alshareef MA, Khan PM, Mallosho AM, AbuElsaoud HM, et al. The prevalence of hypothyroidism in patients with Type 2 diabetes mellitus in Saudi community-based hospital a retrospective single centre study. Arch Diabetes Obes2019; 2.doi: 10.32474/ADO.2019.02.000126.

25. Ahmed AA, Mohamed SB, Elmadi SA, Abdorabo AA, Ismail IM, Ismail AM. Assessment of thyroid dysfunctions in type 2 diabetes mellitus patients in Surman, Western Libya. Int J Clin Exp Med Sci2017; 3:1 4.

26. Sahu S, Dutta SK, KuiriSS, NandiMM, KabirajP, De U. Prevalence of thyroid dysfunction in patients with Type 2 diabetes mellitus and its correlation with insulin resistance and serum markers for autoimmune thyroiditis. Asian Journal of Medical Sciences 2015; 6(6):33-38.

27. United Kingdom Prospective Study Group, 1998. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes mellitus. Lancet. (1998) 352:837–53. doi: 10.1016/S0140-6736(98)07019-6.

28. Diabetes Control and Complications Trial Research Group. Effects of intensive treatment of diabetes on the development of microvascular complications of diabetes mellitus. N Engl J Med. (1993) 329:304–9.

29. Gursoy NT, Tuncel E. The relationship between the glycaemic control and hypothalamus-pituitary-thyroid axis in diabetic patients. Turkish J Endocrinol Metab. (1999) 12:163–8.

30. Bazrafshan HR, Ramezani A, Salehi A, Shir AAA, Mohammadian S, Faraj EM, et al. Thyroid dysfunction and its relationship with diabetes mellitus (NIDDM). J Gorgan Univ Med Sci. (2000) 2:5–11.

31. Ardekani MA, Rashidi M, Shojaoddiny A. Effect of thyroid dysfunction on metabolic response in type 2 diabetic patients. Iranian J Diabetes Obesity. (2010) 2:20–6.

32. Schlienger JL, Anceau A, Chabrier G, North ML, Stephan F. Effect of diabetic control on the level of circulating thyroid hormones. Diabetologia. (1982) 22:486–8. doi: 10.1007/BF00282596.

33. Telwani AA, Wani ZH, Ashraf Y, Shah AA. Prevalence of thyroid dysfunction in type 2 diabetes mellitus: a case control study. Int J Res Med Sci. (2017) 5:4527–31. doi: 10.18203/2320-6012.ijrms20174590.

34. Diez JJ, Sanchez P, Iglesias P. Prevalence of thyroid dysfunction in patients with type 2 diabetes. Exp Clin Endicrinol Diabetes. (2011) 119:201– 7. doi: 10.1055/s-0031-1271691.

35. Radaideh AR, Nusier MK, Amari FL, Bateiha AE, El Khateeb MS, Naser AS, et al. thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. Saudi Med J 2004; 25:1046 50.

36. Yasuda T, Kaneto H, Kuroda A, Yamamoto T, Takahara M, Naka T, et al. Subclinical hypothyroidism is independently associated with albuminuria in people with type 2 diabetes. Diabetes Res Clin Pract. 2011;94: e75–7.

37. Furukawa S, Yamamoto S, Todo Y, Maruyama K, Miyake T, Ueda T, et al. Association between subclinical hypothyroidism and diabetic nephropathy in patients with type 2 diabetes mellitus. Endocr J. 2014; 61:1011–8.

38. Iwakura H, TakagiT, Inaba H, DoiA, Ueda Y, Uraki S et al. Thyroid function, glycemic control, and diabetic nephropathy in patients with type 2 diabetes over 24 months: prospective observational study. BMC Endocrine Disorders 2023; 23:146 :1-8.

ORIGINAL ARTICLE

Correlation of Coronary Angiography Findings with Cardiovascular Risk Factors in a Tertiary Center in Nepal

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ABSTRACT

Introduction: Coronary artery disease is one of the most common heart problems and a major cause of illness and death around the world. It occurs when the coronary arteries become narrower due to atherosclerosis. Risk factors contributing to atherosclerosis include high blood pressure, diabetes, smoking, high cholesterol, being overweight, and physical inactivity. Coronary angiography is a highly effective method for diagnosing coronary disease. Having more than one cardiovascular risk factor at the same time has been linked to more serious and widespread forms of coronary artery disease. **Aims:** To correlate coronary angiographic findings of coronary artery disease with cardiovascular disease risk factors. **Methods:** A hospital-based cross-sectional descriptive study was conducted among 170 patients who had undergone coronary angiograms in a Semi-urban tertiary care center. Participants were enrolled prospectively after taking ethical approval from the Institutional Review Committee, Kathmandu University School of Medical Sciences. Various risk factors and coronary angiogram findings were noted. Data were collected in Microsoft Excel and analyzed in SPSS version 21. **Results:** The mean age of the patients in the study was 60.81±10.70 years, and 35.88% of them were female. The most prevalent risk factor for coronary artery disease was hypertension (73.53%), and the most common symptom was chest pain, seen in 83.50% of cases. ECG changes were seen in 87.65%, and 69.41% of cases had coronary artery disease findings on coronary angiogram. The most common coronary angiogram finding was single-vessel disease, seen in 28.24% of cases. Significant CAD findings correlated well with hypertension, diabetes, smoking, and dyslipidemia, but no correlation was found with obesity and family history of CAD. The risk of having multivessel disease was higher among those who had multiple risk factors. **Conclusion:** This study highlights hypertension as a key modifiable risk factor for CAD. The risk of significant CAD increases in the presence of modifiable cardiovascular risk factors, and the risk of having multivessel disease, i.e., diffuse disease or significant disease burden, is high in the presence of multiple risk factors as compared to single risk factors.

Keywords: Cardiovascular Risk Factors, Coronary Angiography, Coronary Artery Diseases

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death globally, claiming an estimated 17.9 million lives in 2015.[1] Age, gender, smoking, obesity, dyslipidemia, physical inactivity, hypertension and diabetes mellitus (DM) are established risk factors for CVD.[2-5] Coronary artery disease (CAD), one of the major causes of morbidity and mortality worldwide, is characterized by the presence of atherosclerosis in the coronary arteries. CAD still accounts for approximately one-third of all deaths in individuals over 35 years old.[6-7] Mortality from CVD results from CAD, with ACS almost always presenting with symptoms including unstable angina and myocardial infarction.[8] Coronary angiography is an invasive diagnostic procedure used to visualize the coronary circulation and diagnose intracoronary

lesions.[9] Due to its low risk of major complications and the ability to perform interventions, if necessary, hemodynamic data can also be obtained during the procedure.[9] Various studies have examined the effect of multiple risk factors, such as diabetes, hypertension, hyperlipidemia, sex and smoking, on the pattern and severity of CAD, but there is very limited data based on Nepal. This study aims to correlate the findings of coronary artery disease confirmed by coronary angiogram with cardiovascular disease risk factors.

METHODS

This prospective cross-sectional study was conducted in a semi-urban tertiary care center of Nepal from October 2022, to July 2024. The study was conducted after getting ethical approval from the Institutional Review Committee, Kathmandu University School of Medical Sciences (IRC, KUSMS), with an approval number IRC/KUSMS 11/17. Clinical and demographic variables, including age, sex, Body Mass Index (BMI), smoking history, hypertension, diabetes mellitus, dyslipidemia, family history and alcohol consumption were noted. Electrocardiography (ECG), Echocardiography, and Coronary angiography were done, and their findings were also noted. Two cardiologists independently evaluated angiograms. Lesions ≥50% were defined as significant. CAD was categorized as Single-vessel disease (SVD), Double-vessel disease (DVD), and Triple-vessel disease (TVD). Consecutive sampling was done.

Inclusion Criteria: All patients who underwent coronary angiography (CAG) for coronary artery disease and were presented to the Emergency or Cardiology Outpatient Departments were included in the study.

Exclusion Criteria: Patients who did not give consent were excluded from the study. 170 samples were collected randomly from October 2022 to July 2024. The sample size was calculated using the formula for estimating proportions, $N = Z^2p\ (1-p) / e^2$

Where the N is the required sample size, Z = 1.96 at 95% confidence interval, P is the prevalence of coronary artery disease taken from a study[10] and d = margin of error(5%).

According to the Global Burden of Disease, the prevalence of coronary artery disease in Nepal(p) is 12.2%.[10] Using the above formula, the sample size was calculated to be 170. Therefore, a total of 170 samples were collected.

Statistical analysis

The data were entered in Microsoft Excel, and subsequent statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 21.0 software.

RESULTS

The study enrolled 170 patients with suspected coronary artery disease (CAD) who met the inclusion criteria.

Baseline Characteristics

The mean age of the study population was 60.81±10.70, with the youngest age being 30 years. In our study, Males were higher in number (64.12%) compared to females (35.88%).

The following demographic features and risk factor profile were observed as shown in Table I.

Characteristics	Frequency n(%)
(A) Risk Factors	
Mean age	**60.81 ± 10.70years**
Male	109 (64.12)
Female	61 (35.88)
Hypertension	125 (73.53)
Smoking	83 (48.82)
Alcohol	117 (68.82)
Diabetes Mellitus	61 (35.88)
Obesity (BMI >=30)	64 (37.65)
Dyslipidemia	45 (26.47)
Family History of CAD	16 (9.41)
Past myocardial infarction	16 (9.41)
Stroke	8 (4.71)
Peripheral Arterial Diseases	12 (7.06)
(B) Clinical Features	**n (%)**
Chest pain	142 (83.50)
Shortness of breath	99 (58.20)
Palpitation	58 (34.10)
S3 heart sound	5 (2.90)
S4 heart sound	5 (2.90)
Murmur	38 (22.40)
Asymptomatic	5 (2.94)

Table I: Baseline Characteristics of Study Participants

ECG findings	Frequency n(%)
ST depression	120 (70.64)
ST elevation	50 (29.36)
T wave inversion	57 (33.55)
Q wave	19 (11.18)
LBBB	30 (17.65)
RBBB	12 (7.06)
Atrial fibrillation	15 (8.82)

Table II: Electrocardiography (ECG) findings

Echocardiographic Findings		Frequency n(%)
Dilated Left Ventricle	≤ 50%	118 (69.40)
	>50%	52 (30.50)
Left ventricular ejection fraction	>50%	113 (66.47%)
	40-50%	37 (21.70)
	<40%	20 (11.70)
Regional wall motion abnormalities	Present	62 (36.40)
	Absent	108 (63.50)

Table III: Echocardiographic Findings

Coronary Angiographic Findings

Out of a total of 170 patients undergoing coronary angiography, 118 (69.40%) had significant CAD (defined as ≥50% luminal stenosis). SVD was the most common (28.2%), followed by DVD (14.7%) and TVD (12.9%), as shown in Table IV. Left main disease was identified in 4.1%.

Coronary Angiographic Features	Frequency (%)
No significant CAD	52 (30.60)
Single Vessel Disease(SVD)	48 (28.24)
Double Vessel Disease (DVD)	25 (14.71)
Triple Vessel Disease (TVD)	22 (12.94)
Left Main Disease	7 (4.11)
Non-critical CAD	18 (10.59)

Table IV: Coronary Angiographic Findings

Correlation with Risk Factors

In our study, we found that significant coronary artery disease (defined as ≥50% luminal stenosis) was more common in patients with hypertension (OR=4.25), diabetes (OR=0.46), smoking (OR=2.75), and dyslipidemia (OR=2.76), as shown in Table V. Obesity and family history showed no significant correlation. Patients with >= 2 risk factors were significantly more likely to have multivessel disease (OR 4.78, 95% CI 2.17–10.56). Percentages of individual risk factors among CAD patients are shown in Table Va. Those with only one risk factor had lower odds of having multivessel disease (OR 0.29, 95% CI 0.13–0.69).

Risk Factor	Non-Critical CAD/ Normal (N=70)	Significant CAD (N=100)	OR/CI	p-value
1. Hypertension				
Yes	40	85	4.25(2.06-8.77)	<0.001
No	30	15		
2. Diabetes				
Yes	18	43	0.46(0.24-0.89)	0.023
No	52	57		
3. Smoking				
Yes	24	59	2.75(1.46-5.2)	0.002
No	46	41		
4. Dyslipidemia				
Yes	11	34	2.76(1.28-5.94)	0.009
No	59	66		
5. Obesity				
Yes	28	36	0.84(0.45-1.58)	0.59
No	42	64		
6. Family History				
Yes	38	53	1.053(0.57-1.94)	0.87
No	32	47		

Table Va: Correlation of Risk Factors with Normal/Non-Significant CAD Vs Significant CAD

Risk Factor	SVD (N=48)	MVD (N=52)	Odd's Ratio	95% Confidence Interval
1. Hypertension				
Yes	38	47	0.819	(0.31-2.04)
No	10	5		
2. Diabetes				
Yes	19	24	1.30	(0.59-2.89)
No	29	28		
3. Smoking				
Yes	30	29	0.75	(0.34-1.68)
No	18	23		
4. Dyslipidemia				
Yes	13	21	1.26	(0.57-2.77)
No	35	31		
5. Obesity				
Yes	16	20	0.54	(0.23-1.27)
No	32	32		
6. Family History				
Yes	24	29	1.25	(0.5-2.83)
No	24	23		

Table Vb: Correlation of Risk Factors Among Significant CAD Patients with CAD Pattern SVD vs MVD

Risk Factors	Normal/ Nonsignificant CAD with risk factors (N=63)	Significant CAD with risk factors (N=99)	OR/(CI)
Single risk factor	19	10	0.298 (0.129-0.69)
Multiple risk factors	44	89	4.78 (2.165-10.557)

Table Vc: Correlation of Risk Factors Burden with CAD Pattern SVD Vs MVD

DISCUSSION

The age distribution of patients in this study had a mean age of 60.81 years, with the minimum age being 30 years and the maximum age of 87 years. There was a male predominance comprising 64.12% of our total study population. This finding of age and gender is consistent with the findings of Chandramani et al, conducted at a tertiary hospital in Nepal.[11] Based on the Women's Ischemia Syndrome Evaluation (WISE) study, symptoms of coronary artery disease are not typical in females, and present with atypical symptoms and decreased seeking for medical attention, which may suggest a male predominance of CAD.[12] Patients with angina, ACS or those undergoing coronary angiography may present with a variety of symptoms and signs.[13] The most common symptom was chest pain, followed by dyspnea and other symptoms, which is similar to our findings, where chest pain was the predominant symptom seen in 83% of cases, followed by dyspnea in 58% of cases. In a study by June-Sung Kim et al, about 10% of patients undergoing coronary angiography were asymptomatic.[14] In our study, the population of asymptomatic patients was 2.94%, although they had abnormal ECG or echocardiographic findings.

Among the study population, the most common risk factor was hypertension (73.53%), followed by smoking (48.82%), diabetes (35.88%), dyslipidemia (26.47%), and obesity (37.65%). Among smokers, 30.59% were active smokers and 18.24% were past smokers. Regarding the family history of risk factors, a family history of CAD is present in 9.4% of cases. Similarly, the study by Poudel et al (48). showed the prevalence of hypertension (63.6%), smoking (58.6%), diabetes (18.2%), alcohol intake (30.7%), dyslipidemia (7.6%), and the presence of angina/CAD in family members (11.3%) as risk factors, which is nearly consistent with our study.

CAD remains a leading cause of mortality in both type 1 and type 2 diabetes mellitus, and DM is associated with a 2 to 4-fold increased mortality risk from heart disease.[15] In our study, around 36% of patients were diabetic, a finding consistent with the study done by Einarson TR et al, which states that based on analyzing data from articles with 4,549,481 persons having T2DM, approximately 32.2% of all people with T2DM had cardiovascular disease.[16-17] The combination of hyperglycemia, hypercholesterolemia, inflammation, and endothelial dysfunction is the key mechanism involved in the initiation and progression of atherosclerotic coronary artery disease.[18] Elevated blood pressure (BP) is associated with a significant global burden of cardiovascular disease (CVD) and premature death. Among the patients with pre-existing coronary artery disease (CAD), the prevalence of hypertension ranged from 30% to 70%.[17] This result is somewhat consistent with our study, which found a prevalence of hypertension of 73%.

Although LDL cholesterol, total cholesterol and total triglyceride levels are directly related to the prevalence of coronary artery disease, HDL cholesterol is more closely associated. An inverse association between HDL cholesterol and coronary artery disease persists even when adjusted for LDL cholesterol and triglyceride levels.[19] In our study, dyslipidemia was seen in 26.47% of cases, which is not consistent with the study done by Dhungana et al, where dyslipidemia was seen in around 48% of cases.[20] This discrepancy may be due to the limited sample size in our study population. However, the pattern of dyslipidemia was similar to the study where hypercholesterolemia, hypertriglyceridemia, and low HDL were present in 35.3%, 63.0%, and 28.6% of the total study population, respectively.[21] In our study, the most common pattern of dyslipidemia was low HDL, seen in 56% of cases, followed by hypercholesterolemia and hypertriglyceridemia, seen in 38% and 32% of cases, respectively.

In our study, almost 38% of patients were obese, a finding similar to the study done by Powell-Wiley TM et al, where obesity-associated cardiovascular disease was seen in nearly 38% of cases.[22] Visceral adiposity promotes systemic and vascular inflammation, which is fundamental to all aspects of the ath-

erosclerotic process, from fatty streak development to atherothrombosis.[23] Obesity represents one of the overlooked risks for CAD and will likely escalate the global burden of CAD in the coming decades, given its ongoing epidemic worldwide. A family history of coronary artery disease (CAD) is also a major risk factor for CAD. In our study, 9.4% of the total patients recruited for coronary angiography had a family history of CAD, which is consistent with the study done by Wahrenberg et al, where approximately 9% of the study population had a family history of CAD.[24]

The most common ECG finding was ST depression, seen in 70% of cases, followed by T-wave inversion in 33.55% of cases. These patterns of changes are quite similar to those reported in a study by Liu Y et al, where significant ST-T changes in ECG were observed in 66% of patients undergoing coronary angiography for suspected CAD.[25] Additionally, echocardiographic evaluation of our study population revealed normal left ventricular ejection fraction (LVEF) in 66.4% of cases, while reduced EF (LVEF <40%) was only found in 11.7%, and regional wall motion abnormalities (RWMA) were found in 36% of cases. A study on routine echocardiographic assessment in patients undergoing coronary angiography reported reduced left ventricular systolic function in 21.1% and segmental wall motion abnormalities in 32.9% of cases.[26] Though RWMA findings are consistent with our study, the finding of reduced LVEF is not similar, possibly due to selection bias or a smaller sample size of patients with reduced LVEF included in our study.

In a study by Beig Jr et al in Srinagar, single vessel disease was the most common finding, and the most common risk factor was hypertension, followed by smoking, which is consistent with our study.[27] Also, a study by Dhungana et al showed a majority of SVD followed by DVD in 21.1%, and TVD in 31.6% of cases, which also aligns with our study.[28] Among the patients with CAD on angiography, 98.2% had at least one type of risk factor. Among the various risk factors, the most common was hypertension, seen in 58.82% of cases, followed by smoking in 38.82%, diabetes in 28.24%, obesity in 25.88%, dyslipidemia in 22.94%, and family history in 6.4% of cases. The pattern of risk factors is quite similar to a study done at Sahid Gangalal National Heart Centre in a tertiary center, where hypertension (65%), smoking (57.8%) and dyslipidemia (45.5%) were the most common risk factors.[11]

In our study, we found a significant correlation between coronary artery findings on angiograms with coronary risk factors such as hypertension, diabetes, smoking and dyslipidemia. However, there was no significant correlation between family history and obesity, which may be due to the small sample size study single-center study as a study by Dung NJ et al found a significant correlation between angiographic findings of CAD, dyslipidemia and obesity.[22] Studies showed a significant correlation between risk burden and significant CAD patterns, i.e., MVD is more common among patients with multiple risk factors than SVD, based on the Odds ratio and confidence interval. The odds of single risk factor and multiple risk factors with single vessel disease versus multivessel disease are 0.298(0.129-0.69) and 4.78(2.165-10.557), respectively. This is consistent with the study done by Zeinali-Nezhad et al, who also found that with an increase in multiple risk factors, the prevalence of multivessel disease increased significantly with a p-value of <0.00529.

There are a few limitations in our study. The sample size was relatively small, and the study was done in a single center, which limits its generalizability. So the study provides valuable insights into CAD burden and risk stratification in resource-limited settings like Nepal and urges for larger, multicenter research.

CONCLUSION

Hypertension, Diabetes, Dyslipidemia, and Smoking were strongly associated with coronary arterial disease. Also, multivessel disease was strongly correlated with these risk factors. This study highlights the importance of modifying these possible risk factors and focusing public health interventions to halt the growing burden of coronary artery disease in South Asian countries like Nepal.

REFERENCES

1. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016 Oct;388(10053):1459–544.

2. Peters SAE, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014 Aug;57(8):1542–51.

3. Greenland P. Major Risk Factors as Antecedents of Fatal and Nonfatal Coronary Heart Disease Events. JAMA. 2003 Aug 20;290(7):891.

4. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The Lancet. 2004 Sep;364(9438):937–52.

5. Franklin SS, Larson MG, Khan SA, Wong ND, Leip EP, Kannel WB, et al. Does the Relation of Blood Pressure to Coronary Heart Disease Risk Change With Aging?: The Framingham Heart Study. Circulation. 2001 Mar 6;103(9):1245–9.

6. Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, et al. European Society of Cardiology: Cardiovascular Disease Statistics 2017. Eur Heart J. 2018 Feb 14;39(7):508–79.

7. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Murray CJL, et al. Temporal Trends in Ischemic Heart Disease Mortality in 21 World Regions, 1980 to 2010: The Global Burden of Disease 2010 Study. Circulation. 2014 Apr 8;129(14):1483–92.

8. Ralapanawa U, Sivakanesan R. Epidemiology and the Magnitude of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review: J Epidemiol Glob Health. 2021;11(2):169.

9. Porto I, Mattesini A, Valente S, Prati F, Crea F, Bolognese L. Optical coherence tomography assessment and quantification of intracoronary thrombus: Status and perspectives. Cardiovasc Revasc Med. 2015 Apr;16(3):172–8.

10. Global Health Estimates 2020: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2019. Geneva, World Health Organization; 2020.

11. Adhikari CM, Prajapati D, Baniya B, Regmi S, Bogati A, Thapaliya S. Prevalence of Conventional Risk Factors in ST Segment Elevation Myocardial Infarction Patients in Shahid Gangalal National Heart Centre, Nepal. J Nepal Med Assoc. 1970 Jan 1;52(195):914–9.

12. Bairey Merz CN, Kelsey SF, Pepine CJ, Reichek N, Reis SE, Rogers WJ, et al. The Women's Ischemia Syndrome Evaluation (WISE) Study: protocol design, methodology and feasibility report. J Am Coll Cardiol. 1999 May;33(6):1453–61.

13. Jakulla RS, Gunta SP, López-Candales A. Abnormal Resting Myocardial Contrast Echocardiographic Uptake: Clue of an Ongoing Acute Coronary Artery Event. Heart Views. 2023 Oct;24(4):212–6.

14. Kim J sung, Kim YJ, Shin YS, Ahn S, Kim WY. Use of Coronary CT Angiography to Predict Obstructive Lesions in Patients with Chest Pain without Enzyme and ST-Segment Elevation. J Clin Med. 2021 Nov 21;10(22):5442.

15. June-sung Kim, Youn-Jung Kim, Yo Sep Shin, Shin Ahn, Won Young Kim, Use of Coronary CT Angiography to Predict Obstructive Lesions in Patients with Chest Pain without Enzyme and ST-Segment Elevation, Journal of Clinical Medicine, 10, 22, (5442), (2021).

16. Barua RS, Ambrose JA, Srivastava S, et al. Reactive oxygen species are involved in smoking-induced dysfunction of nitric oxide biosynthesis and upregulation of endothelial nitric oxide synthase: an in vitro demonstration in human coronary artery endothelial cells. Circulation 2003

17. Aronson D, Edelman ER. Coronary artery disease and diabetes mellitus. Cardiol Clin. 2014 Aug;32(3):439-55.

18. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation 2019; 139: e56–e528.

19. Hyman DJ, Pavlik VN. Characteristics of patients with uncontrolled hypertension in the United States. N Engl J Med. 2001;345:479–486.

20. Rosendorff C, Lackland DT, Allison M, et al. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. Hypertension. 2015;65(6):1372–1407

21. Wallace SM, McEniery CM, Mäki-Petäjä KM, et al. Isolated systolic hypertension is characterized by increased aortic stiffness and endothelial dysfunction. Hypertension. 2007;50(1):228–233.

22. Dhungana SP, Mahato AK, Ghimire R, Shreewastav RK. Prevalence of Dyslipidemia in Patients with Acute Coronary Syndrome Admitted at Tertiary Care Hospital in Nepal: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2020 Apr 30;58(224):204-208

23. Mahalle N, Garg MK, Naik SS, Kulkarni MV. Study of pattern of dyslipidemia and its correlation with cardiovascular risk factors in patients with proven coronary artery disease. Indian J Endocrinol Metab. 2014 Jan;18(1):48-55.

24. Wahrenberg A, Magnusson PK, Discacciati A, Ljung L, Jernberg T, Frick M, Linder R, Svensson P. Family history of coronary artery disease is associated with acute coronary syndrome in 28,188 chest pain patients. Eur Heart J Acute Cardiovasc Care. 2020 Oct;9(7):741-747.

25. Liu Y, Ping J, Qiu L, Sun C, Chen M. Comparative analysis of ischemic changes in electrocardiogram and coronary angiography results: A retrospective study. Medicine (Baltimore). 2021 Jun 18;100(24):e26007

26. Germing A, Ulrich S, Fadgyas T, Grewe P, Mügge A, Lindstaedt M. Echocardiographic findings in patients with acute coronary syndrome and normal angiogram. Eur J Med Res. 2008 Aug 18

27. Dung NJ, Tettey MM, Tamatey M, Sereboe LA, Doku A, Adu-Adadey M, Agyekum F. Angiographic severity of coronary artery disease and the influence of major cardiovascular risk factors. Ghana Med J. 2023 Dec;57(4):262-269.

28. Castelli WP, Doyle JT, Gordon T, Hames CG, Hjortland MC, Hulley SB, Kagan A, Zukel WJ: HDL cholesterol and other lipids in coronary heart disease: The Cooperative Lipoprotein Phenotyping Study. Circulation 55: 767, 1977

29. Zeinali-Nezhad, N., Najafipour, H., Shadkam, M. et al. Prevalence and trend of multiple coronary artery disease risk factors and their 5-year incidence rate among adult population of Kerman: results from KERCADR study. BMC Public Health 24, 25 (2024)

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3. Haas AN, de Castro GD, Moreno T, Susin C, Albandar JM, Oppermann RV, et al. Azithromycin as a adjunctive treatment of aggressive periodontitis: 12-months randomized clinical trial. J Clin Periodontol 2008 Aug;35(8):696-704.

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