ISSN (Print): 2958-1281
ISSN (Online): 3006-5690

Mugda Medical College Journal

Volume 09 Number 01 January 2026

ISSN (Print): 2958-1281
ISSN (Online): 3006-5690

MuMC Journal
Mugda Medical College Journal

Published by
MUGDA MEDICAL COLLEGE, BANGLADESH
If any query please correspond with
The Chief Editor, Mugda Medical College Journal (MuMc Journal)
Mugda Medical College, Dhaka, Bangladesh
E-mail: mumcjournal@gmail.com

Editorial

Breaking Bad: What It Means and How We Do It

The well-known American TV series "Breaking Bad" follows a high school chemistry teacher in Albuquerque who, after being diagnosed with lung cancer, teams up with a former student – now an unsuccessful drug dealer – to manufacture and sell drugs (crystal methamphetamine). Although the show was widely praised by both viewers and critics, its title puzzled many people. What does "breaking bad" actually mean, and where did the phrase originate? The answers are fairly straightforward, though not easy to trace in reference books. For much of its history, "to break bad" was not a fixed expression but simply a regular verb phrase, similar to combinations like "break good," "break lucky," or "break ice." It was not until the 1960s that "break bad" became established in slang, particularly in African American vernacular, with the meaning of becoming angry or behaving aggressively. In the context of the series, the lead actors' descent into crime and violence reflects this later slang meaning, which is likely the inspiration behind the show's title.

However, in medical science, the phrase 'breaking bad' is used to deliver news related to the diagnosis of life-threatening diseases, progressive diseases, poor prognosis, failure in treatment, treatment complications, amputation and death.[1] We know that communication is crucial in the physician-patient relationship in healthcare. However, 'breaking bad' news in healthcare is quite different from other forms of clinical communication. It often triggers strong emotional reactions in patients, which can interfere with how they understand the information and often may lead to distress or unpredictable behaviour.[2] The way bad news is delivered can significantly shape the physician-patient relationship – enhancing it, damaging it, or even leading to exploitation. As a result, such situations can be difficult to manage and may cause healthcare professionals, especially interns and residents, to feel hesitant about communicating bad news. Still in modern healthcare, patients have the right to know the truth about their condition to make their decisions independently. Concealing any part of information, even with good intent, violates the principle of autonomy unless overtly requested by the patient. However, in the cultural context of Bangladesh, physicians often allow family dominance, where relatives request to withhold the truth partially, especially when the information can lead to loss of hope and distress for their loved ones. Implementing such requests demands ethical sensitivity and clarity. Besides, physicians have the obligation to "do good" which must be balanced with "do no harm" through their truth-telling.[1,3] In the medico-legal context, concealment of critical information can be seen as medical negligence or deficiency in service. However, our court system often recognise a doctor's right to withhold part of information from their patient under "therapeutic privilege" (only in rare cases where disclosure would cause serious psychological harm or complete loss hope of life). Any blanket non-disclosure is discouraged and may be seen as paternalistic.[3]

Communicating bad news is a complex task, requiring not only verbal, paraverbal, and nonverbal skills, but also the ability to manage emotional responses, involve patients and their families in decision-making, cope with stress for both parties, and maintain a sense of hope even in difficult circumstances.[4] Unfortunately, medical doctors in Bangladesh hardly receive any formal training or guidance on how to communicate with such patients and their families or to do formally 'breaking bad'.[5] Mostly they learn such communication through day-to-day practices by the senior professors, which is an important part of the "hidden curriculum" (including the customs, behavioural norms and communication style), to which they are exposed in their clinical rounds in hospital wards. However, it often limits personal growth by fostering imitation over authenticity, leading to the adoption of a model having bias or

outdated perspectives.[6] Moreover, in the absence of proper and effective (bio)ethics training, they may adopt inappropriate motives and methods of 'breaking bad' news, which may lead other parties to distress and emotional outburst and an increased risk of litigation.[3,7] Nurunnabi et al. proposed a four-step communication method for the first time to formally educate/train our physicians (targeting communication with the patients having an incurable illness).[5] Recently, Bangladesh Medical & Dental Council (BM&DC) has brought some changes in our MBBS curriculum in teaching and training methods emphasizing communication, ethics and professionalism in Medicine. Similar steps have been taken from the Bangladesh College of Physicians & Surgeons (BCPS). Recognition of our shortcomings in education and training, medical educators need to come forward which may lead to several initiatives ranging from designing communication skills training to the development of guidelines and protocols both national and institutional levels, which will meet expectations – ethically sound, culturally appropriate, practically applicable, and addressing patients' needs.

We have seen form our decades of experience that when physicians are well trained and 'breaking bad' is done with compassion and care, it can help patients and families navigate the challenging journey ahead, fostering a sense of trust, understanding, and support. To educate our interns and residents, the 'SPIKES' protocol – a validated, six-step approach[8] and 'BAD' – an established communication strategy,[7] can be easily implemented. Besides, video-based training session, role-play and simulation-based training can be arranged under medical education unit (MEU) of the respective institution. Currently we are piloting a similar formal training on 'goals of care' discussion in surgical settings for faculty members and residents.[9] We must continue to review and modify our current curricula and teaching methodologies (both in undergraduate and postgraduate medical education) to determine their adequacy in making medical doctors more competent in communication skills including 'breaking bad' tasks.

'Breaking bad' is a challenging communication task that requires empathy, honesty, and sensitivity. By preparing carefully, delivering the news with compassion, and responding to emotional reactions with empathy and understanding, our physicians can help patients and families navigate their difficult journey. Prioritizing self-care is also essential to avoid burnout and ensure that physicians can continue to provide high-quality care.

Mugda Med Coll J. 2026; 9(1): 1-2.
DOI: https://doi.org/10.3329/mumcj.v9i1.90748

Dr. Riffat Rahim
Associate Professor
Department of Obstetrics & Gynaecology
Mugda Medical College & Hospital, Dhaka-1214.
Email: riffatrahim@yahoo.com

REFERENCES

1. Jalali R, Jalali A, Jalilian M. Breaking bad news in medical services: a comprehensive systematic review. Heliyon. 2023;9(4):e14734.
2. Yurdakul ES, Coskun ZY, Sari O, Coskun AK. Characteristics affecting the attitude and approach of physicians to breaking bad news: uncertain medical situations. Humanit Soc Sci Commun. 2024;11:490.
3. Kumar V, Sarkhel S. Clinical practice guidelines on breaking bad news. Indian J Psychiatry. 2023; 65(2):238-44.
4. Karnieli-Miller O, Palombo M, Laor N. The hidden curriculum of breaking bad news: identification of three dimensions and four communication patterns. Patient Educ Couns. 2023;114:107807.
5. Nurunnabi ASM, Ahmad N, Chakma S, Asaduzzaman M, Mohammad A. Talking about end-of-life care: how should physicians act. Community Based Med J. 2020;9(1):38-42.
6. Nurunnabi ASM, Alam MB, Wazed F, Khaleque SA, Muqueet MA. Role modelling in medical education. Community Based Med J. 2025;14(2):208-13.
7. Christoph B, Katharina B, Alessia V, Sabina H. Communication challenges in end-of-life decisions. Swiss Med Wkly. 2020;150:w20351.
8. Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES – a six-step protocol for delivering bad news: application to the patient with cancer. Oncologist. 2000;5(4):302-11.
9. Nurunnabi ASM, Jamal ABM, Rahim R, Rashid MM, Hossain MA, Alam QS, et al. 'Goals of care' discussion in surgical settings: a pilot curriculum for the training of the faculty members and residents under faculty of surgery. Mugda Med Coll J. 2025;8(2):133-7.

Original Article

Terminal Ileal Endoscopic Findings in Chronic Diarrhoea: Experience of A Tertiary Teaching Hospital in Bangladesh

Haque MT[1], Hossain MJ[2], Islam MS[3], Rahman MO[4], Hossain MA[5], Hasan M[6], Bhuyian R[7], Mobin AQM[8]

ABSTRACT

Terminal ileal intubation is an integral part of colonoscopy in patients with chronic diarrhoea. Besides colonic diseases, terminal ileum can be involved in chronic diarrhea pathogenesis. The aim of this study was to assess the additional diagnostic yield of ileal intubation in chronic diarrhea. This cross-sectional study was conducted in the Department of Gastroenterology of National Gastroliver Institute and Hospital, Dhaka, Bangladesh, between July and December of 2021. One hundred and sixteen consecutive patients with chronic diarrhoea were enrolled. Thirteen patients were not fulfilling the inclusion criteria were excluded. In all patients, routine terminal ileal intubation was done as a part of routine colonoscopy and biopsies were taken from any visible lesion. Histopathology and GeneX-pert for detection of MTB were done from biopsy specimen. One-third (35.9%) of patients belonged to the 26-40 years age group. The mean age was 35.63±15.21 years (ranging between 18 and 74 years). Almost two-thirds (63.1%) of patients were male. More than three fourth (77.9%) of the patients were nonsmoker. In this study, isolated macroscopic abnormal ileum was found in 12(11.65%) patients and 13(12.62%) patients had macroscopic abnormality in both ileum and colon, which gave a diagnostic yield of 24.27% of all ileal intubation. No association was observed between macroscopic features and age or gender of the patients (p>0.05); however, significant association was found between macroscopic features and alarming features of the patients (p=0.001).

Keywords: *Colonoscopy, terminal ileal intubation, diarrhoea.*

Mugda Med Coll J. 2026; 9(1): 3-8
DOI: https://doi.org/10.3329/mumcj.v9i1.90800

1. Dr. Mohammed Tozammel Haque, Assistant Registrar, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212. Email: tozammel_jch@yahoo.com (Corresponding author)
2. Dr. Mir Jakib Hossain, Associate Professor, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212.
3. Dr. Mohammad Shohidul Islam, Registrar, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212.
4. Dr. Mohammad Obayedur Rahman, Registrar, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212.
5. Dr. Md. Altaf Hossain, Registrar, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212.
6. Dr. Monirul Hasan, Registrar, Department of Gastroenterology, National Gastroliver Institute and Hospital (NGIH), Dhaka-1212.
7. Dr. Rokanuzzaman Bhuyian, Professor, Department of Gastroenterology, NGIH, Dhaka 1212.
8. Dr. AQM Mobin, Associate Professor, Department of Gastroenterology, Mugda Medical College & Hospital, Dhaka-1214.

INTRODUCTION

Chronic diarrhoea, defined as the passage of loose or watery stools persisting for more than four weeks[1,2], represents a common yet diagnostically challenging clinical condition. It encompasses a wide spectrum of underlying etiologies, ranging from functional gastrointestinal disorders to inflammatory, infectious, and neoplastic diseases.[3] Identifying the precise cause is critical for effective management, especially when alarm features such as weight loss, anemia, or gastrointestinal bleeding are present. The terminal ileum (TI) plays a crucial role in the absorption of bile acids and vitamin B_{12} and serves as a common site for several pathological conditions including Crohn's disease, intestinal tuberculosis, lymphoma, and drug-induced enteritis. Despite its clinical relevance, the TI is often under-evaluated due

to the technical challenges associated with its visualization during colonoscopy. Advancements in endoscopic techniques have improved access to the TI, allowing for direct mucosal inspection and targeted biopsies. Endoscopic evaluation of the TI can reveal a range of findings, from normal mucosa to subtle or overt pathological changes, which may significantly influence diagnostic outcomes and therapeutic decisions in patients with chronic diarrhoea.

Chronic diarrhoea affects around 7.3% of adults and 14.2% of the elderly in the United States[4], where as in developing countries only limited data exist regarding the burden of chronic diarrhoea. Once clinical examination is unyielding and intestinal infection has been excluded by microbiological and serological investigations, colonoscopy with biopsy is usually performed.[3] But colonoscopy with ileal intubation is not routinely performed. However, alterations of the colonic mucosa have been involved in chronic diarrhoea pathogenesis in 15-18% of cases.[5] Chronic diarrhoea may also be caused by diseases involving the terminal ileum. In patients with chronic diarrhoea macroscopically abnormal ileum was found in 5% cases.[6] Ileoscopy has been regarded as a meaningful procedure in specific conditions, including inflammatory and some infectious disease.[7-9] Ileal intubation with biopsy is a key element for the diagnostic evaluation of chronic diarrhea, especially in patients suspected of having inflammatory bowel disease.[10,11] Histology of terminal ileal biopsy may be of greatest value when an macroscopic abnormal terminal ileum is identified during colonoscopy with ileal intubation.[12,13] Some studies from western population have reported the additional diagnostic benefit of terminal ileum intubation.[3,5,6,10,14] Most studies of routine terminal ileal intubation during colonoscopy have been performed in western population. Only a few studies have been conducted in Asian or other tropical regions.[15,16] These regions have different spectrum of gastrointestinal disease, relatively low prevalence of Crohn's disease and higher prevalence of gastrointestinal infections, including TB.[16,17] There is a paucity of data in our countries. Therefore, the study was designed to performed routine terminal ileal intubation during colonoscopy as part of the workup for chronic diarrhoea. The aim of this study was to assess the value of routine terminal ileal intubation during colonoscopy in patients with chronic diarrhoea in a tertiary teaching hospital of Bangladesh.

METHODS

This cross-sectional study was done in the Department of Gastroenterology of National Gastroliver Institute and Hospital (NGIH), Dhaka, Bangladesh, between July and December of 2021. Consecutive patients of chronic diarrhoea attending the inpatient and outpatient Department of Gastroenterology for evaluation of chronic diarrhoea were included. All adult patients of both sexes with chronic diarrhea who had complete colonoscopic examination with successful ileal intubation were included. Patients who refused to participate in the study or already known to be suffering from diarrhea associated disorder such as inflammatory bowel disease, celiac disease, pancreatic disease, intestinal tuberculosis or had a history of drug induced diarrhea, prior GI surgery or were pregnant not allowed to participate in the study. After obtaining informed written consent they were screened through history, clinical examination and some routine investigations such as full blood count, erythrocyte sedimentation rate, routine microscopic examination of stool, stool culture, RBS, C-reactive protein. Further specific investigations including IgA anti tTG antibody, distal duodenal biopsy, fecal calprotectin, hydrogen breath test, MR enterography and thyroid hormones were done on selected cases based on clinical suspicion. In all patients, terminal ileal intubation was done as a part of routine colonoscopy. All colonoscopic examinations were performed by experienced endoscopists by using video colonoscope Olympus 190 after preparation with 20% mannitol solution. Ileocolonoscopic findings were carefully recorded and biopsies were taken from any visible ileocolonoscopic lesion. Biopsy specimens were sent in 10% formalin for histopathological study in Department of Histopathology of the same institution and in normal saline for GeneXpert test for detection of MTB to the Laboratory Services of ICDDR,B, Dhaka. Information was collected in a predesigned data collection sheet which included demographic characteristics, duration of symptoms, associated symptoms, findings of colonoscopic and ileoscopic examination, histopathologic and GeneXpert for MTB detection of biopsy specimen.Data was recorded systematically in preformed data collection form (questionnaire). Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 25.0 for Windows. Categorical data were presented as numbers and percentages. Numerical

data were presented as mean and standard deviation, median and range. Student t-test was used for comparing continuous variables, ANOVA test was used for comparing means of more than two groups and Chi-square test for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 116 consecutive patients who attended for evaluation of chronic diarrhoea were recruited. Thirteen patients were excluded during the study – three patients had failed ileal intubation, while six patients were unwilling to do colonoscopy and four patients had known diagnosis of inflammatory bowel disease. Successful ileal intubation was achieved in 107(97.27%) patients. Table-I shows the demographic profile of the patients. In this study, more than one third (35.9%) of study population belonged to age level 26-40 years. The mean age was 35.63±15.21 years (ranging from 18 to 74 years). Almost two-thirds (63.1%) of the patients were male and more than three-fourths (77.9%) of them were nonsmoker.

Among all study participants, isolated macroscopic abnormality of ileum was found in 12(11.65%) of the patients and 13(12.62%) had macroscopic abnormality in both ileum and colon, which gave a diagnostic yield of 24.27% of all ileal intubation (Table-II). Alarm features were present in 80% of patients with macroscopic abnormality in ileum, on the other hand 19.04% of patients had alarm features with macroscopic normal ileum. Histopathological examination of terminal ileal biopsy reveals 40% chronic ileitis, 28% acute ileitis, 20% non-specific ileitis and 12% granuloma (Fig. 1). Gene X-pert for MTB were detected in three patients from 24 of terminal ileal biopsy. It was observed that more than one fourth (29.1%) of study population had irritable bowel syndrome followed by 22(21.4%) functional diarrhoea, 13(12.62%) intestinal TB, 9(8.7%) Crohn's disease, 6(5.8%) ulcerative colitis, 2(1.9%) colonic malignancy and 1(1.0%) patient had tropical sprue. However, in 20(19.5%) patients, the etiology of chronic diarrhoea was not determined. No association was observed between macroscopic features and age or gender of the patients (p>0.05); in contrast, significant association was found between macroscopic features and alarming features of the patients (p=0.001) (Table-III).

Table-I: *Demographic profile of the study participants (n=103)*

Variables	Frequency	Percentage
Age group (in years)		
≤25	35	33.98
26-40	37	35.90
41-55	15	14.56
>56	16	15.53
Mean±SD	35.63±15.21	
Range	18-74	
Gender		
Male	65	63.1
Female	38	36.9
Marital status		
Married	74	71.8
Unmarried	29	28.2
Occupation		
Housewife	29	28.2
Service	23	22.3
Student	20	19.4
Day labourer	15	14.56
Business	10	9.7
Others	6	5.8
Education		
Illiterate – Class V	15	14.6
Class VI – Class X	25	24.3
SSC – HSC	35	33.9
Graduate –Postgraduate	28	27.2
Religion		
Muslim	97	94.2
Hindu	6	5.8
Smoking history		
Non-smoker	80	77.6
Smoker	23	22.4

Table-II: *Distribution of the study population according to isolated macroscopic abnormality of ileum (n=12)*

Macroscopic	Frequency	Percentage
Abnormality		
Ulcer	11	10.67
Nodule	1	1
Total	12	11.65

Table-III: *Association of the macroscopic features and age, gender and alarming features of the study participants*

Variables	Macroscopic normal ileum (n=63)	Isolated macroscopic abnormal ileum (n=12)	Isolated macroscopic abnormal colon (n=15)	Macroscopic abnormal in both ileum and colon (n=13)	p-value
Age in years	34±14.8	37.7±15.6	35.5±12.0	41.8±19.4	[a]0.381[ns]
Gender					
Male	41(65.1%)	7(58.3%)	8(53.3%)	9(69.2%)	[b]0.789[ns]
Female	22(34.9%)	5(41.7%)	7(46.7%)	4(30.8%)	
Alarming features	12(19.04)	10(83.33)	12(80.0)	13(100)	[b]0.001[s]

[a]p-value reached from ANOVA test, [b]p-value reached from Chi-square test; s= significant, ns=not significant.

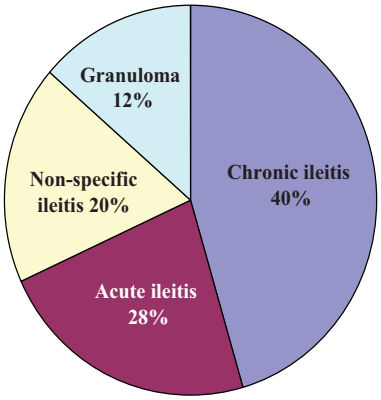

Fig. 1: *Pie chart showing the histopathological findings of ileal biopsy*

DISCUSSION

Chronic diarrhoea of unknown origin is one of the major indications for gastrointestinal endoscopy and accounts for approximately 4%-7% of all the colonoscopies performed in Western countries.[5,18,19] This study showed high prevalence of chronic diarrhoea with male preponderance, which is in concordance with several previous studies.[20-24] It was observed that 66% of the study population had abdominal pain. Shah et al. reported that 43% of their study subject had abdominal pain. This figure is much lower than our study results.[25]

This study reported that 24.27% of the study population have macroscopic abnormalities in the terminal ileum. Another study done by Melton et al. retrospectively examined 9785 unselected patients who underwent ileocolonoscopy with biopsy had abnormal ileum in 24.9% of patients. That study result is almost similar with our findings.[20]

Geboes et al. reported that among 257 immunocompetent patients with acute or chronic diarrhea with abdominal pain, 47.95% patients were found to have endoscopic abnormalities of the terminal ileum. This is a higher incidence compared to our study.[7] However, our study results showed a higher incidence compared to the studies conducted in the Western countries.[21-23] Another study showed that 2% to 7.2% diagnostic findings of TB were reported when routine terminal ileal intubation was performed in unselected patients.[16] Wijewantha et al. found 10.6% of their patients had macroscopic abnormalities in the terminal ileum. This is much lower figure compared to our study when routine terminal ileal intubation was performed not only for the evaluation of chronic diarrhoea.[26] A study from India showed 14% (8/57) study population had ileal abnormality when routine terminal ileal intubation was done in unselected patients.[15] In another study, diagnostic yield of routine terminal ileal intubation was as low as 0.3%.[23] This study had been carried out on asymptomatic patients undergoing screening colonoscopy.[23]

This study reported colonoscopic findings were normal in the majority of cases (72.81%). Specific changes like ulcers, polyps and diverticula were seen in 27.2% (28 cases); whereas 23.3%(24) of cases showed ulcers, 2.9%(3) polyps and 1%(1) diverticula. In this study, we found almost similar figure compared to another Indian study.

This study reported 13/103(12.6%) patients were diagnosed to have intestinal tuberculosis. Whereas Wijewantha et al. study described only 1.8%(14/764) of cases had evidence of ITB, this result was much

lower than our study results.[26] Although this study was conducted in tropical setting like Sri Lanka, they had recruited unselected patients. Kolhe et al. reported 7.5% (9/120) patients had intestinal tuberculosis which was also lower than our study results.[27]

In this study, we found 9/103(8.7%) patients were diagnosed to have CD. However, this study was conducted in a referral center. The high frequency of CD among patients undergoing colonoscopy with ileal intubation in this hospital was likely to be due to a referral bias. Another study from Sri Lanka reported that 3.6% (28/764) patients had Crohn's disease of unselected patients. Their lower incidence could be explained by the fact that they recruited unselected patients.[26]

This study reported 6/103(5.8%) patients were diagnosed to have ulcerative colitis. Kolhe et al study had 16.7% (20/120) of UC, this result was much higher than our study result.[27] A significant number of the patients (29.1%) in this study population subsequently diagnosed with IBS. These findings were consistent with the study findings of Read et al.[28], as they reported that (30%) (8/27) patients underwent an extensive evaluation for chronic diarrhoea were found to have the IBS. Shah et al. reported 31% of their study participants had IBS; this result is almost similar with the present study results.[25]

CONCLUSION

Routine terminal ileal intubation during colonoscopy, yield additional benefit to the diagnosis, especially in cases where routine investigations yield inconclusive results. Early identification of terminal ileal lesions can facilitate timely diagnosis and appropriate management, ultimately improving patient outcomes.

Conflict of Interest: None declared by the authors.

Funding Statement: No external funding received.

Ethical Approval: This study was approved by the Institutional Review Committee of the National Gastroliver Institute and Hospital (NGIH), Dhaka, Bangladesh.

Authors' Contribution: Conception and design: MT Haque, MJ Hossain, patient selection: MT Haque, MJ Hossain; acquisition, analysis and interpretation of data: MT Haque, MS Islam, MO Rahman, MA Hossain, M Hasan; manuscript writing, critical revision, final approval and submission of the manuscript: MT Haque, MJ Hossain, MS Islam, MO Rahman, MA Hossain, M Hasan, R Bhuyian, AQM Mobin.

REFERENCES

1. Schiller LR, Pardi DS, Sellin JH. Chronic diarrhea: diagnosis and management. Clinical Gastroenterology and Hepatology. 2017;15(2):182-93.
2. Arasaradnam RP, Brown S, Forbes A, Fox MR, Hungin P, Kelman L, et al. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology. Gut. 2018;67(8):1380-99.
3. Fine KD, Schiller LR. AGA technical review on the evaluation and management of chronic diarrhea. Gastroenterology. 1999;116(6):1464-86.
4. Talley NJ, O'Keefe EA, Zinsmeister AR, Melton III LJ. Prevalence of gastrointestinal symptoms in the elderly: a population-based study. Gastroenterology. 1992;102(3):895-901.
5. Patel Y, Pettigrew NM, Grahame GR, Bernstein CN. The diagnostic yield of lower endoscopy plus biopsy in nonbloody diarrhea. Gastrointest Endosc. 1997;46(4):338-43.
6. Yusoff IF, Ormonde DG, Hoffman NE. Routine colonic mucosal biopsy and ileoscopy increases diagnostic yield in patients undergoing colonoscopy for diarrhea. J Gastroenterol Hepatol. 2002;17(3):276-80.
7. Geboes K, Ectors N, D'Haens G, Rutgeerts P. Is ileoscopy with biopsy worthwhile in patients presenting with symptoms of inflammatory bowel disease? Am J Gastroenterol. 1998;93(2):201-6.
8. Zwas FR, Bonheim NA, Berken CA, Gray S. Diagnostic yield of routine ileoscopy. Am J Gastroenterol. 1995;90(9):1441-3.
9. Bhasin DK, Goenka MK, Dhavan S, Dass K, Singh K. Diagnostic value of ileoscopy: a report from India. J Clin Gastroenterol. 2000;31(2):144-6.
10. Morini S, Lorenzetti R, Stella F, Martini MT, Hassan C, Zullo A. Retrograde ileoscopy in chronic nonbloody diarrhea: a prospective, case-control study. Am J Gastroenterol. 2003;98(7):1512-5.
11. Shen B, Khan K, Ikenberry SO, Anderson MA, Banerjee S, Baron T, Ben-Menachem T, Cash BD, Fanelli RD, Fisher L, Fukami N. The role of endoscopy in the management of patients with diarrhea. Gastrointest Endosc. 2010;71(6):887-92.

12. McHugh JB, Appelman HD, McKenna BJ. The diagnostic value of endoscopic terminal ileum biopsies. Am J Gastroenterol. 2007;102(5):1084-9.

13. Tontini GE, Vecchi M, Pastorelli L, Neurath MF, Neumann H. Differential diagnosis in inflammatory bowel disease colitis: state of the art and future perspectives. World J Gastroenterol. 2015;21(1):21-46.

14. Shah RJ, Fenoglio-Preiser C, Bleau BL, Giannella RA. Usefulness of colonoscopy with biopsy in the evaluation of patients with chronic diarrhea. Am J Gastroenterol. 2001;96(4):1091-5.

15. Bhasin DK, Goenka MK, Dhavan S, Dass K, Singh K. Diagnostic value of ileoscopy: a report from India. J Clin Gastroenterol. 2000;31(2):144-6.

16. Jeong SH, Lee KJ, Kim YB, Kwon HC, Sin SJ, Chung JY. Diagnostic value of terminal ileum intubation during colonoscopy. J Gastroenterol Hepatol. 2008;23(1):51-5.

17. Niriella MA, de Silva AP, Dayaratne AH, Ariyasinghe MH, Navarathne MM, Peiris RS, et al. Prevalence of inflammatory bowel disease in two districts of Sri Lanka: a hospital based survey. BMC Gastroenterology. 2010;10:32.

18. Tontini GE, Pastorelli L, Spina L, Fabris F, Bruni B, Clemente C, et al. Microscopic colitis and colorectal neoplastic lesion rate in chronic nonbloody diarrhea: a prospective, multicenter study. Inflamm Bowel Dis. 2014;20(5):882-91.

19. Meral M, Bengi G, Kayahan H, Akarsu M, Soytürk M, Topalak Ö, et al. Is ileocecal valve intubation essential for routine colonoscopic examination? Eur J Gastroenterol Hepatol. 2018;30(4):432-7.

20. Melton SD, Feagins LA, Saboorian MH, Genta RM. Ileal biopsy: clinical indications, endoscopic and histopathologic findings in 10,000 patients. Dig Liver Dis. 2011;43(3):199-203.

21. Cherian S, Singh P. Is routine ileoscopy useful? An observational study of procedure times, diagnostic yield, and learning curve. Am J Gastroenterol.| 2004;99(12):2324-9.

22. Yoong KK, Heymann T. It is not worthwhile to perform ileoscopy on all patients. Surg Endosc. 2006;20(5):809-11.

23. Kennedy G, Larson D, Wolff B, Winter D, Petersen B, Larson M. Routine ileal intubation during screening colonoscopy: a useful maneuver?. Surg Endosc. 2008;22:2606-8.

24. Bhagyalakshmi A, Venkatalakshmi A, Praveen L, Sunilkumar K. Clinico-pathological study of colonoscopic biopsies in patients with chronic diarrhea. Int J Res Med Sci. 2016;4(7):2738-44.

25. Shah RJ, Fenoglio-Preiser C, Bleau BL, Giannella RA. Usefulness of colonoscopy with biopsy in the evaluation of patients with chronic diarrhea. Am J Gastroenterol. 2001;96(4):1091-5.

26. Wijewantha HS, de Silva AP, Niriella MA, Wijesinghe N, Waraketiya P, Kumarasena RS, et al. Usefulness of routine terminal ileoscopy and biopsy during colonoscopy in a tropical setting: a retrospective record-based study. Gastroenterol Res Pract. 2014;2014:343849.

27. Kolhe HS, Mahore SD, Patil SS, Patil RN. To study the endoscopic colonic biopsies of patients presenting with chronic watery diarrhea or constipation with special emphasis on microscopic colitis. IOSR J Dent Med Sci. 2014;13(12):84-8.

28. Read NW, Krejs GJ, Read MG, Santa Ana CA, Morawski SG, Fordtran JS. Chronic diarrhea of unknown origin. Gastroenterology. 1980;78(2):264-71.

Original Article

Renoprotective Effect of Desloratadine on Streptozotocin-induced Diabetic Nephropathy in Adult Male Long-Evans Rats

Aktar S[1], Rahman MS[2], Chowdhury IH[3], Mitu FH[4], Sultana S[5], Shovah ST[6], Tabassum M[7]

ABSTRACT

Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD) worldwide and a major microvascular complication of diabetes mellitus (DM). Despite current treatments, particularly those targeting the renin–angiotensin system, the progression of DN remains inadequately controlled. Histamine H1 receptors have emerged as potential contributors to glomerular dysfunction, mediating inflammation and oxidative stress in diabetic kidneys. Desloratadine, a potent H1 receptor antagonist, exhibits anti-inflammatory and antioxidant properties, suggesting its therapeutic potential in DN. This experimental, randomized controlled study aimed to evaluate the renoprotective effects of desloratadine in streptozotocin (STZ)-induced DN in adult male Long-Evans rats. Seventy adult male rats were divided into eight groups. Group I served as a blank control, and Group II received vehicle for STZ. Groups III–VIII were rendered diabetic via a single intraperitoneal injection of STZ (50 mg/kg). Groups III, V, and VII served as diabetic controls, while Groups IV, VI, and VIII received daily oral desloratadine (10 mg/kg) for varying durations, initiated at different stages of DN progression. Serum creatinine was measured as a marker of renal function. Renal oxidative stress were assessed by malondialdehyde (MDA), reduced glutathione (GSH), and histopathological changes in renal tissue were also evaluated. In diabetic control groups, serum creatinine, and MDA levels were significantly elevated ($p<0.01$), while GSH was significantly reduced ($p<0.01$) compared to control. Histopathological examination showed marked renal damage, and body weight was significantly decreased ($p<0.01$). Desloratadine treatment significantly improved biochemical and histological parameters at all stages of DN ($p<0.05$ to $p<0.01$), though values did not return to normal control levels. Longer duration treatment, initiated after DN onset, yielded the most pronounced histological improvements. Desloratadine also significantly prevented diabetes-induced weight loss ($p<0.01$). Desloratadine attenuated the progression of diabetic nephropathy, likely through its antioxidant mechanisms. While it may not prevent DN onset, its therapeutic benefits in slowing disease progression warrant further investigation in advanced animal models and clinical trials.

Keywords: *Diabetic nephropathy, diabetes mellitus, desloratadine, long-Evans rats*

Mugda Med Coll J. 2026; 9(1): 9-17
DOI: https://doi.org/10.3329/mumcj.v9i1.90802

1. Dr. Shirin Aktar, Lecturer, Department of Pharmacology & Therapeutics, Sylhet MAG Osmani Medical College, Sylhet-3100. Email: dr.shirinaktarcmc@gmail.com (Correspondong author)
2. Prof. Md. Sayedur Rahman, Ex-Chairman, Department of Pharmacology & Therapeutics, Bangladesh Medical University (BMU), Dhaka-1000.
3. Dr. Iftekhar Hossain Chowdhury, Assistant Professor, Department of Pharmacology & Therapeutics, Mugda Medical College, Dhaka-1214.
4. Dr. Farjana Haque Mitu, Assistant Professor, Department of Pharmacology & Therapeutics, Shahabuddin Medical College, Gulshan-2, Dhaka-1212.
5. Dr. Shahrin Sultana, Assistant Professor, Department of Pharmacology & Therapeutics, Eastern Medical College, Cumilla-3520.
6. Dr. Sharmeen Tania Shovah, Assistant Professor, Department of Pharmacology & Therapeutics, Sir Salimullah Medical College, Dhaka-1100.
7. Dr. Masuma Tabassum, Medical Officer, Department of Pharmacology & Therapeutics, Dhaka Medical College, Dhaka-1000.

INTRODUCTION

Diabetic nephropathy (DN) is one of the most serious microvascular complications of diabetes mellitus (DM), accounting for approximately 40% of cases of end-stage renal disease (ESRD) globally and remaining its leading cause.[1] In addition to being a primary contributor to renal failure, DN independently increases the risk of cardiovascular diseases, adding to its burden on global health With roughly 30–45% of diabetic individuals developing DN during the course of their disease,[2] it poses a major clinical and public health challenge, particularly in low- and middle-income countries, where 80% of diabetic patients reside.[3] DM is a chronic metabolic disorder marked by persistent hyperglycemia due to insulin secretion defects, insulin resistance, or both. Sustained hyperglycemia triggers a cascade of metabolic and hemodynamic disturbances that lead to long-term organ damage, notably to the kidneys. DN typically progresses from a state of glomerular hyperfiltration and microalbuminuria to overt proteinuria and eventually ESRD, characterized by a reduced glomerular filtration rate (GFR<60ml/min/1.73m²) and irreversible histological changes such as glomerular sclerosis, interstitial fibrosis, and tubular atrophy.[1,4] Current treatment strategies for DN primarily focus on strict glycemic control and management of associated risk factors like hypertension and dyslipidemia.[5] Although pharmacological interventions such as renin–angiotensin–aldosterone system (RAAS) blockers have been shown to delay progression, they are insufficient in halting disease advancement in many patients.[6] Consequently, there is growing interest in exploring alternative therapeutic targets, particularly those addressing underlying oxidative mechanisms. In recent years, increasing evidence has highlighted the pivotal role of oxidative stress in the pathogenesis of DN.[6] Interestingly, histamine has recently been identified as a novel player in the pathophysiology of DN. Released predominantly from mast cells in response to AGEs and ROS, histamine exerts potent pro-inflammatory effects via histamine receptors (H1–H4), with the H1 receptor (H1R) being most abundantly expressed in renal tissues.[7,8] Studies have shown that blocking H1R signaling can modulate inflammatory responses, reduce oxidative stress, and confer renoprotection in diabetic models.[9-11]

Desloratadine, a second-generation, non-sedating H1 receptor antagonist, is widely used for allergic disorders. In addition to its antihistaminic effects, desloratadine has demonstrated antioxidant properties through inhibition of NF-KB activation, reduction in pro-inflammatory cytokine release, and attenuation of ROS generation.[12-14] Animal studies further support its protective effects in various models of oxidative and inflammatory injury, including renal ischemia-reperfusion and toxin-induced nephropathy.[15,16] However, its potential role in mitigating diabetic nephropathy has not yet been explored. Given the promising anti-inflammatory and antioxidant profile of desloratadine and the multifactorial pathogenesis of DN, the present study aims to evaluate the renoprotective effects of desloratadine in a streptozotocin (STZ)-induced diabetic nephropathy model in adult male Long-Evans rats. STZ is a widely used compound for inducing type 1 diabetes in animal models by selectively destroying pancreatic β-cells, resulting in persistent hyperglycemia and renal injury closely resembling human DN.[17] Exploring the therapeutic impact of desloratadine in this model may provide valuable insights into its utility as a repurposed drug for managing DN, especially in resource-limited settings where drug affordability and availability are major concerns.

METHODS

This experimental, randomized controlled study was conducted in the Department of Pharmacology & Therapeutics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, between March 2021 and January 2023. Seventy adult male Long-Evans rats (7–10 weeks old, 180–220 gm in weight) were used. Male rats were selected based on greater susceptibility to STZ-induced diabetes and diabetic nephropathy (DN). The rats were housed under standard laboratory conditions (24±1°C, 12:12 h light-dark cycle), with free access to water and standard pellet diet. Animals were randomly assigned into eight groups. Two groups served as controls (blank and vehicle), while the remaining six were diabetic groups induced by streptozotocin (STZ, 50 mg/kg, intraperitoneal), divided into three untreated and three desloratadine-treated subgroups:

Group I: Blank control (n=8).

Group II: Vehicle control (0.5 ml sodium citrate buffer, pH 4.5; n=8).

Group III, V, VII: Diabetic controls (n=9 each, sacrificed at weeks 4, 8, and 12).

Group IV (STZ+DESL1): Desloratadine-treated from diabetes onset, for 3 weeks (n=9).

Group VI (STZ+DESL2): Desloratadine-treated from week 4 to 7, for 4 weeks (n=9); and

Group VIII (STZ+DESL3): Desloratadine-treated from week 4 to 11, for 8 weeks (n=9).

A total of five rats died during the study due to suspected STZ toxicity or complications; these were excluded from analysis.

Diabetes was induced by a single intraperitoneal injection of freshly prepared STZ (50 mg/kg) in 0.1 M sodium citrate buffer (pH 4.5). Rats were fasted for 12 hours prior to injection. Blood glucose was measured from the tail vein using a glucometer (Accu-Chek Instant S, Roche, Germany). Rats with fasting blood glucose ≥15 mmol/L on day 7 post-STZ injection were included in the diabetic groups.

Desloratadine tablets (Deslor 5 mg, Orion Pharma) were crushed and dissolved in distilled water. Based on an average body weight of 200 g, each rat received 2 mg/day (10 mg/kg/day) orally via gavage using a flexible ball-tipped feeding needle. Dosing volumes were within recommended limits (10–20 ml/kg/day). Treatment schedules varied by group, as outlined above.

Random blood glucose was monitored twice weekly. Rats with RBS >30 mmol/L received subcutaneous long-acting insulin (2–4 units) per a predefined scale. Hypoglycemic rats (RBS <15 mmol/L) were treated with 20% glucose solution. At designated time points (weeks 4, 8, and 12), rats were euthanized under light anesthesia using chloroform. Blood was collected via carotid artery into plain test tubes, allowed to clot, and centrifuged to obtain serum, stored at –20°C. **Blood glucose was m**easured using glucose oxidase strip method, while s**erum creatinine was e**stimated by Jaffe's Alkaline-Picrate method. For r**enal oxidative stress,** kidney homogenates were assayed for malondialdehyde (MDA), reduced glutathione (GSH), using standard spectrophotometric methods and ELISA kits (SunLong Biotech, made in China). Both kidneys were excised; the left kidney was stored at –80°C for biochemical assays, and the right kidney fixed in 10% formalin for histopathological analysis. Kidney sections were stained with hematoxylin and eosin (H&E) and periodic acid-Schiff (PAS) for assessment of glomerular and tubular changes.

Data was analyzed using SPSS software version 26.0 for Windows. Results were expressed as mean±SD (standard deviation). One-way ANOVA followed by post-hoc unpaired and paired t-tests were used for group comparisons. A p-value <0.05 was considered statistically significant.

RESULTS

Table-I shows fasting blood glucose levels were significantly elevated in all STZ-induced diabetic groups (Groups III–VIII) compared to the control Group II (5.24±0.60 mmol/L; $p<0.001$), confirming successful induction of diabetes. No significant differences were observed among the diabetic groups themselves ($p>0.05$). To evaluate the progression of diabetic nephropathy over time, serum creatinine levels were measured in STZ-induced diabetic rats sacrificed at three different time points and compared with the non-diabetic control group (Table-II). In Group II (control), the mean±SD of serum creatinine level was 0.54±0.06 mg/dl. A time-dependent elevation in serum creatinine was observed in diabetic rats. Desloratadine significantly reduced serum creatinine levels in diabetic rats at all time points. At week 4, levels decreased from 0.90±0.15 mg/dl (Group III) to 0.73±0.05 mg/dl in Group IV ($p<0.05$). At week 8, creatinine dropped from 1.82±0.09 mg/dl (Group V) to 1.62±0.14 mg/dl in Group VI ($p<0.01$). At week 12, levels declined from 2.35±0.15 mg/dl (Group VII) to 2.06±0.16 mg/dl in Group VIII ($p<0.01$). Despite improvements, all desloratadine-treated groups remained above the control Group II level (0.54±0.06 mg/dl) (Table-III). Table-IV shows renal tissue MDA levels significantly increased with the progression of diabetes. Compared to the control Group II (0.84±0.11 µmol/L), MDA concentrations were elevated in Group III (1.83±0.34 µmol/L; $p<0.01$), Group V (2.82±0.31 µmol/L; $p<0.001$), and Group VII (4.06±0.21 µmol/L; $p<0.001$). The increases were also significant between Group V vs. III and Group VII vs. V ($p<0.001$). Renal GSH levels decreased progressively with the duration of diabetes. Compared to the control Group II (3.33±0.18 mg/ml), significant reductions were observed in Group III (2.23±0.20 mg/ml; $p<0.01$), Group V (1.60±0.15 mg/ml; $p<0.001$), and Group VII (1.16±0.16 mg/ml; $p<0.001$). The decline was also significant between Group V vs. III and Group VII vs. V ($p<0.001$), indicating worsening oxidative stress with prolonged diabetes. Table-V shows that desloratadine treatment significantly reduced renal MDA concentrations in all diabetic

groups. At week 4, MDA levels decreased from 1.83±0.34 µmol/L in Group III to 1.43±0.22 µmol/L in Group IV ($p<0.05$). At week 8, Group VI showed reduced MDA (2.47±0.19 µmol/L) compared to Group V (2.82±0.31 µmol/L) ($p<0.05$). Similarly, at week 12, Group VIII had lower MDA (3.77±0.17 µmol/L) than Group VII (4.06±0.21 µmol/L) ($p<0.05$). Despite these reductions, MDA levels remained higher than the control (Group II: 0.84±0.11 µmol/L). Desloratadine significantly improved renal GSH concentrations in diabetic rats at all time points. At week 4, GSH increased from 2.23±0.20 mg/ml (Group III) to 2.66±0.22 mg/ml in Group IV ($p<0.01$). At week 8, GSH rose from 1.60±0.15 mg/ml (Group V) to 1.96±0.10 mg/ml in Group VI ($p<0.01$). At week 12, GSH increased from 1.16±0.16 mg/ml (Group VII) to 1.56±0.28 mg/ml in Group VIII ($p<0.01$). Despite these improvements, GSH levels remained lower than the control Group II (3.33±0.18 mg/ml). Table-VI illustrates results of histopathological examination of kidney tissues in different groups of rats. Group I (blank control) and Group II (vehicle control) showed normal glomerular and tubular structures with no pathological changes (mean scores: 0.00±0.00 for all parameters). In Group III (STZ-induced, 4th week), mild renal changes were observed, including glomerular hypertrophy (0.86±0.38) and mesangial expansion (0.71±0.49), with a significant increase in mesangial expansion ($p<0.01$). Group IV (STZ+desloratadine, 4th week) showed reduced histological scores, with a significant decrease in mesangial expansion (0.13±0.35) ($p<0.05$). In Group V (STZ-induced, 8th week), further deterioration occurred with significant increases in glomerular hypertrophy (2.38±0.52, $p<0.001$), GBM thickening, and mesangial expansion (both $p<0.05$). Group VI (STZ+desloratadine, 8th week) showed improvements, with significant reduction in glomerular hypertrophy (1.00±0.54) ($p<0.01$), though other changes were not statistically significant. By the 12th week, Group VII (STZ-induced) exhibited severe damage, including nodular sclerosis (0.25±0.46), with significant increases in all other parameters ($p<0.001$). Group VIII (STZ+desloratadine, 12th week) showed marked renoprotection, with significant reduction in glomerular hypertrophy, mesangial expansion, GBM thickening, and mononuclear cell infiltration ($p<0.05$). Nodular sclerosis was absent. Group II (Vehicle control, sacrificed on Day 1 of Week 4): H&E stained sections showed normal histoarchitecture with well-defined glomeruli, intact renal tubules, and unremarkable interstitium (Fig. 1). Group III (STZ-induced diabetic group, sacrificed on Day 1 of Week 4): H&E stained sections demonstrated mild glomerular hypertrophy and early mesangial expansion (Fig. 2). Group IV (Desloratadine-treated diabetic group, sacrificed on Day 1 of Week 4): H&E stained sections showed mild amelioration of glomerular hypertrophy, with near-normal mesangial appearance and preserved tubular structure (Fig. 3). Group V (STZ-induced diabetic group, sacrificed on Day 1 of Week 8): H&E stained sections revealed glomerular hypertrophy, marked mesangial expansion, prominent mononuclear cell infiltration, and glomerular basement membrane thickening (Fig. 4). Group VI (Desloratadine-treated diabetic group, sacrificed on Day 1 of Week 8): H&E stained sections displayed amelioration of glomerular hypertrophy, reduced mesangial expansion, and decreased mononuclear cell infiltration compared to Group V (Fig. 5). Group VII (STZ-induced diabetic group, sacrificed on Day 1 of Week 12): H&E stained sections exhibited severe mesangial expansion, podocyte loss and vacuolization, mononuclear cell infiltration, and pronounced glomerular basement membrane thickening (Fig. 6). Group VIII (Desloratadine-treated diabetic group, sacrificed on Day 1 of Week 12): H&E stained sections revealed notable amelioration of me1sangial expansion, improved podocyte morphology, and decreased mononuclear cell infiltration compared to Group VII (Fig. 7).

Table-I: *Comparison of blood glucose level among control and experimental groups of rats*

	Group II n=8 Mean±SD	Group III n=7 Mean±SD	Group IV n=8 Mean±SD	Group V n=8 Mean±SD	Group VI n=8 Mean±SD	Group VII n=8 Mean±SD	Group VIII n=7 Mean±SD
Blood glucose (mmol/L)	5.24±0.60	24.49±4.65	25.58±3.54	24.78±4.61	25.41±3.62	25.66±4.30	25.14±3.04
p-value	–	0.000^{a} 0.624^{x}	0.000^{b} -	0.000^{c} 0.763^{y}	0.000^{d} -	0.000^{e} 0.789^{z}	0.000^{f} -

Table-II: *Comparison of serum creatinine level (mg/dl) among STZ induced diabetic groups (Group III, Group V, Group VII) and control group (Group II) of rats*

	Group II n=8 Mean±SD	Group III n=7 Mean±SD	Group V n=8 Mean±SD	Group VII n=8 Mean±SD
Serum creatinine (mg/dl)	0.54±0.06	0.90±0.15	1.82±0.09	2.35±0.16
p-value	0.003[a]	0.000[b]	0.000[c]	0.000[x]0.000[y]

Table-III: *Comparison of serum creatinine level among STZ induced diabetic groups and concomitantly desloratadine treated groups*

	Group III n=7 Mean±SD	Group IV n=8 Mean±SD	Group V n=8 Mean±SD	Group VI n=8 Mean±SD	Group VII n=8 Mean±SD	Group VIII n=7 Mean±SD
Serum creatinine(mg/dl)	0.90±0.15	0.73±0.05	1.82±0.09	1.62±0.14	2.35±0.15	2.06±0.16
p-value	-	0.022[x]	-	0.005[y]	-	0.003[z]

Table-IV: *Comparison of renal tissue homogenate MDA and GSH concentration among STZ induced diabetic groups and control group of rats*

Variables	Group II n=8 Mean±SD	Group III n=7 Mean±SD	Group V n=8 Mean±SD	Group VII n=8 Mean±SD
MDA conc.(µmol/L)	0.84±0.11	1.83±0.34	2.82±0.31	4.06±0.21
p-value	0.001[a]	0.000[b]	0.000[c]	0.000[x]0.000[y]
GSH conc.(mg/ml)	3.33±0.18	2.23±0.20	1.60±0.15	1.16±0.16
p-value	0.001[a]	0.000[b]	0.000[c]	0.000[x]0.000[y]

Table-V: *Comparison of MDA and GSH concentration (µmol/L) among STZ induced diabetic groups and concomitantly desloratadine treated groups*

Variables	III n=7 Mean±SD	IV n=8 Mean±SD	V n=8 Mean±SD	VI n=8 Mean±SD	VII n=8 Mean±SD	VIII n=7 Mean±SD
MDA conc.(µmol/L)	1.83 ± 0.34	1.43±0.22	2.82±0.31	2.47±0.19	4.06±0.21	3.77±0.17
p value	-	0.025[x]	-	0.021[y]	-	0.011[z]
GSH conc.(mg/ml)	2.23±0.20	2.66±0.22	1.60±0.15	1.96±0.10	1.16±0.16	1.56±0.28
p value	-	0.002[x]	-	0.001[y]	-	0.008[z]

Table-VI: *Histopathology of renal tissue with qualitative changes and arbitrary score*

Variables	Group I n=8 Mean±SD	Group II n=8 Mean±SD	Group III n=7 Mean±SD	Group IV n=8 Mean±SD	Group V n=8 Mean±SD	Group VI n=8 Mean±SD	Group VII n=8 Mean±SD	Group VIII n=7 Mean±SD
Glomerular hypertrophy Mean±SD	0.00±0.00	0.00±0.00	0.86±0.38	0.38±0.52	2.38±0.52	1.00±0.54	3.13±0.35	1.29±0.49
p^Avalue	-	-	0.009[a]	0.058[b]	0.000[c]	0.001[d]	0.000[e]	0.000[f]
Mononuclear cell infiltration Mean±SD	0.00±0.00	0.00±0.00	0.43±0.54	0.00±0.00	0.75±0.46	0.25±0.46	1.5±0.54	0.57±0.53
p^B value	-	-	0.078[a]	0.078[b]	0.003[c]	0.049[d]	0.000[e]	0.005[f]
Podocyte injury Mean±SD	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.25±0.46	0.00±0.00	0.88±0.64	0.29±0.49
p^C value	-	-	-	-	0.170[c]	0.170[d]	0.006[e]	0.065[f]
Glomerular basement membrane thickening Mean±SD	0.63±0.52	1.88±0.84	0.71±0.49	0.00±0.00	0.00±0.00	0.43±0.54	0.00±0.00	1.13±0.64
p^D value	-	-	0.078[a]	0.078[b]	0.002[c]	0.110[d]	0.000[e]	0.007[f]
Mesangial cell expansion Mean±SD	0.00±0.00	0.00±0.00	0.71±0.49	0.13±0.35	1.13±0.64	0.50±0.54	1.88±0.35	0.86±0.38
p^E value	-	-	0.008[a]	0.023[b]	0.002[c]	0.053[d]	0.000[e]	0.001[f]
Nodular sclerosis Mean±SD	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00± 0.00	0.25±0.46	0.00± 0.00
p^F value	-	-	-	-	-	-	0.170[e]	0.170[f]

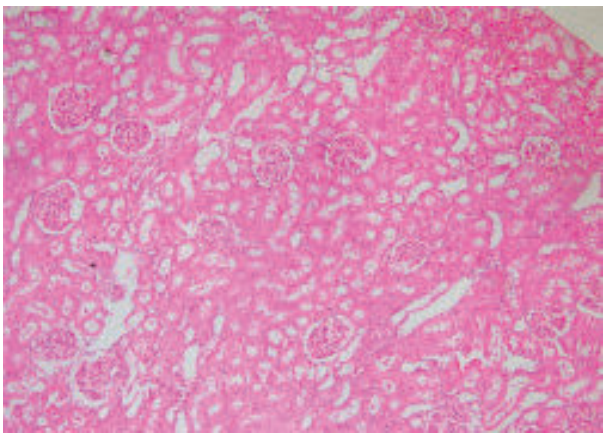

Fig. 1: *Histopathology slide showing normal histoarchitecture with well-defined glomeruli, intact renal tubules, and unremarkable interstitium (H&E stain; ×100).*

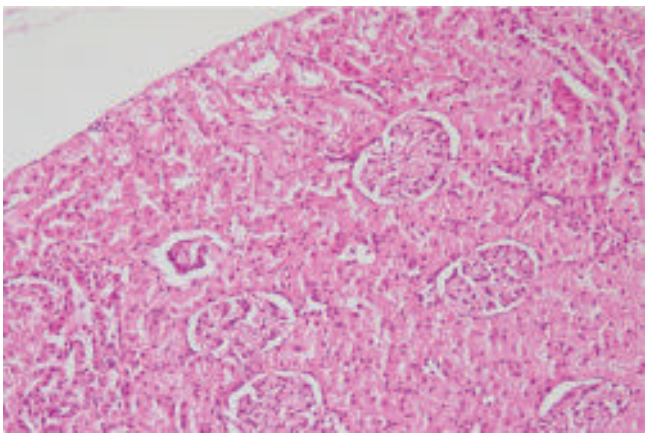

Fig. 2: *Histopathology slide showing mild glomerular hypertrophy and early mesangial expansion (H&E stain; ×100).*

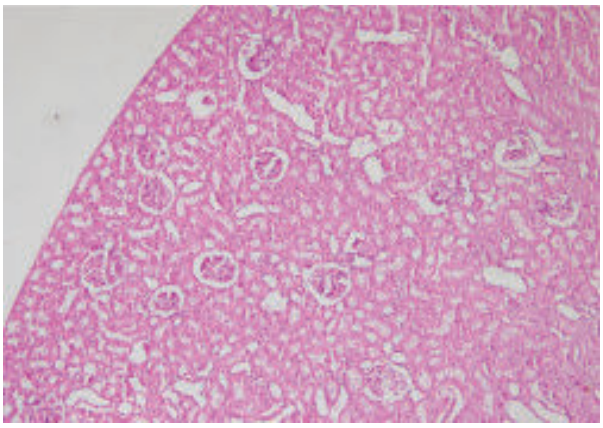

Fig. 3: *Histopathology slide showing mild amelioration of glomerular hypertrophy, with near-normal mesangial appearance and preserved tubular structure (H&E stain; ×100).*

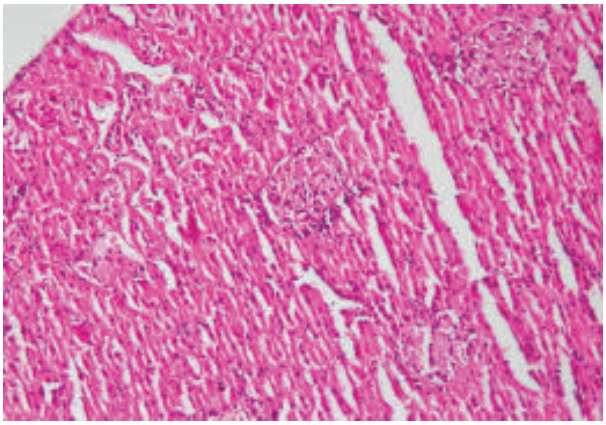

Fig. 6: *Histopathology slide showing severe mesangial expansion, podocyte loss and vacuolization, mononuclear cell infiltration, and pronounced glomerular basement membrane thickening (H&E stain; ×100).*

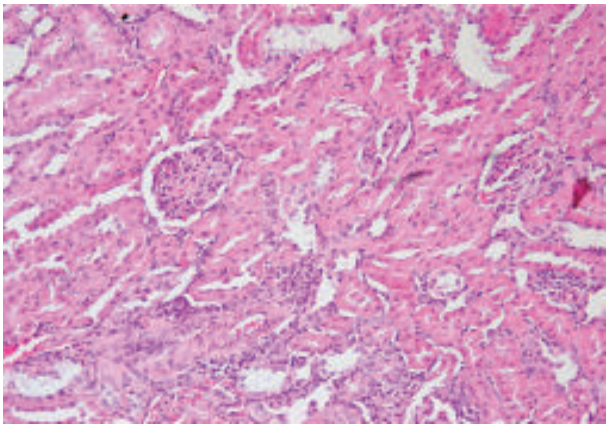

Fig. 4: *Histopathology slide showing glomerular hypertrophy, marked mesangial expansion, prominent mononuclear cell infiltration, and glomerular basement membrane thickening (H&E stain; ×100).*

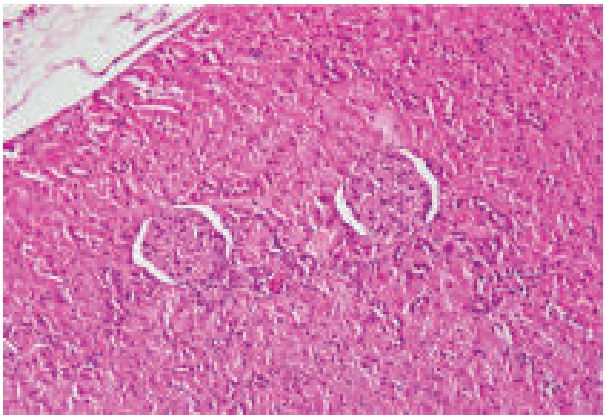

Fig. 7: *Histopathology slide showing notable amelioration of mesangial expansion, improved podocyte morphology, and decreased mononuclear cell infiltration (H&E stain; ×100).*

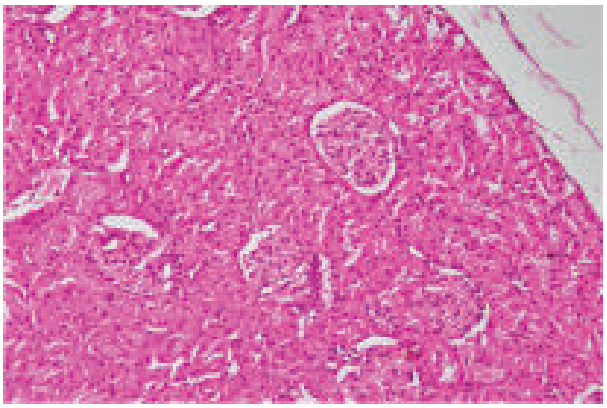

Fig. 5: *Histopathology slide showing amelioration of glomerular hypertrophy, reduced mesangial expansion, and decreased mononuclear cell infiltration (H&E stain; ×100).*

DISCUSSION

To our knowledge, this is the first study to investigate the potential renoprotective effects of desloratadine in a rat model of streptozotocin (STZ)-induced diabetic nephropathy (DN). The present findings demonstrate that desloratadine exerts beneficial effects across multiple stages of DN progression, possibly through its antioxidant mechanisms.STZ-induced diabetes in rats resulted in significant renal functional impairment, as evidenced by elevated serum creatinine levels. This aligns with previous reports indicating kidney dysfunction as a hallmark of DN. Treatment with desloratadine significantly attenuated serum creatinine elevation when administered both at the early stage of diabetes and at established DN stages, suggesting a protective

effect on renal function irrespective of treatment onset. While creatinine levels in treated groups remained higher than in normal controls, the consistent reduction observed supports a functional renoprotective role. These results are consistent with earlier studies where H1 receptor antagonists such as levocetirizine, cetirizine, and rupatadine also conferred renal protection in diabetic rats.[9,11] Oxidative stress is another central contributor to DN pathophysiology. Diabetic control rats showed significantly elevated malondialdehyde (MDA) levels and depleted reduced glutathione (GSH) content, indicating increased lipid peroxidation and compromised antioxidant defense. Desloratadine treatment significantly lowered MDA levels and restored GSH content, irrespective of treatment timing. These findings suggest that desloratadine mitigates oxidative damage, possibly via direct antioxidant activity or by reducing reactive oxygen species through inflammatory pathway modulation. Previous in vivo and in vitro studies support the antioxidant effects of desloratadine,[14,18] reinforcing its potential as a therapeutic agent in oxidative stress-related renal damage.Histopathological examination of renal tissue revealed structural abnormalities in diabetic control rats, which worsened with disease progression. Desloratadine-treated groups showed non-significant improvements in early intervention phases but demonstrated significant structural preservation when treatment was initiatedat the DN stage and continued for a longer duration. These histological improvements likely reflect the antioxidative actions of desloratadine. Notably, the renoprotective histological changes are consistent with findings from previous studies using other H1 receptor antagonists[9,11] and from desloratadine's effects in other organ systems subjected to ischemia-reperfusion injury.[15,16] Collectively, the current data provide compelling evidence that desloratadine confers renoprotection in STZ-induced DN, regardless of the stage at which treatment is initiated. Its capacity to modulate oxidative stress pathways may underlie these beneficial effects. However, it should be noted that while desloratadine ameliorated renal damage, it did not fully restore all parameters to baseline, suggesting a partial protective effect that might be enhanced through combination therapies or higher dosing strategies.

CONCLUSION

Our findings suggest that desloratadine holds promise as a novel therapeutic candidate for diabetic nephropathy. Its renoprotective effects, observed across various stages of disease progression, appear to be mediated through attenuation of oxidative stress. Further mechanistic studies and clinical investigations are needed to validate these preclinical findings and to explore desloratadine's potential as a pharmacological intervention for diabetic nephropathy.

Conflict of Interest: None declared.

Funding Statement: Self-funding.

Ethical Approval: Ethical approval was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh (Ref: BSMMU/2022/3780). All animal procedures adhered to the standard ethical guidelines on animal welfare and care and use of laboratory animals for research.[19,20]

Authors' Contribution: Concept and design of the study: S Aktar, MS Rahman; Data collection, compilation and analysis: S Aktar, IH Chowdhury, FH Mitu, S Sultana, SS Tania, M Tabassum; Manuscript preparation, review, editing and final submission: S Aktar, MS Rahman, IH Chowdhury, FH Mitu, S Sultana, SS Tania, M Tabassum.

REFERENCES

1. Keri KC, Samji NS, Blumenthal S. Diabetic nephropathy: newer therapeutic perspectives. J Community Hosp Intern Med Perspect. 2018 ;8(4):200-7.
2. Pini A, Grange C, Veglia E, Argenziano M, Cavalli R, Guasti D, et al. Histamine H4 receptor antagonism prevents the progression of diabetic nephropathy in male DBA2/J mice. Pharmacol Res. 2018;128:18-28.
3. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF Diabetes Atlas: Estimation of Global and Regional Gestational Diabetes Mellitus Prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes Res Clin Pract. 2022;183:109050.
4. Diabetes Canada Clinical Practice Guidelines Expert Committee; McFarlane P, Cherney D, Gilbert RE, Senior P. Chronic kidney disease in diabetes. Can J Diabetes. 2018;42(Suppl 1):S201-9.
5. Umanath K, Lewis JB. Update on diabetic nephropathy: core curriculum 2018. Am J Kidney Dis. 2018;71(6):884-95.
6. Matoba K, Takeda Y, Nagai Y, Yokota T, Utsunomiya K, Nishimura R. Targeting redox

imbalance as an approach for diabetic kidney disease. Biomedicines. 2020;8(2):40.

7. Pini A, Obara I, Battell E, Chazot PL, Rosa AC. Histamine in diabetes: is it time to reconsider? Pharmacol Res. 2016;111:316-24.

8. Veglia E, Grange C, Pini A, Moggio A, Lanzi C, Camussi G, et al. Histamine receptor expression in human renal tubules: a comparative pharmacological evaluation. Inflam Res. 2015;64(3):261-70.

9. Anbar HS, Shehatou GS, Suddek GM, Gameil NM. Comparison of the effects of levocetirizine and losartan on diabetic nephropathy and vascular dysfunction in streptozotocin-induced diabetic rats. Eur J Pharmacol. 2016;780:82-92.

10. Verta R, Grange C, Gurrieri M, Borga S, Nardini P, Argenziano M, et al. Effect of bilastineon diabetic nephropathy in DBA2/J mice. Int J Mol Sci. 2019;20(10):2554.

11. Hafez HM, Abdel-Hakeem EA, Hassanein H. Rupatadine, a dual antagonist of histamine and platelet-activating factor (PAF), attenuates experimentally induced diabetic nephropathy in rats. Naunyn Schmiedebergs Arch Pharmacol. 2020;393(8):1487-1500.

12. Chen M, Xu S, Zhou P, He G, Jie Q, Wu Y. Desloratadine citrate disodium injection, a potent histamine H1 receptor antagonist, inhibits chemokine production in ovalbumin-induced allergic rhinitis guinea pig model and histamine-induced human nasal epithelial cells via inhibiting the ERK1/2 and NF-kappa B signal cascades. Eur J Pharmacol. 2015;767:98-107.

13. Roumestan C, Henriquet C, Gougat C, Michel A, Bichon F, Portet K, et al. Histamine H1 receptor antagonists inhibit nuclear factor kappaB and activator protein 1 activities via H1 receptor dependent and independent mechanisms. Clin Exp Allergy. 2008;38(6):947-56.

14. Sadowska-Woda I, Bieszczad-Bedrejczuk E, Rachel M. Influence of desloratadine on selected oxidative stress markers in patients between 3 and 10 years of age with allergic perennial rhinitis. Eur J Pharmacol. 2010;640(1-3):197-201.

15. Kocaturk H, Bedir F, Altay MS, Bakan E, Suleyman B, Yazici GN, et al. The effect of desloratadine on ischemia reperfusion induced oxidative and inflammatory renal injury in rats. Ren Fail. 2020;42(1):531-8.

16. Kadýoglu BG, Gundogdu B, Kurt N, Suleyman H, Suleyman Z. Effect of desloratadine on oxidative and inflammatory ovarian ischemia-reperfusion injury in female rats: biochemical and histopathological evaluation. Anal Quant Cytopathol Histopathol. 2020;42(2):61-8.

17. Tesch GH, Allen TJ. Rodent models of streptozotocin-induced diabetic nephropathy. Nephrology (Carlton). 2007;12(3):261-6.

18. Tatar A, Parlak SN, Yayla M, Ugan RA, Polat E, Halici Z. Effects of allergic rhinitis and desloratadine on the submandibular gland in a rat allergy model. Int Forum Allergy Rhinol. 2015;5(12):1164-9.

19. Nurunnabi ASM, Afroz RD, Alam SN. Ethical debate on animal research. Bangladesh J Bioethics. 2013;4(3):11-8.

20. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals. 8th ed. Washington DC: National Academies Press; 2011.

Original Article

CD3+ Tumor Infiltrating Lymphocytes (TILs) in Gastric Adenocarcinoma

Tahira UQ[1], Ara J [2], Jakia SMN[3], Ahmed S[4], Rahman S[5], Fatema SK[6], Begum S[7]

ABSTRACT

Gastric cancer is the fifth most common cancer worldwide. Early and proper diagnosis and proper assessment of prognosis is one of the most important things for treatment response. The presence and activity of tumor-infiltrating lymphocytes (TILs) is a key parameter related to the antitumor immune response. The role of CD3+ TIL as a prognostic marker as well as the role in targeted immunotherapy has been studied in many cancers including adenocarcinoma of the stomach. A cross-sectional study was conducted in the Department of Pathology, Sir Salimullah Medical College, Dhaka, Bangladesh, from March 2022 to February 2024, to evaluate the expression of CD3+ tumor infiltrating lymphocytes in gastric adenocarcinoma and their association with histological grade and pathological stage. This. A total of 50 gastrectomy samples with histopathologically confirmed diagnosis of gastric adenocarcinoma were included in this study. The expression of CD3+ in TILs were evaluated in formalin-fixed and paraffin embedded specimens by immunohistochemistry. The CD3+ TILs were categorized as positive and negative expressions. The mean age of the participants was 54.98±12.10 years. Most of the tumors were located in the lesser curvature (34%), while most of the tumors were intestinal type (60%). On staging of tumors, 52% cases were in stage T3, followed by stage T1 (22%), stage T2 (14%) and stage T4 (12%). CD3+ intratumoral and stromal TIL expression was positive in 34(68%) and 28(56%) cases respectively. Significant association was found between intratumoral CD3+ TILs and tumor grade, pathological stage and nodal status ($p<0.05$). However, no association was observed between the stromal CD3+ TILs and tumor grade, pathological stage and nodal status ($p>0.05$). As part of tumor microenvironment, CD3+ TIL influence the progression and differentiation of gastric adenocarcinoma. These expression levels can be utilized as indicators of biological behavior and prognosis as well as in therapeutic purpose of gastric adenocarcinoma.

Keywords: *Adenocarcinoma, stomach cancer, tumor infiltrating lymphocytes, immunohistochemistry.*

Mugda Med Coll J. 2026; 9(1): 18-24
DOI: https://doi.org/10.3329/mumcj.v9i1.90803

1. Dr. Ummey Qoraiman Tahira, Lecturer, Department of Pathology, Manikganj Medical College, Manikganj-1800.
2. Dr. Jannat Ara, Lecturer, Department of Pathology, Patuakhali Medical College, Patuakhali-8600.
3. Dr. S.M.N. Jakia, Lecturer, Department of Microbiology, Sher-E-Bangla Medical College, Barishal-8200.
4. Dr. Shamim Ahmed, Assistant Professor, Department of Pathology, Brahmanbaria Medical College, Brahmanbaria-3400.
5. Dr. Sanjida Rahman, Curator, Department of Pathology, Uttara Adhunik Medical College, Uttara, Dhaka-1230.
6. Dr. Syeda Kaniz Fatema, Lecturer, Department of Pharmacology & Therapeutics, Mugda Medical College, Dhaka-1214. Email: kfatema416@gmail.com (Corresponding author)
7. Prof. Shahnaj Begum, Professor & Head, Department of Pathology, Sir Salimullah Medical College, Dhaka-1100.

INTRODUCTION

Gastric cancer is the seventh most common cancer worldwide and the fifth most frequently diagnosed.[1] Gastric adenocarcinoma is the term for cancer that develops in the stomach's epithelium lining. Over a million cases of gastric cancer are detected globally each year. Approximately 75.3% of gastric cancer cases in Asia.[2] The most common type of stomach cancer, adenocarcinoma, originates in the glandular tissue of the stomach and accounts for 90–95% of all stomach cancer cases. Stomach cancers are classified based on the type of tissue in which they originate.[3] It frequently involves a combination of environmental

and genetic factors, making it multifactorial. Diet, H. pylori and EBV infection, smoking, alcohol, prior stomach surgery, atrophic gastritis, bile reflux, radiation exposure, race, ethnicity, and other environmental variables are all linked to the development of gastric cancer.[4] Despite advancements in diagnosis and treatment, the prognosis for patients with gastric cancer remains poor, with 5-year overall survival rates ranging from 28% to 51%.[5] Recent research indicates that this aggressive behavior can be attributed to the immune system during the progression of the cancer and therapeutic interventions. Approximately 60% of patients with stomach cancer exhibit late-stage cancer diagnosis. Over 40% of patients who underwent curative resection experienced recurrence within 2 years after surgery.[6]

The "Cancer immune editing Theory" states that tumors develop as a result of immune system failure, which happens when tumor development and immune surveillance are out of balance.[7] Generally, there is a correlation between the infiltration of immune cells within a tumor and tumor development. Therefore, the distribution of various immune cell types detected in gastric carcinoma may provide helpful information for patient's progress.[8,9] Blood and lymphoid tissue contain lymphocytes, which are immune cell types produced in the bone marrow. Tumor-infiltrating lymphocytes are white blood cells that have moved from the circulation to a tumor. The term "tumor-infiltrating immune cells" refers to a broader category of immune cells that include T-cells, B-cells, natural killer cells, macrophages, neutrophils, dendritic cells, mast cells, eosinophils, basophils, and other immune cells in varying proportions. Their frequency fluctuates according to the type and stage of the tumor and occasionally correlates with the prognosis of the illness.[10] T-cells aid in immune response regulation and tumor cell destruction. The cell membrane of TILs contains a variety of distinct antigens, including CD3, CD4, CD8, FOXP3, CD20, and CD57. Typically, distinct cell surface antigens attach to particular lymphocyte types. For instance, T-cells are bound by CD3, CD4, CD8, and FOXP3. Consequently, TILs regulate the immune response linked to tumors in both directions. The majority of the infiltrating T-cells are lymphocytes that are CD3 and CD8 positive. In an immunocompetent host, they either create a tumor microenvironment that promotes tumor propagation or selectively protects tumor cell survival. They play a crucial role in inhibiting tumor growth by decreasing their outgrowth or destroying cancer cells.[7] All mature lymphocytes in the peripheral circulation, including CD4+ and CD8+ cells, are classified as CD3+ T lymphocytes. These cells provide a comprehensive picture of T lymphocytes, including all of its subgroups. Analyzing CD3+ TILs in tumors may help us understand the overall T cell composition of the host immune response and tumor microenvironment.[11] The existence of tumor-infiltrating T-cell, cytotoxic T-cells has been linked to a survival advantage. Various studies demonstrate that high numbers of CD3+ T-cells in tumor are significantly associated with lower frequencies of lymph node metastasis or disease recurrence or longer survival.[12,13] Therefore, the immune response to gastric cancer may serve as a novel prognostic and therapeutic marker. This study aimed to evaluate CD3 expression in the tumor infiltrating lymphocytes in gastric adenocarcinoma specimens and to find out its association with histological grade and pathological stage.

METHODS

This cross-sectional study was conducted between March 2022 and February 2024. We studied on a total of 50 specimens. Thirty-five cases were fresh resected specimens and rest of the fifteen cases were paraffin blocks of resected and diagnosed cases of primary gastric adenocarcinoma, which were collected from the Department of Pathology of Sir Salimullah Medical College and Bangabandhu Sheikh Mujib Medical Univerity, Dhaka, Bangladesh. The patients were enrolled according to patients of any age group with histopathologically diagnosed cases of gastric adenocarcinoma. Patients having prior radiotherapy or chemotherapy or both, inadequate formalin fixed and paraffin embedded (FFPE) tissue block, poorly preserved sample, patients having secondary metastasis of stomach and tumors other than adenocarcinoma were excluded from this study. Data was collected in approved data collection form and privacy of the patient's was maintained. All the cases were numbered chronologically and the same number was

given to histopathological as well as in immunohistochemical slides. After receiving fresh samples (partial and total gastrectomy), gross examination was done as per standard procedure.

All the tissues were submitted for routine processing, paraffin embedding and the blocks were sectioned in 3-4 micrometer thickness and finally slides were stained with routine Hematoxylin & Eosin (H&E) stain. All the slides were thoroughly evaluated by microscopic examination and grading and staging were done. The collected paraffin blocks of fifteen cases were given re-cut and subsequent staining was done. Relevant information was collected from previous reports. After following standard protocols two slides were made from each tumor block. One slide was stained with Hematoxylin & Eosin (H&E) stain for reviewing the diagnosis and grading, while another one was used for immunohistochemical analysis with CD3+ immuno-marker.

For immunohistochemistry, 3-4 micrometer sections of formalin-fixed, paraffin embedded tissues were mounted on poly-L-lysine coated slides. The sections were deparaffinized in xylene and rehydrated in a descending ethanol series. Sections were incubated for five minutes in 3% hydrogen peroxide to block endogenous tissue peroxidase. The sections were incubated with primary antibodies against CD3+ in appropriate dilutions. Mouse anti-human monoclonal primary antibodies against the said antigens were used. Standard immunohistochemical method was applied for subsequent staining. For visualizing the section, DAKO En Vision+ HRP (Horseradish peroxidase) system was used. Each assay included a positive control slide. Polyclonal Rabbit Anti-Human CD3+ (1:100, Code A0452, Dako Cytomation, Glostrup, Denmark) was used as primary antibody. Secondary antibody used as with DAKO REALTM En Vision TM (HRP RABBIT/MOUSE). An acute appendicitis specimen with positive lymphocytes was taken as a positive control. After that immunostained sections of CD3+was examined under light microscope. Immunopositively cells are defined as those showing partial or complete staining within the cytoplasm and/or plasma-membrane. The semi quantitative immunohistochemical grading of CD3+ TILs were determined by high power microscopy. Five fields of view with the most abundant lymphocyte infiltration area was selected by the "hot spot" method.

The percentage of CD3+ positive T-cells among total lymphocytes were calculated. The average values of five fields were taken as the density (%) of CD3+ TILs. Percentage of immunopositively cells among total cells was calculated as: 1=<1% of cells; 2=1–10% of cells; 3=11–33% of cells; 4=34–66% of cells; and 5=67–100% of cells. Then, intensity score was estimated as: 0 =negative/no staining;1+ =mild; 2+ =moderate; and 3+ =intense. Finally, scores (ranging from 1 to 8) were calculated by adding the percentage positivity scores and the intensity scores for each section. The cases were divided into two groups using the median value, with negative or positive CD3+ expression.[13] Final score was calculated as: ≥ Median value (positive) = CD3+intra tumoral ≥5 (positive); stromal ≥6 (positive); and <Median value (negative) = CD3+intra tumoral <5 (negative); stromal <6 (negative).

Tumor staging was done was using TNM classification of gastric adenocarcinoma according to the American Joint Committee of Cancer (AJCC). Tumors were observe both for the depth of invasion of primary tumor (pT) and the involvement of regional lymph nodes by the tumor (pN).[14]

Statistical analysis was conducted using Statistical Package for Social Sciences version 28.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables were expressed as frequency (percentile). Continuous variables were expressed as mean±SD and range. The association of CD3+ tumor infiltrating lymphocytes with histological grade, stage and nodal status were evaluated using Chi-square test. A p-value ≤0.05 was considered statistically significant. Results were presented in the tabulated form.

RESULTS

Out of total 50 cases, the majority of the cases belonged to the age group of 50–59 years (32%) and 60–69 years (22%). The mean age was 54.98±12.10 years (Table-I). Most of the tumors were located in the lesser curvature 17(34%), followed by antrum 12(24%), body and greater curvature 6(12%) each, pylorus 5(10%) and fundus 4(8%). Most of the tumors were intestinal type 30(60%), followed by diffuse type 17(34%), mucinous type 3(6%). Regarding the staging of tumors, 26(52%) cases were in stage T3, followed by stage T1 11(22%),

stage T2 7(14%) and stage T4 6(12%) cases (Table-II). A significant association was found between intra tumoral CD3+ TILs and tumor grade (p=0.031), pathological stage (p=0.049) and nodal status (p=0.049). However, no significant association was seen between the stromal CD3+ TILs and tumor grade (p=0.145), pathological stage (p=0.085) and nodal status (p=0.826) (Table-III).

Table-I: *Distribution of the study subjects by age group (N=50)*

Age group (in years)	Frequency	Percentage
20–29	1	2.0
30–39	4	8.0
40–49	9	18.0
50–59	16	32.0
60–69	11	22.0
≥70	9	18.0

Mean±SD = 54.98±12.10 years
Range (Min–Max) (24–76 years)

Table-II : *Distribution of study subjects based tumor characteristics (N=50)*

Variables	Frequency	Percentage
Location of the tumor		
Fundus	4	8
Body	6	12
Greater curvature	6	12
Lesser curvature	17	34
Antrum	12	24
Pylorus	5	10
Histological types		
Intestinal	30	60
Diffuse	17	34
Mucinous	3	6
Pathological stage		
T1	11	22
T2	7	14
T3	26	52
T4	6	12

Table-III : Comparison between CD3+TILs distribution within intratumoral and stromal compartments

Variables	CD3+ Intratumoral TILs		p-value	CD3+ stromal TILs		p-value
	Positive	Negative		Positive	Negative	
Histological Grade						
G-I	3 (33.3%)	6 (66.7%)	0.031^{S}	3 (33.3%)	6 (66.7%)	0.145^{NS}
G-II	16 (69.6%)	7 (30.4%)		16 (69.6%)	7 (30.4%)	
G-III	15 (83.3%)	3 (16.7%)		9 (50%)	9 (50%)	
Pathological Stage						
T1 T2	6 (17.6%)	5 (31.3%)	0.049^{S}	6 (54.5%)	5 (45.5%)	0.085^{NS}
T3	4 (11.8%)	3 (18.8%)		7 (100%)	-	
T4	19 (55.9%)	7 (43.8%)		12 (46.2%)	14 (53.8%)	
	5 (14.7%)	1 (6.3%)		3 (50%)	3 (50%)	
Nodal involvement						
Present	25 (69.4%)	11 (30.5%)	0.049^{S}	20 (55.5%)	16 (44.5%)	0.826^{NS}
Absent	9 (71.4%)	5 (30.4%)		8 (57.1%)	6 (42.9%)	

Chi-square test was applied to reach p-value; S=significant, NS=not significant.

DISCUSSION

Gastric cancer is the fifth most commonly diagnosed malignancy and the third leading cause of cancer related mortality worldwide[15]. In this study, the ages of patients ranging from 24 to 76 years (mean age was 54.98±12.10 years), and we observed that 32% of patients were in the 50–59 years age group. These results are in congruence with another Indian study

done by Pramanik et al.,[16] as they found the mean age of gastric carcinoma patients 55.3±12.71 years, with age group ranged from 20 to 81 years. It is also consistent with the study of Abdel-Aziz et al.,[17] in which it was found that patient age ranged from 27 to 75 years and mean age was 54.04±11.98 years. Another study by Saeed & Saeed[18] reported that the mean age was 54 years and ranged between (30–72) years. Among the present study cases, 60% of gastric adenocarcinoma were intestinal type. Rest were diffuse type (34%) and mucinous type (6%). It aligns with the results of Abel-Aziz et al.,[17] which showed that among 32 cases of gastric adenocarcinoma 66.7% were intestinal subtype and 29.2% were diffuse subtype. However, our findings slightly differ with the findings of Kang et al.,[19] where the most common type of gastric adenocarcinoma was diffuse type (70%).

In the present study, most of the tumor located along the lesser curvature of the stomach 17(34%), followed by antrum 12(24%), body and greater curvature 6(12%) cases each, pylorus 5(10%) and fundus 4(8%). However, those findings are different from the findings of Kang et al.,[19] as they found that the most common site was the body of the stomach (74.2%). In our study, 26(52%) patients were in stage T3. Stage T1 comprised 11(22%) cases, stage T2 7(14%) cases and stage T4 were found in 6(12%) cases. It matches the results of Lu et al.,[13] as they found that most of the cases were in the stage 3 (50%).

We observed that 34(68%) cases were positive for intra tumoral CD3+ TILs and 16 (32%) were negative for intra tumoral CD3+ TILs. Whereas 28(56%) cases were positive for stromal CD3+ TILs and 22 (44%) were negative for stromal CD3+ TILs. This finding is in congruence with the results of Saeed & Saeed, as they found positive results for CD3 in 28(60.86%) out of 43 samples. Our results are also comparable to that of with Kang et al.,[19] where stromal TILs were positive in 60.83% cases and intra tumoral TILs were positive in 50% cases. Similar results were reported by Kim et al.[20] and Ishigami et al.[21] as they found higher levels of CD3 expressions in gastric cancer samples.

In search of the association of intra tumoral CD3+ TILs with histopathological grades of gastric adenocarcinoma, we observed that intratumoral CD3+ TILs positivity was mostly found in grade 3 tumors (83.3%) cases. Grade 2 tumors showed intra tumoral CD3+ TILs positivity in 69.6% cases and grade 1 tumors showed intratumoral CD3+ TILs positivity in 33.3% cases, which was statistically significant ($p<0.05$). Moreover, stromal CD3+ TILs positivity was mostly found in grade 2 tumors (69.6%). Grade 3 tumors showed stromal CD3+ TILs positivity in 50% cases and grade 1 tumors showed stromal CD3+ TILs positivity in 33.3% cases; however, the difference was not statistically significant ($p>0.05$). Similar results were found by Saeed & Saeed,[18] where CD3+ TILs were mostly positive in grade 3 tumors (50%), followed by grade 1 (35.71%) and grade 3 (14.29%). When considering the association of CD3+ TILs with pathological stage of gastric adenocarcinoma, we found that intratumoral CD3+ TILs positivity was mostly found in stage T3 tumors (55.9%), followed by stage T1 tumors in (17.6%), stage T4 tumors (14.7%) and stage T2 tumors (11.8%); the difference was statistically significant ($p<0.05$). Nonetheless, stromal CD3+ TILs positivity was mostly found in stage T2 tumors (100%), followed by stage T1 tumors (54.5%), stage T4 tumors (50.0%) and stage T3 tumors (46.2%); the difference was not statistically significant ($p>0.05$). Our findings are closely related to the findings of Saeed & Saeed,[18] where 71.43% CD3+ TILs positive tumors were in stage I–II and 28.57% were in stage III–IV. When assessing the association of nodal positivity with CD3+ TILs, we found that intra tumoral CD3+ TILs positivity was found mostly in the patients with no nodal involvement (71.4%) and intratumoral CD3+ TILs was positive in 69.4% of patients with lymph node involvement; the differences were statistically significant ($p<0.05$). Similar results were found regarding stromal TILs, as stromal CD3+ TILs positivity was found in 57.1% cases with no nodal involvement, while stromal CD3+ TILs were positive in 55.5% of the node involved cases; however, the difference was not statistically significant ($p>0.05$). Our findings are similar to that of Kang et al.,[19] as they observed both stromal and intratumoral TILs were mostly positive in the cases without lymph node involvement (83.3% and 79.5% cases respectively).

CONCLUSION

Our data suggests that expression of intratumoral CD3+ TILs is associated with tumor grade, pathological stage and nodal status of the patients. Such expression levels can be utilized as indicators of biological behavior and prognosis as well as in therapeutic purpose of gastric adenocarcinoma. To conclude, immunophenotyping and evaluation of TILs subsets might be considered as a valuable supplementary tool for predicting prognosis of

patients and further management by application of immunotherapy.

Conflict of Interest: Nothing to disclose.

Funding Source: Self-funded.

Ethical Clearance: This study was approved by the Institutional Ethics Committee of Sir Salimullah Medical College, Dhaka, Bangladesh.

Authors' Contribution: Concept and design: UQ Tahira, S Begum; Specimen collection and experiment: UQ Tahira, J Ara, S Ahmed, S Rahman; Data collection, compilation and analysis: UQ Tahira, J Ara, SMN Jakia, S Ahmed, S Rahman; Manuscript preparation, critical review, editing and final submission: UQ Tahira, J Ara, SMN Jakia, S Ahmed, S Rahman, SK Fatema, S Begum.

REFERENCES

1. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. Prz Gastroenterol. 2019;14(1):26-38.
2. World Health Organization (WHO). International Agency for Research on Cancer. Global Cancer Observatory (GCO). Bangladesh Fact Sheet 2022. Retrieved from: https://gco.iarc.who.int/media/globocan/factsheets/populations/50-bangladesh-fact-sheet.pdf (Accessed February 16, 2023).
3. Grantham T, Ramachandran R, Parvataneni S, Budh D, Gollapalli S, Gaduputi V. Epidemiology of gastric cancer: global trends, risk factors and premalignant conditions. J Community Hosp Intern Med Perspect. 2023;13(6):100-6.
4. Bertuccio P, Chatenoud L, Levi F, Praud D, Ferlay J, Negri E, et al. Recent patterns in gastric cancer: a global overview. Int J Cancer. 2009;125(3):666-73.
5. Tian C, Jing H, Wang C, Wang W, Cui Y, Chen J, et al. Prognostic role of tumour-infiltrating lymphocytes assessed by H&E-stained section in gastric cancer: a systematic review and meta-analysis. BMJ Open. 2021;11(1):e044163.
6. Curiel TJ, Coukos G, Zou L, Alvarez X, Cheng P, Mottram P, et al. Specific recruitment of regulatory T cells in ovarian carcinoma fosters immune privilege and predicts reduced survival. Nat Med. 2004;10(9):942-9.
7. Schreiber RD, Old LJ, Smyth MJ. Cancer immunoediting: integrating immunity's roles in cancer suppression and promotion. Science. 2011;331(6024):1565-70.
8. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
9. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. 2010;60(5):277-300.
10. Gentles AJ, Newman AM, Liu CL, Bratman SV, Feng W, Kim D, et al. The prognostic landscape of genes and infiltrating immune cells across human cancers. Nat Med. 2015;21(8):938-45.
11. Taube JM, Galon J, Sholl LM, Rodig SJ, Cottrell TR, Giraldo NA, et al. Implications of the tumor immune microenvironment for staging and therapeutics. Mod Pathol. 2018;31(2):214-34.
12. Lee K, Hwang H, Nam KT. Immune response and the tumor microenvironment: how they communicate to regulate gastric cancer. Gut Liver. 2014;8(2):131-9.
13. Lu J, Xu Y, Wu Y, Huang XY, Xie JW, Wang JB, et al. Tumor-infiltrating CD8+ T cells combined with tumor-associated CD68+ macrophages predict postoperative prognosis and adjuvant chemotherapy benefit in resected gastric cancer. BMC Cancer. 2019;19(1):920.
14. Rice TW, Rusch VW, Ishwaran H, Blackstone EH; Worldwide Esophageal Cancer Collaboration. Cancer of the esophagus and esophagogastric junction: data-driven staging for the seventh edition of the American Joint Committee on Cancer/International Union Against Cancer Cancer Staging Manuals. Cancer. 2010;116(16):3763-73.
15. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.
16. Pramanik P, Sarkar R, Maity M. Study of HER2/neu and ki-67 expression in gastric and esophagogastric junction adenocarcinoma and their correlation with grade and stage. Int J Sci Res. 2020;9(2):1617.
17. Abdel-Aziz A, Ahmed RA, Ibrahiem AT. Expression of pRb, Ki67 and HER 2/neu in gastric carcinomas: Relation to different histopathological grades and stages. Ann Diagn Pathol. 2017;30:1-7.
18. Saeed NAAAH, Saeed HA. Correlation between lymphocytes CD3, CD8 in patients with gastric

adenocarcinoma by using Immunohistochemical assay. Al-Mustansiriyah J Sci. 2013;24(2):31-38.

19. Kang BW, Seo AN, Yoon S, Bae HI, Jeon SW, Kwon OK, et al. Prognostic value of tumor-infiltrating lymphocytes in Epstein-Barr virus-associated gastric cancer. Ann Oncol. 2016;27(3):494-501.

20. Kim CW, Choi SH, Chung EJ, Lee MJ, Byun EK, Ryu MH, et al. Alteration of signal-transducing molecules and phenotypical characteristics in peripheral blood lymphocytes from gastric carcinoma patients. Pathobiology. 1999;67(3): 123-8.

21. Ishigami S, Natsugoe S, Miyazono F, Tokuda K, Nakajo A, Matsumoto M, et al. CD3 zeta expression of regional lymph node and peripheral blood lymphocytes in gastric cancer. Anticancer Res. 2004;24(3b):2123-6.

Original Article

Evaluation of Computed Tomography Scans of Neck Masses and Their Histopathological Correlation

Ahmed L[1], Rayhan MF[2], Ahmed M[3], Yasmin MS[4], Gaffar F[5], Al Mamun MA[6]

ABSTRACT

A cross-sectional, comparative study was conducted in the Department of Radiology & Imaging, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh, between July and December of 2019, to assess the diagnostic usefulness of multi-detector computed tomography scans in the evaluation of neck mass by comparing with histopathological reports. A total of 40 patients were enrolled in the study. All relevant data was collected from history sheet of the patients and investigation reports. Computed Tomography findings and histopathological diagnosis were recorded in a pre-designed structured data collection sheet. Then histopathology reports were compared with computed tomography (CT) scan findings. The most common age group was 40-70 years (45%), followed by 15-40 years (35%) and <15 years (12.5%). A male predominance was observed with male-female ratio of 2.33:1. Based on CT scans, 14 patients were diagnosed as benign lesions such as thyroglossal duct cyst 1case, abscess 2 cases, tubercular lymphadenopathy 2 cases, reactive lymphadenopathy 1 case, multinodular goiter 3 cases, thyroid cyst 1 case, hemangioma 1 case, pleomorphic adenoma 2 cases and carotid body tumor 1 case. The rest 26 cases were diagnosed as malignant: carcinoma larynx 5 cases, metastatic lymphadenopathy 3 cases, carcinoma thyroid 2 cases, parotid carcinoma 3 cases, submandibular gland malignant tumor 1 case, carcinoma tonsil 2 cases, nasopharyngeal carcinoma 4 cases, hypopharyngeal carcinoma 1 case, carcinoma base of tongue 2 cases and lymphoma 3 cases. Based on histopathology reports, 13 patients were diagnosed as having benign pathology like thyroglossal duct cyst 1case, abscess 3 cases, tubercular lymphadenopathy 2 cases, reactive lymphadenopathy 1 case, multinodular goiter 2 cases, thyroid cyst 1 case, pleomorphic adenoma 2 cases and carotid body tumor 1 cases. Remaining 27 cases were diagnosed as malignant which included carcinoma larynx 5 cases, metastatic lymphadenopathy 4 cases, carcinoma thyroid 2 cases, parotid carcinoma 3 cases, submandibular gland malignant tumor 1 case, carcinoma tonsil 2 cases, nasopharyngeal carcinoma 4 cases, hypopharyngeal carcinoma 1 case, carcinoma base of the tongue 2 cases and lymphoma 3 cases The present study showed that CT scans were significantly precise to differentiate between benign and malignant neck masses with 92.6% sensitivity, 92.3% specificity and 92.5% diagnostic accuracy. Our study demonstrated that computed tomography scan proved to be a useful tool for assessing and characterization of neck mass as either benign or malignant.

Keywords: *Neck mass, computed tomography scan, histopathology, malignancy.*

Mugda Med Coll J. 2026; 9(1): 25-30
DOI: https://doi.org/10.3329/mumcj.v9i1.90804

INTRODUCTION

The head and neck possess a complex anatomy and contains many small anatomic structures that are closely spaced.[1] This necessitates a thorough understanding of normal spatial relationships and anatomical variants for the diagnosis of lesions. Cancer of the head and neck, which includes cancers of the larynx, nasal passages and nose, oral cavity, pharynx, salivary glands, buccal regions, and thyroid, is the sixth most frequent cancer worldwide.[1] A mass

1. Dr. Luna Ahmed, Junior Consultant, Department of Radiology & Imaging, Shaheed Suhrawardy Medical College Hospital, Dhaka-1207. Email: lunaahmed57@gmail.com (Corresponding author)
2. Dr. Md. Ferdoush Rayhan, Junior Consultant, Department of Surgery, Manikganj 250 Bed District Hospital, Manikganj-1800.
3. Dr. Mina Ahmed, Assistant Professor, Department of Surgery, Chattogram Medical College & Hospital, Chattogram-4203.
4. Dr. Mst. Sabina Yasmin, Assistant Registrar, Department of Radiology & Imaging, National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR), Dhaka-1207.
5. Dr. Faria Gaffar, Radiologist, Department of Radiology & Imaging, Government Homoeopathic Medical College Hospital, Mirpur-14, Dhaka-1206.
6. Dr. Md. Abdullah Al Mamun, Associate Professor, Department of ENT & Head-Neck Surgery, Mugda Medical College Hospital, Dhaka-1214.

in the neck is a common clinical problem that presents in patients of all ages. With regard to age, the neck masses were classified into three groups: paediatric (≤15 years old), young adults (16–40 years of age), and older adults (≥40 years old).[2]

Application of computed tomography (CT) scans in the evaluation of neck masses has gained popularity in different clinical settings. Provision of better visualization using computed tomography (CT) helps clinicians with key information relating to both diagnosis and prognosis and ensures improved management in modern medicine.[3] It is currently recognized as one of the most powerful and versatile imaging procedure for the evaluation of neck masses.[3,4] Spiral computed tomography or multidetector computed tomography (MDCT) permits the rapid scanning of large volumes of tissue during quiet respiration and it is less susceptible to patient motion when compared to the conventional computed tomography.[5,6] Volumetric helical data permits the optimal multiplanar and 3D reconstructions. Spiral-CT is standard one for imaging neck tumours. Secondary coronal reconstructions of axial scans are very helpful in the evaluation of the crossing of the midline by small tumors of the palate or tongue base. Multislice spiral CT allows almost isotropic imaging of the head and neck region and also improves the assessment of tumor spread and lymph node metastases in arbitrary oblique planes. Multislice CT scan has a special feature in defining the critical relationships of tumor and lymph nodes metastases and for functional imaging of the hypopharynx and larynx, not only in the transverse plane but also in the coronal plane.[5,6]

In the last decade, along with other malignancies the prevalence of head-neck malignancy has increased much in our country, as we observed in our day to day practice. However, at the same time, diagnostic modalities for the diagnosis of neck mass lesions have been advanced all over the world. Considering the low-economic condition of the vast majority of our population we must design some diagnostic procedures that would be very accurate in differentiating between benign and malignant as well as affordable. Computed tomography (CT) Scan is often the first-line imaging tool used as it is readily available, relatively cheaper than magnetic resonance imaging (MRI) and is rapidly acquired.[3,7] Therefore, we proposed this study to evaluate neck masses using CT scans and compare to histopathological diagnosis (as gold standard), which would determine the efficacy of CT scans in such lesions. The results will help our radiologists especially who are working in the oncoradiology units gain more information and confidence in early detection and management of neck mass lesions.

METHODS

This cross-sectional, comparative study was conducted in the Department of Radiology & Imaging of Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh, between July and December of 2019. All the patients with clinically suspicious neck masses who underwent computed tomography (CT) scan followed by a biopsy and histopathological examination by biopsy were our study population. For sample size estimation, we considered that head and neck cancer was 3% among the total cancer cases in the UK in 2014. In adults, however, a malignant tumor may be expected in more than 50% cases. Considering such incidence rate of neck mass 50% with 5% significance level and 5% marginal error, our sample size was estimated 42.6.[8] However, we adopted a convenience sampling technique. We included all the patients with clinically suspected neck masses who underwent multidetector computed tomography (CT) scans and surgical biopsy for histopathological examination (within the study period). However, patients who did not give consent, or unable to undergo computed tomography scanning (e.g., pregnancy, hypersensitivity to contrast medium) and sugical biopsy were excluded from the study. Finally, a total of 40 patients were enrolled in the study.

The study was performed with 16 slice multidetector CT scanner (TOSHIBA, Activion 16, made in Japan). After taking axial pre-contrast scan, post-contrast scanning was done. Contrast agent was a non-ionic iodinated compound named iopamiro 370 given at a dose of 1ml/kg body weight. Arterial phase starts 20-35 sec. after the start of injection of contrast medium and venous phase starts 70-80 sec. after injection and delayed phase was at about 1 to 3 minutes. These three phases were evaluated according to the lesions.[1,9]

CT criteria of benign lesions: These were characterized by: i) the presence of a well defined margin, ii) a density less than that of muscle, iii) coarse globular or rim like calcification, iv) displaced but maintained

fat plane and v) homogenous contrast on post-contrast studies.

CT criteria of inflammatory lesions (benign): These were characterized by: i) ill defined margin, ii) a density less than that of muscle, iii) presence of necrosis, iv) perilesional blurred fat plane, v) heterogeneous or peripheral thick rim enhancement and vi) lymphadenopathy with benign criteria enlarged size (>1cm) but oval contour, presence of hilum, well defined margins with no infiltration of surrounding structures, no loss of fat planes and usually no necrosis.

CT criteria of malignant lesion: These were characterized by: i) an ill-defined margin, ii) a density equal to or more than that of muscle, iii) presence of necrosis, iv) blurring of fat plane, v) eterogeneous enhancement, and vi) lymphadenopathy with malignant criteria like enlarged size (>1cm), rounded contour, absence of hilum, eccentric cortical thickening, necrosis, ill-defined margins with infiltration of surrounding structures and loss of fat planes and infiltration into surrounding tissue and bones or cartilage erosion.

Postoperative resected tissues were examined histopathologically in the Department of Pathology of the same institution. Relevant data was collected from history sheet of the patients and investigation reports. Computed Tomography findings and histopathological diagnosis were recorded in a pre-designed structured data collection sheet. Then the histopathology reports were compared with computed tomography (CT) scan findings.

Collected data was scrutinized, compiled, coded and entered into the computer. Statistical analysis was done by using MS-Excel sheet. Then data was presented as frequency and percentages. For the validity of study outcome, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CT scans in the diagnosis of neck masses were estimated after confirmation of diagnosis by histopathology reports accordingly.

RESULTS

A total of 40 patients with neck masses were included in this study. Among them, 5 patients were below 15 years (12.5%), 14(35%) belonged to the 15-40 years age group, 18(45%) were in the 40-70 years age group, and 3(7.5%) aged >70 years. A male predominance was observed (male-female ratio was 2.33:1) (Table-I). Based on CT scans, 14 patients were diagnosed as benign lesions such as thyroglossal duct cyst 1case, abscess 2 cases, tubercular lymphadenopathy 2 cases, reactive lymphadenopathy 1 case, multinodular goiter 3 cases, thyroid cyst 1 case, hemangioma 1 case, pleomorphic adenoma 2 cases and carotid body tumor 1 case. The rest 26 cases were diagnosed as malignant: carcinoma larynx 5 cases, metastatic lymphadenopathy 3 cases, carcinoma thyroid 2 cases, parotid carcinoma 3 cases, submandibular gland malignant tumor 1 case, carcinoma tonsil 2 cases, nasopharyngeal carcinoma 4 cases, hypopharyngeal carcinoma 1 case, carcinoma base of tongue 2 cases and lymphoma 3 cases (Table-II, Fig.1-3). Based on histopathology reports, 13 patients were diagnosed as having benign pathology like thyroglossal duct cyst 1case, abscess 3 cases, tubercular lymphadenopathy 2 cases, reactive lymphadenopathy 1 case, multinodular goiter 2 cases, thyroid cyst 1 case, pleomorphic adenoma 2 cases and carotid body tumor 1 cases. Remaining 27 cases were diagnosed as malignant which included carcinoma larynx 5 cases, metastatic lymphadenopathy 4 cases, carcinoma thyroid 2 cases, parotid carcinoma 3 cases, submandibular gland malignant tumor 1 case, carcinoma tonsil 2 cases, nasopharyngeal carcinoma 4 cases, hypopharyngeal carcinoma 1 case, carcinoma base of the tongue 2 cases and lymphoma 3 cases (Table-III). The sensitivity of CT scan to evaluate neck masses was found 92.6% and specificity was 92.3%. Diagnostic Accuracy was found 92.5%, whereas positive predictive value was 96.2% and negative predictive value was 85.7% (as estimated from Table-IV).

Table-I: *Age and sex distribution of the patients (N=40)*

Variables	Frequency	Percentage
Age group (in years)		
<15	5	12.5
15-40	14	35.0
40-70	18	45.0
>70	3	7.5
Sex		
Male	28	70.0
Female	12	30.0

Table-II: *Diagnosis of neck masses based on CT scans (N=40)*

Findings	Frequency	Percentage
Benign (n= 14)		
Thyroglossal duct cyst	1	2.5
Abscess	2	5
Tubercular lymphadenopathy	2	5
Reactive lymphadenopathy	1	2.5
Multinodular goiter	3	7.5
Thyroid cyst	1	2.5
Hemangioma	1	2.5
Pleomorphic adenoma	2	5
Carotid body tumor	1	2.5
Malignant (n=26)		
Carcinoma larynx	5	12.5
Metastatic lymphadenopathy	3	7.5
Carcinoma thyroid	2	5
Parotid carcinoma	3	7.5
Submandibular gland malignant tumor	1	2.5
Carcinoma tonsil	2	5
Nasopharyngeal carcinoma	4	10
Hypopharyngeal carcinoma	1	2.5
Carcinoma base of tongue	2	5
Lymphoma	3	7.5

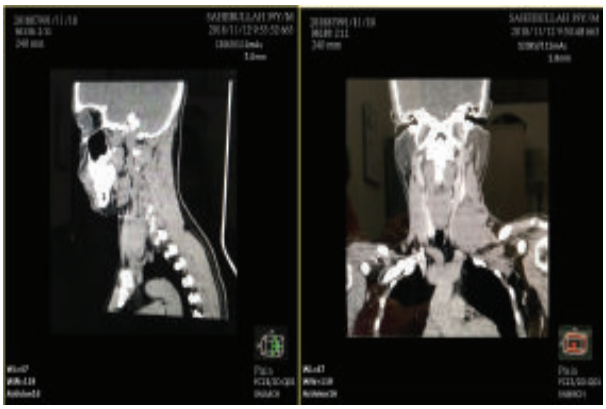

Fig. 1: *Post-contrast sagittal and coronal CT scans showing left cervical lymphadenopathy.*

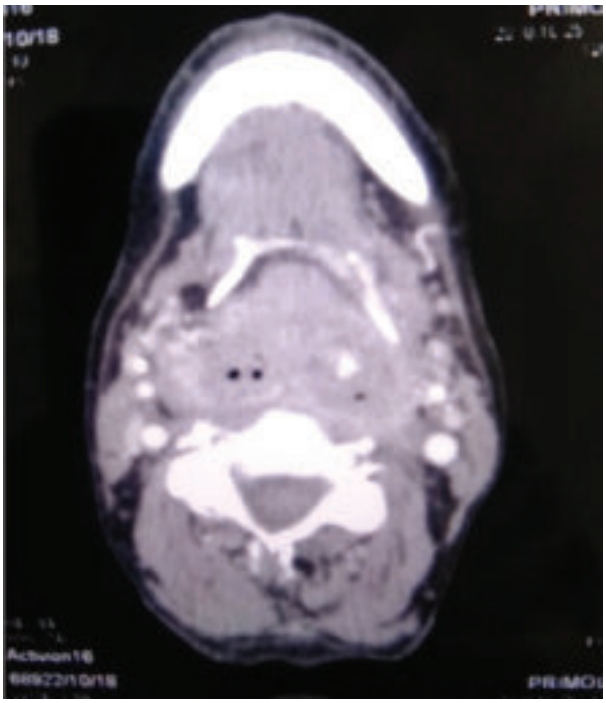

Fig. 2: Axial post-contrast CT scan of neck showing large mixed density mass at glottic and supraglottic part of larynx.

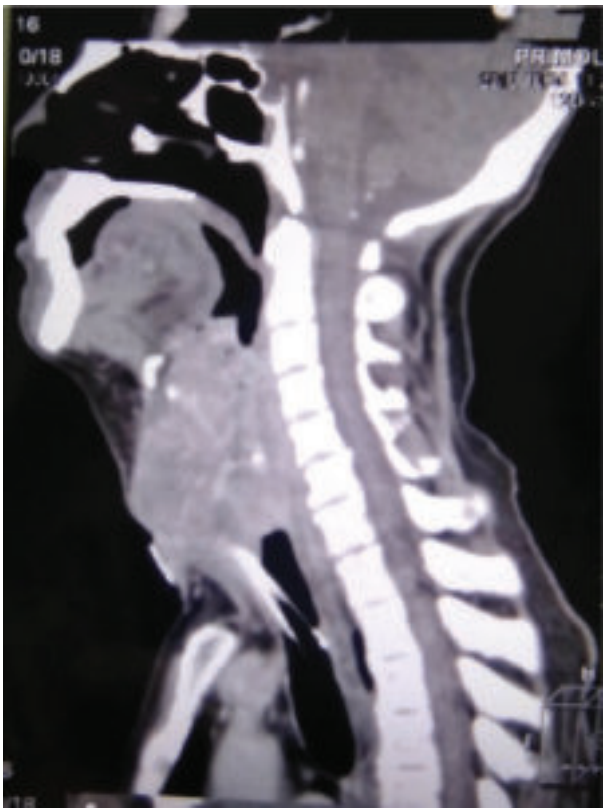

Fig. 3: Sagittal post-contrast CT scan of neck showing large laryngeal growth (Ca-larynx).

Table-III: *Diagnosis of neck masses based on histopathological examination (N=40)*

Findings	Frequency	Percentage
Benign (n= 13)		
Thyroglossal duct cyst	1	2.5
Abscess	3	7.5
Tubercular lymphadenopathy	2	5
Reactive lymphadenopathy	1	2.5
Multinodular goiter	2	5
Thyroid cyst	1	2.5
Hemangioma	0	0
Pleomorphic adenoma	2	5
Carotid body tumor	1	2.5
Malignant (n=27)		
Carcinoma larynx	5	12.5
Metastatic lymphadenopathy	4	10
Carcinoma thyroid	2	5
Parotid carcinoma	3	7.5
Submandibular gland malignant tumor	1	2.5
Carcinoma tonsil	2	5
Nasopharyngeal carcinoma	4	10
Hypopharyngeal carcinoma	1	2.5
Carcinoma base of tongue	2	5
Lymphoma	3	7.5

Table-IV: *CT scans and histopathological correlation of benign versus malignant lesions (N=40)*

CT scan	Histopathological diagnosis		
diagnosis	Malignant	Benign	Total
Malignant	25	1	26
Benign	2	12	14
Total	27	13	40

Sensitivity 92.6%, Specificity 92.3%, Diagnostic accuracy 92.5%, Positive predictive value 96.2%, Negative predictive value 85.7%

DISCUSSION

In this study, a total of 40 patients were enrolled and their age was ranging between 2 and 82 years. The most common age group was 40–70 years (45%), followed by 15–40 years (35%) and <15 years (12.5%). A study done by Shrestha et al. reported that 29% of the patients of neck masses belonged to the age group 51–60 years, followed by 41–50 years and 61–70 years respectively.[10] Another study done by Charan et al. reported that the majority of patients with neck mass malignancy was found in the 46–60 years age group (29%), followed by 31–45 years age group (24%).[11] A previous study done by Siddiqua et al. found that most of the patients were in the was in 51–60 years age group (26.3%), followed by 41–50 years age group (17.5%).[12] All those findings are quite similar to our results.

A male predominance was noted in the present study. 28(70%) were male and 12(30%) were female (male-female ratio was 2.33:1). Kaur et al., Siddiqua et al., and Vazquez et al. also observed a male predominance in their studies (male-female ratio were reported as 2:1, 1.9:1 and 2.1:1 respectively),[3,12,13] which are also in congruence with our study finding. However, Balakrishnan observed that malignant lesions prevailed among male population with a male to female ratio of 1.6:1, while an equal incidence was observed in benign lesions with a male to female ratio of 1:1.[14] These findings are lower than that of our observation.

We observed in our study that the sensitivity of CT scan in diagnosis of neck masses was 92.6%, while its specificity was 92.3%, diagnostic accuracy 92.5%, positive predictive value 96.2%, negative predictive value 85.7%. Kaur et al. found sensitivity of CT 96.4%, specificity of 100%, positive predictive value of 100% and a negative predictive value of 91.67%.[3] Shrestha et al. reported the sensitivity of CT in detecting malignant/benign lesions was 96.5% with a specificity of 100%. The positive predictive value was 100% and the negative predictive value 95.2%.[10] Siddiqua et al. reported 94.6% sensitivity and 95% specificity, while positive predictive value was 97.2%, negative predictive value 90.5% and diagnostic accuracy 94.7%.[12] Vazquez et al. reported 91.4% diagnostic accuracy of CT scans.[13] Begum et al. reported that CT in the diagnosis of laryngeal carcinoma showed 97.9% sensitivity, 66.7% specificity, 96% accuracy and 97.9% positive predictive value.[15] Those findings are more or less similar to our results. We also observed that CT scans can ensure accurate anatomical localization and characterization of lesion as benign and malignant. Moreover, in malignant tumors, it plays a very useful

role for staging and provide essential information about the tumor extent that directly affects the surgical approach necessary for curative resection. Our findings are also supported by several previous studies.[12,13]

However, our study has some limitations. We did not evaluate the inter-reader variability between radiologists in the interpretation of the CT scan images. Moreover, patients were recruited from a single centre in Dhaka city; we could recruit a small sample due to time and budget constraint. Therefore, further studies with larger sample and longer duration involving more hospitals from different regions of the country are recommended to obtain more precise results.

CONCLUSION

To summarize, computed tomography (CT) scan definitely plays a major role in the evaluation of neck masses both in adult and paediatric patients; it has an excellent correlation with postoperative histopathological diagnosis. It also assists in the pretreatment planning in neck masses, by better defining the local extension of infiltrating tumours, and detecting local and distant metastasis. Such diagnostic and prognostic information helps clinicians determine the relative value of surgical intervention as well as chemo- and radiotherapy, in selecting patients who might be benefited from adjuvant treatment, and also in identifying patients at high risk for recurrence to be followed up more closely.

Conflict of Interest: None declared by the authors.

Funding Statement: Self-funded.

Ethical Approval: This study was approved by the Ethical Committee of Bangladesh College of Physicians and Surgeons (BCPS), Dhaka, Bangladesh.

Authors' Contribution: Concept and design: L Ahmed; Patient selection, data collection, compilation and analysis: L Ahmed, MF Rayhan, M Ahmed, MS Yasmin, F Gaffar; Manuscript writing, editing and final submission: L Ahmed, MF Rayhan, M Ahmed, MS Yasmin, F Gaffar, MAA Mamun.

REFERENCES

1. Pynnonen MA, Gillespie MB, Roman B, Rosenfeld RM, Tunkel DE, Bontempo L, et al. Clinical practice guideline: evaluation of the neck mass in adults. Otolaryngol Head Neck Surg. 2017;157(Suppl 2):S1-S30.
2. McGuirt WF. The neck mass. Med Clin North Am. 1999;83(1):219-34.
3. Kaur R, Singh P, Kaur N, Bhatnagar S, Dahuja A. Role of computed tomography (CT) in localisation and characterisation of suprahyoid neck masses. Pol J Radiol. 2017;82:263-70.
4. Schwetschenau E, Kelley DJ. The adult neck mass. Am Fam Physician. 2002;66(5):831-8.
5. Rydberg J, Buckwalter KA, Caldemeyer KS, Phillips MD, Conces DJ Jr, Aisen AM, et al. Multisection CT: scanning techniques and clinical applications. Radiographics. 2000;20(6):1787-806.
6. Martinez CR, Kashima H, Gayler BW, Siegelman SS. Computed tomography of the neck. Ann Otol Rhinol Laryngol Suppl. 1982;99:1-31.
7. Junn JC, Soderlund KA, Glastonbury CM. Imaging of head and neck cancer with CT, MRI, and US. Semin Nucl Med. 2021;51(1):3-12.
8. Buderer NM. Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Acad Emerg Med. 1996;3(9):895-900.
9. Plant RL. Image analysis of benign and malignant neck masses. Ann Otol Rhinol Laryngol. 1998;107(8):689-96.
10. Shrestha MK, Ghartimagar D, Ghosh A. Diagnostic accuracy of computed tomogram in the evaluation of a neck mass. J Nepal Med Assoc. 2011;51(184):164-70.
11. Charan I, Kapoor A, Kumar N, Jagawat N, Singhal MK, Kumar HS. Evaluation of neck mass with computed tomography: an observational study. Int J Sci Stud. 2014;2(7):118-22.
12. Siddiqua UI, Halder BA, Hossain MR, Roy SK, Al-Amin A, Sultana S. Evaluation of neck mass by multidetector computed tomography and histopathological comparison. Bangladesh Med Res Counc Bull. 2017;43(3):115-9.
13. Vazquez E, Enriquez G, Castellote A, Lucaya J, Creixell S, Aso C, et al. US, CT, and MR imaging of neck lesions in children. Radiographics. 1995;15(1):105-22.
14. Balakrishnan K. Multidetector CT evaluation of neck masses. J Evid Based Med Healthc. 2018;5(53):3658-63.
15. Begum M, Yiasmeen S, Arabi SN, Siddique AB, Chowdhury MN. Diagnostic performance of computed tomography in laryngeal carcinoma and its extension. J Monno Med Coll. 2023;9(2):63-7.

Original Article

Prescription Pattern of Antihypertensive Agents in Chronic Kidney Disease Patients of Two Tertiary Care Hospitals in Bangladesh

Akter N[1], Moon KJ[2], Fatema SK[3], Akkas N[3], Yusuf R[5], Nahar K[6], Sultana S[7]

ABSTRACT

Occurrence of chronic kidney disease (CKD) is significantly high in Bangladesh. CKD is viewed as a common cause of hypertension, also as a complication of uncontrolled hypertension. Therefore, blood pressure control is vital in all stages of CKD. Early control of hypertension can prevent further CKD progression. A cross-sectional study was conducted in the Department of Nephrology of Sir Salimullah Medical College & Mitford Hospital and National Institute of Kidney Diseases & Urology (NIKDU), Dhaka, Bangladesh, to assess the current antihypertensive prescription pattern in chronic kidney disease patients. A total of 264 diagnosed hypertensive CKD (all stages) patients were included in this study. Among 264 CKD patients, 52.7% were female and 47.3% were male. 23.9% were smokers and 52.3% had habits of extra salt intake. Most of the patients were in CKD stage 1, followed by CKD stage 5 in both hospitals. Common comorbidities of the CKD patients were anemia (51.5%), followed by diabetes mellitus (29.7%) and ischemic heart disease (18.8%). Regarding anti-hypertensive medications, angiotensin receptor blockers (ARBs) were prescribed to 58 patients; they were the highest prescribed agents observed in our study. Among them, losartan was the most common prescribed drug (44.8%), followed by olmesartan (31.0%), telmisartan (20.7%), and irbesartan (3.5%). Calcium channel blockers (CCBs) were prescribed to 16 patients, with amlodipine accounting for 50% of those prescriptions. Angiotensin converting enzyme (ACE) inhibitors were used in 13 patients; ramipril (61.5%) and lisinopril (38.5%) were two drugs of choice. Blood pressure control is very crucial for CKD patients to minimize cardiovascular risks associated with CKD progression and to decrease morbidity and mortality.

Keywords: *Chronic kidney disease, hypertension, antihypertensive agent, cardiovascular risks*

Mugda Med Coll J. 2026; 9(1): 31-36
DOI: https://doi.org/10.3329/mumcj.v9i1.90805

1. Dr. Nazia Akter, Lecturer, Department of Pharmacology & Therapeutics, Dinajpur Medical College, Dinajpur-5200. Email: naziadjmc@gmail.com (Corresponding author)
2. Dr. Kawsar Jahan Moon, Associate Professor, Department of Pharmacology & Therapeutics, Sir Salimullah Medical College, Dhaka-1100.
3. Dr. Syeda Kaniz Fatema, Lecturer, Department of Pharmacology & Therapeutics, Mugda Medical College, Dhaka-1214.
4. Dr. Nafisa Akkas, Lecturer, Department of Pharmacology & Therapeutics, Chattogram Medical College, Chattagram-4203.
5. Dr. Riti Yusuf, Assistant Professor, Department of Pharmacology & Therapeutics, Sir Salimullah Medical College, Dhaka-1100.
6. Dr. Kamrun Nahar, Assistant Professor, Department of Pharmacology & Therapeutics, Mugda Medical College, Dhaka-1214.
7. Dr. Sadia Sultana, Assistant Professor, Department of Pharmacology & Therapeutics, Mugda Medical College, Dhaka-1214.

INTRODUCTION

Hypertension stands as a key risk factor for cardiovascular disease, and ranks among the top reasons for early death worldwide.[1] Uncontrolled hypertension can lead to serious adverse cardiovascular and cerebrovascular events including acute coronary syndrome, stroke, heart failure, and even death.[2] Hypertension happens when one's systolic BP is above 140 mm of Hg and/or diastolic BP is above 90 mm of Hg or is on anti-hypertensive drug.[3] In Bangladesh, the rate of hypertension is 26.2%.[4] About 1.28 billion people age range 30-79

years, suffer from hypertension. Low- and middle-income countries have almost two-thirds of hypertensive people.[5] In 2017, hypertension caused 10.4 million deaths and 218 million disability. Hypertension is an important etiological factor for cardiovascular diseases and cerebrovascular diseases. Those who have hypertension are more likely to develop CVD sooner than those who do not have hypertension.[4] Due to regional heterogenicity various risk factors are seen in hypertension prevalence, for example: intake of high salty food, intake of food containing low potassium food, obesity, consumption of alcohol, being physically inactive and unhealthy diet.[1]

Chronic kidney disease is considered as a fatal condition. This disease is life threatening which has turned into a global public health challenge with an accelerated risk for ESKD, cardiovascular disorder and other health problems.[6] Renal function gets progressively lost because of chronic kidney disease, in most cases present with high blood pressure which should be managed by antihypertensive medications.[7] The global burden of morbidity and mortality is directly affected by CKD.[6] In 2017, almost 697.5 million cases of CKD were submitted. Among them, about 1.2 million people lost lives[8]. In Bangladesh, occurrence of CKD was 22% in 2020[9]. The global estimated chronicity is 13.4% (11.7-15.1) & dialysis or renal transplant needed ESKD patients are about 4.9-7.1 million[6]. An authentic study shows that the occurrence of CKD was 21.2%, 10.2% and 13.4% for Pakistan, India and Nepal respectively.[10] Due to the excessive occurrence of diabetes mellitus, hypertension, hyperlipidemia & aging, CKD is increasing globally. In a few areas, other causes i.e. infection, herbal and environmental toxins are common.[6] CKD patients have renal impairment that causes hemodynamic overload, metabolic & endocrine abnormalities which damages the cardiovascular system. CKD causes many other health issues for example: hypertension, anemia, dyslipidemia, electrolyte imbalances, mineral disorders and bony abnormalities.[11] The link between hypertension and CKD is bi-directional. Hypertension can be the reason for CKD also it can be the cause of uncontrolled hypertension. CKD picks up its pace as hypertension has its contribution to it.[12] It has been reported approximately 80-85% CKD patients develop hypertension and almost 15.8% hypertensive patients suffer from CKD.[13] Due to volume overload and peripheral vascular resistance, progressive kidney disease can lead to uncontrolled hypertension. Heightened blood pressure causes injury to endothelium resulting in vascular damage within the kidney's ability to excrete fluid and waste from blood, causing fluid retention and it causes hypertension[11]. CKD patients have higher chance to develop cardiovascular diseases. When kidney function and cardiovascular diseases get worse, risk of death also increases. Once kidney impairment begins, it progresses to a stage where expensive treatments like dialysis and renal transplantation are required.[14]

Antihypertensive medications have three main purposes in CKD patients, they are: decreasing blood pressure in hypertensive patients, lowers the CVD in hypertensive patients and slows the declination of kidney disease in patients with or without hypertension. There also lessens proteinuria which results in improved health outcome and reduces healthcare expenses.[15] Proper treatment must be provided to CKD patients with hypertension to prevent the risk of poor prognosis of chronic kidney disease.[16,17]

Evidence showed that angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) decrease the prevalence of kidney dysfunction by 39% and 30% respectively in CKD patients with or without diabetes mellitus. These medications also reduce the risk of major cardiovascular events from 18% to 24%. Blockade of renin-angiotensin system might prevent new onset or deterioration of albuminuria in renal impaired patients.[6]

Understanding of utilization pattern of anti-hypertensive drugs in hypertensive CKD patients is essential to know the current prescription pattern, to observe patient compliance with medication, to understand common comorbidities associated with CKD and to study the impact on overall health condition of the patient. Prescribing patterns are powerful and important tools to exhibit the role of drugs in society. Drug utilization studies at regular intervals help physician to prescribe drug rationally. This study is helpful to observe the appropriate anti-hypertensive drug prescription pattern among the patients of chronic kidney disease for control of hypertension.

METHODS

This cross-sectional study was conducted in the Department of Nephrology of Sir Salimullah Medical College & Mitford Hospital and National Institute of Kidney Diseases & Urology (NIKDU), Dhaka, Bangladesh, between July 2023 and June 2024. A total of 264 patients who diagnosed with CKD and having anti-hypertensive therapy were enrolled in this study. However, patients aged <18 years, having acute renal injury, renal transplantation or stroke were excluded. Participants were interviewed using a pretested semi-structured questionnaire through the face-to-face interview. Blood pressure (BP) was assessed according to the Kidney Disease: Improving Global Outcomes (KDIGO) 2021 Clinical Practice Guideline for the Management of BP in CKD. BP was considered controlled when systolic blood pressure was <120 mmHg, provided that the target was tolerated by the participant. Data was collected including demographic characteristics, clinical history, smoking habit, salt intake, comorbidities, laboratory findings, CKD staging and record of anti-hypertensive medication.

Collected data was compiled, coded and analyzed. Data analysis was carried out using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). Data was presented as frequency and percentage for qualitative variables. To find out relation between dependent and independent variables (both are qualitative variables), Chi-square test was done. A p-value <0.05 was considered statistically significant. The results were presented in tables.

RESULTS

Out of 264 hypertensive CKD patients enrolled, 52.7% were female and 47.3% were male, indicating a slight female predominance. The mean age was 48.48±14.2 years. Most of the patients had normal BMI (61%), while 21.6% were overweight and 17% underweight. Extra salt intake was reported by 52.3% and smoking by 23.9% of the patients (Table-I). Regarding multiple comorbidities, anemia was the most common, affecting 184 (69.7%) patients, followed by diabetes mellitus 106 (40.2%) and ischemic heart disease 67(25.4%) (Table-II). Only 19.7% of the CKD patients had no associated comorbidities. Controlled BP was observed in 10(9.8%) stage 1 patients, 2(4.6%) stage 2 patients, 2(11.1%) stage 4 patients and 2(2.7%) stage 5 patients. In contrast, all patients in stage 3a and 3b had uncontrolled BP. The variation in BP control across different CKD stages was statistically significant (p=0.023) (Table-III). Regarding anti-hypertensive medications, angiotensin receptor blockers (ARBs) were prescribed to 58 patients; they were the highest prescribed agents observed in our study. Among them, losartan was the most common prescribed drug (44.8%), followed by olmesartan (31.0%), telmisartan (20.7%), and irbesartan (3.5%). Calcium channel blockers (CCBs) were prescribed to 16 patients, with amlodipine accounting for 50% of those prescriptions. Angiotensin converting enzyme (ACE) inhibitors were used in 13 patients; ramipril (61.5%) and lisinopril (38.5%) were two drugs of choice (Table-IV).

Table-I : *BMI and risk factors among CKD patients (n=264)*

Variables	Frequency	Percentage
BMI		
Underweight	45	17.0
Normal	161	61.0
Overweight	57	21.6
Obese	1	0.4
Extra salt intake		
Yes	138	52.3
No	126	47.7
Smoking		
Yes	63	23.9
No	201	76.1

Table-II: *Multiple comorbidities observed among CKD patients (n=264)*

Comorbidities	Frequency (n)	Percentage of cases (%)
Anemia	184	69.7
Diabetes Mellitus	106	40.2
Ischemic Heart Disease	67	25.4
Response	357	

Multiple responses were allowed; therefore, percentages do not sum to 100%

Table-III: *Status of blood pressure of the patients in different stages of CKD (n=264)*

CKD Stage	Blood Pressure Controlled	Blood Pressure Uncontrolled	p-value
1	10 (9.8)	92 (90.2)	0.023[S]
2	2 (4.6)	41 (95.4)	
3a	-	21 (100)	
3b	-	6 (100)	
4	2 (11.1)	16 (88.9)	
5	2 (2.7)	72 (97.3)	

Chi-sqaure test was applied to reach p-value; S=significant.

Table-IV: *Distribution of antihypertensive agents used in CKD patients*

Antihypertensive agents	Frequency	Percentage
Angiotensin receptor blockers (n=58)		
Losartan	26	44.8
Olmesartan	18	31.0
Telmisartan	12	20.7
Irbesartan	2	3.5
Calcium channel blockers (n=16)		
Amlodipine	8	50.0
Cilnidipine	6	37.5
Nifedipine	2	12.5
Angiotensin converting enzyme inhibitors (n=13)		
Ramipril	8	61.5
Lisinopril	5	38.5
Combination therapy	177	67.0

DISCUSSION

In the present study, the mean age of the patients was 48.48±14.2 years. This finding resembled to the study done by Oommen et al.[18], where the mean age was observed 49.53±15.1 years. Kidney function deteriorates with aging due to decrease in number of glomeruli and decreased glomerular filtration rate. Our study showed that hypertension along with CKD is more prevalent in women than in men. This findings similar to another study done by Sarker et al.[9] in Bangladesh. In contrast, Thomas et al.[7] observed a male predominance in their study.

In this study, it was observed that anemia was the most prevalent comorbidity among hypertensive CKD patients, affecting 69.7% of the cohort. This finding aligns with the findings of several previous studies conducted in Bangladesh, which also reported high prevalence rates of anemia among CKD patients. For instance, Yousuf et al.[19] reported higher anemia prevalence rates with progression of CKD reaching up to 86% in stage 5 patients, while Rahman et al.[20] found reduced hemoglobin levels in CKD patients, which was directly associated with the severity of the disease (i.e., more anemia in advanced stages of CKD). Those findings highlight the commonality of such complication among Bangladeshi CKD patients.

Regarding blood pressure control, this study found that a significant proportion of patients, especially those in advanced CKD stages, had uncontrolled hypertension. Specifically, all patients in stages 3a and 3b, and 97.3% of stage 5 patients, exhibited poor BP control in those CKD stages. This trend is also consistent with the findings from previous studies that reported poorer BP control and outcomes in advanced stages of CKD.[21,22] Similar patterns have been documented by Lee & Han[17], who emphasized the challenges of blood pressure regulation due to fluid retention and vascular resistance in advanced CKD. We observed a significant difference in BP control across different CKD stages ($p<0.05$), which underscores the importance of tailored anti-hypertensive strategies.

ARBs were the most frequently prescribed anti-hypertensive agents, particularly losartan (44.8%), corroborating global and regional prescribing trends. Previous studies confirmed ARBs' dual role of reducing blood pressure as well as proteinuria, which ultimately slower down the progression of CKD.[23,24] However, the risk of hyperkalemia and need for renal function monitoring especially in later CKD stages always remain clinical concerns for those patients.[16] Amlodipine was the most commonly used calcium channel blocker preferred for its renal safety and effective blood pressure control and among ACE inhibitors, ramipril dominated in our observation, which is consistent with the findings of Prabitha et al.[14]; however, those drugs require dose adjustments in renal impairment.[14]

Overall, our study findings highlight a high prevalence of anemia and poor BP control among hypertensive CKD patients in Bangladesh. The prescribing patterns observed are consistent with national trends, emphasizing the need for individualized treatment strategies and regular monitoring to improve patient outcomes.

However, in our study, patients were recruited from two selected hospitals in Dhaka city; we could recruit a small sample due to time and budget constraint. Therefore, the study results may not reflect the exact picture of the whole country. Further studies with larger sample and longer duration involving hospitals from different regions of the country are recommended.

CONCLUSION

The study concluded that the control of hypertension is necessary in all stages of CKD to minimize cardiovascular risk associated with CKD progression and to decrease morbidity and mortality. ARBs were most prescribed single drug therapy in both hospitals

among adherent prescriptions. The findings of this study may offer additional information for healthcare professionals about anti-hypertensive therapies in CKD patients in our country. However, we observed that inconsistencies exist towards anti-hypertensive treatment approach. There is need for further improvement in the prescribing patterns of anti-hypertensive and strategies to improve patient adherence to drug treatment for ensuring safety, efficacy and rationality.

Conflict of Interest: None declared.

Funding Statement: Self-funded.

Ethical Approval: Ethical approval was obtained from the Institutional Ethics Committee of Sir Salimullah Medical College, Dhaka, Bangladesh (Ref: 59.14.1100.031.18.001.24.566).

Authors' Contribution: Concept and design of the study: N Akter; Data collection, compilation and analysis: N Akter, SK Fatema, N Akkas, R Yusuf, K Nahar, S Sultana; Manuscript preparation, review, editing and final submission: N Akter, SK Fatema, N Akkas, R Yusuf, K Nahar, S Sultana.

REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223-37.
2. Kim KM, Oh HJ, Choi HY, Lee H, Ryu DR. Impact of chronic kidney disease on mortality: a nationwide cohort study. Kidney Res Clin Pract. 2019;38(3):382-90.
3. Amin MR, Khan FA, Chowdhury RI, Chowdhury AW, Banerjee SK, Choudhury SR, et al. eds. National guideline on hypertension. 2nd ed. Dhaka, Bangladesh: Non Communicable Disease Control Programme, Directorate General of Health Services (DGHS), Ministry of Health & Family Welfare; 2023.
4. Khan MN, Oldroyd JC, Chowdhury EK, Hossain MB, Rana J, Renzetti S, et al. Prevalence, awareness, treatment, and control of hypertension in Bangladesh: Findings from National Demographic and Health Survey, 2017-2018. J Clin Hypertens (Greenwich). 2021;23(10):1830-42.
5. World Health Organization (WHO). Guideline for the pharmacological treatment of hypertension in adults. Geneva, Switzerland: WHO; 2021.
6. Liyanage T, Ninomiya T, Jha V. Worldwide access to treatment for end-stage kidney disease: a systematic review. Lancet. 2015;385:1975-82.
7. Thomas R, Sam S, Neelaphar P, Shabeeb P, Vishwanath BA. A study on prescribing pattern of antihypertensive in chronic kidney disease patients. J Drud Deliv Ther. 2020;10(3-s):75-81.
8. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2020;395(10225):709-33.
9. Sarker MHR, Moriyama M, Rashid HU, Chisti MJ, Rahman MM, Das SK, et al. Community-based screening to determine the prevalence, health and nutritional status of patients with CKD in rural and peri-urban Bangladesh. Ther Adv Chronic Dis. 2021;12:20406223211035281.
10. Hasan M, Sutradhar I, Gupta RD, Sarker M. Prevalence of chronic kidney disease in South Asia: a systematic review. BMC Nephrol. 2018;19(1):291.
11. Burnier M, Damianaki A. Hypertension as cardiovascular risk factor in chronic kidney disease. Circ Res. 2023;132(8):1050-63.
12. Horowitz B, Miskulin D, Zager P. Epidemiology of hypertension in CKD. Adv Chronic Kidney Dis. 2015;22(2):88-95.
13. Huang QF, Hoshide S, Cheng HM, Park S, Park CG, Chen CH, et al. Management of hypertension in patients with chronic kidney disease in Asia. Curr Hypertens Rev. 2016;12(3):181-5.
14. Prabitha P, Reshmi TR, Jayakumar KP. Analysis of prescription pattern of antihypertensives in various stages of chronic kidney disease. Int J Basic Clin Pharmacol. 2019;8:524-8.
15. Hernandez MF, Chang TI. Revisiting hypertension treatment in patients with chronic kidney disease. Semin Nephrol. 2024;44(2):151514.
16. Pugh D, Gallacher PJ, Dhaun N. Management of hypertension in chronic kidney disease. Drugs. 2019;79(4):365-79.
17. Lee JY, Han SH. Blood pressure control in patients with chronic kidney disease. Korean J Intern Med. 2021;36(4):780-94.
18. Oommen JM, Nerurkar DP, Sajith M, Jawale S, Ambike S. Prescription pattern of chronic kidney disease patients undergoing hemodialysis in tertiary and private hospital. J Young Pharm. 2019;11(2):202-6.
19. Yousuf MA, Ahsan T, Hossain M, et al. Prevalence of anemia among chronic kidney disease patients: a study in tertiary care hospitals in Dhaka. Bangladesh Renal J. 2020;9(2):45-50.

20. Rahman MA, Shanjana Y, Ahmed MS, Dhama K, Hasan Fahim M, Mahmud T, et al. Hematological abnormalities and comorbidities are associated with the severity of kidney disease: a hospital-based cross-sectional study in Bangladesh. Clin Pathol. 2022;15:2632010X221114807.

21. Khan MSH, Chy UK, Islam MR, Alam D, Habib R, Latif ZA. State of blood pressure control in adult type 2 diabetic patients with chronic kidney disease and hypertension: experience from a tertiary care centre of Bangladesh. BIRDEM Med J. 2021;11(3): 212-7.

22. Liu B, Wang Q, Wang Y, Wang J, Zhang L, Zhao M, et al. Utilization of antihypertensive drugs among chronic kidney disease patients: results from the Chinese cohort study of chronic kidney disease (C-STRIDE). J Clin Hypertens (Greenwich). 2020; 22(1):57-64.

23. Al-Mirza A, Al-Subhi HR, Abdelrahman AM. Utilization patterns of antihypertensive drugs in the management of hypertension among patients with chronic kidney disease at a tertiary hospital. Int J Basic Clin Pharmacol 2021;10(5):466-70.

24. Magvanjav O, Cooper-DeHoff RM, McDonough CW, Gong Y, Segal MS, Hogan WR, et al. Antihypertensive therapy prescribing patterns and correlates of blood pressure control among hypertensive patients with chronic kidney disease. J Clin Hypertens (Greenwich). 2019;21(1):91-101.

Original Article

Autopsy Findings in Suicidal Hanging – A Cross-Sectional Study Based on the Documentation of the Department of Forensic Medicine & Toxicology in a Tertiary Level Institution in Dhaka, Bangladesh

Sultana N[1], Khan MZR[2], Bari FJ[3], Biswas M[4], Sultan MT[5], Alam S[6], Hossain MS[7]

ABSTRACT

A cross-sectional, descriptive study was carried out in the Department of Forensic Medicine & Toxicology of Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, to determine the characteristics of the autopsy findings in suicidal hanging cases. A total of 157 cases with complete external and internal examination details were included in this study. Data was obtained from the inquest reports, chalan, and death certificates (for hospital deaths) between January and December of 2023. The mean age of victims was 29.9±7.8 years. Most of the victims belonged to the 21–30 years age-group (41.4%). A female predominance was observed (65%). Married (72%) were more affected than unmarried (28%). Most of them belonged to middle-class families (52.2%). Regarding occupation, most of them were students (39.5%), and homemakers (28.7%). The most commonly used ligature material was rope (44%), followed by dupatta (29%), sari (17%) and lungi (10%). Autopsy report revealed that the positions of the knots were found predominantly on the left side (58.6%), followed by the right side (29.3%) and the back of the neck (12.1%). Slip-type knots were more common (62%) compared to fixed knots (38%). Most of the ligature marks were located above the thyroid cartilage (89.8%). Grooving of the ligature mark was observed in 86%, while petechial hemorrhage was noted in 54.1% cases. Tongue bite was observed in 36.9% and subconjunctival hemorrhage was seen in 39.4% cases. Damage to the neck muscle fibers was identified in 78.3%, while damage to the cervical vertebrae were found in 15.9% cases. Regarding fractures, the thyroid cartilage was involved in 16% and the hyoid bone in 30% cases. Parchmentization was observed in 53.5% cases. The most common reported cause of suicidal hanging was familial disharmony (34%), followed by romantic/relationship distress (23%), academic pressure and examination failure (18%), financial crisis (17%), and depressive illness (8%). These findings play a decisive role in ascertaining the manner of death, especially if doubt exists over whether this was suicidal, accidental or homicide in nature and highlight the urgent need for targeted suicide prevention, including improved mental health care, public awareness, and support for at-risk individuals.

Keywords: *Autopsy, hanging, ligature mark, ligature material, suicide.*

Mugda Med Coll J. 2026; 9(1): 37-42
DOI: https://doi.org/10.3329/mumcj.v9i1.90813

1. Dr. Nahid Sultana, Assistant Professor, Department of Forensic Medicine & Toxicology, Holy Family Red Crescent Medical College, Dhaka-1000. Email: nstateart 2009@gmail.com (Corresponding author)
2. Dr. Muhammad Zillur Rahman Khan, Associate Professor & Head, Department of Psychiatry, Shaheed Suhrawardy Medical College & Hospital, Dhaka-1207.
3. Dr. Fatema Jahan Bari, Lecturer, Department of Forensic Medicine & Toxicology, Shaheed Suhrawardy Medical College, Dhaka-1207.
4. Dr. Mitra Biswas, Assistant Professor, Department of Forensic Medicine & Toxicology, M. H. Samorita Hospital & Medical College, Tejgaon, Dhaka-1208.
5. Dr. Mohammad Tipu Sultan, Assistant Professor, Department of Forensic Medicine & Toxicology, Pabna Medical College, Pabna-6602.
6. Dr. Shoeb Alam, Professor, Department of Urology, Holy Family Red Crescent Medical College & Hospital, Dhaka-1000.
7. Dr. Mohammad Shakhawat Hossain, Senior Consultant, Department of Paediatrics, Mugda Medical College Hospital, Dhaka-1214.

INTRODUCTION

According to the World Health Organization (WHO), an estimated 727,000 people died by suicide globally in 2021. Suicide is a global phenomenon and occurs throughout the lifespan. Effective and evidence-based interventions can be implemented at population, sub-population and individual levels to prevent suicide and suicide attempts.[1] Hanging is defined as "death due to suspension of the body by a ligature around the neck, hanging leads to death primarily by asphyxia, venous congestion, or cerebral ischemia depending on the position of the knot, the force of suspension, and the body weight of the victim".[2] The forensic examination of a hanging case involves a meticulous assessment of various factors and each of which provided crucial clues about the circumstances surrounding the death.[3] In our country, the ligature materials usually used are rope, shari, scarves (orna) etc. which can reveal details about the method chosen.[4] Moreover, the pattern of neck injuries can help distinguish self-infliction (suicidal or otherwise including accidental means such as auto-erotic asphyxiation) from homicidal causes of such deaths with greater certainty.[4,5] Fractures of the thyroid cartilage, particularly the superior horns, is the commonest fracture identified in hanging, the majority of which being sustained within the lower third toward the base. Conversely, cricoid fracture is very rare in hanging.[4-6] From a forensic standpoint, distinguishing between suicidal, homicidal, and accidental hanging requires careful evaluation of autopsy findings, ligature characteristics, scene investigation, and injury patterns.[6]

Autopsy plays a crucial role in confirming the cause and manner of death, assessing features like ligature marks, hyoid and laryngeal fractures, and the presence or absence of defensive injuries.[4,7] Several studies have examined the pattern of injuries in hanging cases to aid in medico-legal classification. In many cases, incomplete hanging, dribbling of saliva and oblique ligature marks are indicative of suicide.[4-9] However, occasional inconsistencies and overlapping features make comprehensive postmortem evaluation essential.[4,9]

By analyzing multiple forensic cases of suicidal hanging in Bangladesh, this study seeks to identify prevalent patterns and features. Such insights can strengthen forensic investigations, guide suicide prevention initiatives, and broaden our understanding of the factors driving suicide in the country. Ultimately, a thorough comprehension of suicidal hangings may support the development of targeted interventions suited to the needs of the Bangladeshi population.

METHODS

This cross-sectional, descriptive study was conducted in the Department of Forensic Medicine & Toxicology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, from January to December of 2023. Relevant data was obtained from the autopsy reports, inquest papers, and police challans preserved in the corresponding department. The study population comprised individuals of all ages and genders whose deaths were confirmed as suicidal hangings through medico-legal investigations. Finally, a total of 157 autopsy-confirmed cases of suicidal hanging were included in this study based on our inclusion and exclusion criteria. Inclusion criteria included: i) autopsy confirmed cases of suicidal hanging and ii) deaths reported within the specified study period. Exclusion criteria were: i) suicides by other means except hanging and ii) victims having conflicting or insufficient information.

Variables included age, gender, marital status, socioeconomic status, occupation, ligature material, and autopsy findings (e.g., ligature marks, characteristics of injuries, fractures, petechiae etc.) and suspected causes behind suicide. A structured data extraction form was used to ensure consistency.

Data was analyzed using Microsoft Excel sheet in the computer. Descriptive statistics (e.g., frequency and percentage) were used to summarize categorical variables. Results were presented in tables and pie charts. No inferential statistical tests were applied, as the study was descriptive.

RESULTS

A total of 157 suicidal hanging cases were included in this study. The mean age of victims was 29.9±7.8 years. Most of the victims belonged to the 21–30 years age-group (41.4%). Females 102(65%) outnumbered males 55(35%). Married 113(72%) were more affected than unmarried 44(28%). Most belonged to middle-class families (52.2%), followed by lower and higher socio-economic status (32.5% and 15.3% respectively). Regarding occupation, most of them were students 62(39.5%), followed by homemakers 45(28.7%), business owners 25(15.9%), service holders 12(7.6%) and street vagrant 9(5.7%) (Table-I).

Table-I: *Sociodemographic characteristics of the victims (n=157)*

Variables Category	Frequency	Percentage
Age group (years)		
01–10	1	0.6
11–20	32	20.3
21–30	65	41.4
31–40	49	31.2
41–50	7	4.5
>50	3	2.0
Mean ± SD	29.9 ± 7.8 years	
Gender		
Male	55	35
Female	102	65
Marital status		
Married	113	72.0
Unmarried	44	28.0
Socio-economic status		
Lower class	51	32.5
Middle class	82	52.2
Higher class	24	15.3
Occupation		
Student	62	39.5
Homemaker	45	28.7
Business owner	25	15.9
Service holder	12	7.6
Street vagrant	9	5.7
Others	4	2.5

The most commonly used ligature material was rope, accounting for 69(44%) cases, followed by dupatta 45(29%), sari 27(17%), and lungi 16(10%) (Fig. 1). Autopsy report revealed that the positions of the knots were predominantly found on the left side (58.6%), followed by the right side (29.3%) and the back of the neck (12.1%). Slip-type knots were more common (62%) compared to fixed knots (38%). Most of the ligature marks were located above the thyroid cartilage as found in 141(89.8%) cases, while in 11(7%) cases over the thyroid cartilage and in 5(3.2%) cases below the thyroid cartilage. Grooving of the ligature mark was observed in 135 (86%) cases, while petechial hemorrhage was noted in 85(54.1%) cases. Tongue bite was observed in 58(36.9%) cases and subconjunctival hemorrhage was seen in 62(39.4%) cases. Damage to the neck muscle fibers was identified in 123(78.3%) cases, while damage to the cervical vertebrae were found in 25(15.9%) cases. Regarding fractures, the thyroid cartilage was involved in 25(16%) cases, while the hyoid bone was fractured in 47(30%) cases. Parchmentization was observed in 84(53.5%) cases (Table-II). The most common reported cause of suicidal hanging was familial disharmony (34%), followed by romantic/ relationship distress (23%), academic pressure and examination failure (18%), financial crisis (17%), and depressive illness (8%) (Fig. 2).

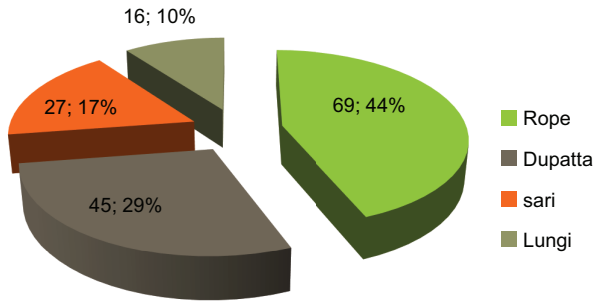

Fig. 1: *Type of ligature materials*

Table-II: *Autopsy findings of the victims (n=157)*

Autopsy Findings	Frequency	Percentage
Ligature mark over the neck		
Above the thyroid cartilage	141	89.8
Over thyroid cartilage	11	7.0
Below the thyroid cartilage	5	3.2
Position of the knot		
Left side	92	58.6
Right side	46	29.3
Back	19	12.1
Grooving of ligature	135	86.0
Evidence of a slip knot	98	62.4
Petechial hemorrhage	85	54.1
Tongue bite	58	36.9
Subconjunctival hemorrhage	62	39.4
Damaged neck muscle fibers	123	78.3
Damaged cervical vertebrae	25	15.9
Parchmentization	84	53.5
Fracture		
Thyroid cartilage	25	16.0
Hyoid bone	47	30.0

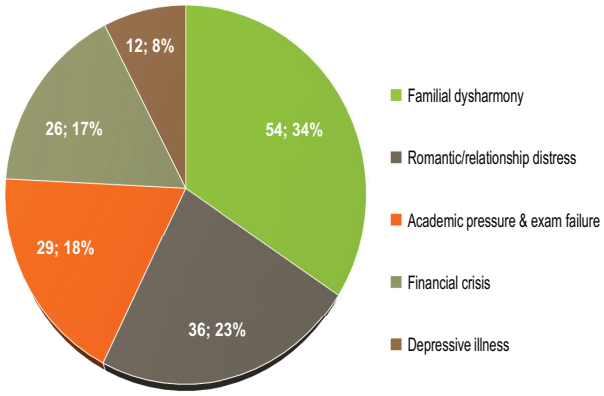

Fig. 2: *Suspected causes behind suicidal hanging (n=157)*

DISCUSSION

Suicides are horrific tragedies of premature end of the lives and have profound effects on the lives of families and communities.[1] Unnatural deaths like suicidal hanging pose a significant burden in the society, particularly in low-income countries like Bangladesh.[10] Our study was based on the autopsy findings of 157 victims who committed suicide by hanging in Dhaka city, Bangladesh. The cases were documented between January and December of 2023. The findings of the present study were analyzed and compared with those reported in previously published literature. In this study, the majority of hanging cases (41.4%) were observed in the 21–30 years age-group, which is more or less consistent with the findings of several previous studies done in Bangladesh.[9,11-15] This may be attributable to the fact that individuals in this age-group represent the most active phase of life, during which individuals are particularly susceptible to diverse psychosocial challenges that lead to suicidality. Our study also revealed a predominance of female victims in suicidal hanging cases, which is consistent with findings from studies conducted in our country.[9,11,12] In contrast, a male predominance was reported by several previous studies.[13,14,16-18] Equal gender distribution was also evident.[15,19]

This study also brings attention to the contextual factors in Bangladesh, including poverty, social discrimination, and limited mental health resources for this fatality. For example, in our study, hanging deaths were uncommon among the elite people. Conversely, the highest incidence was observed in the middle class group, who may struggle to accept reality, suggesting a predominantly psychological origin for these deaths. These findings are consistent with results reported in other studies on suicidal hanging.[15,16,19] Students were the most victims, followed by homemakers in our study, which is in congruence with the previous studies. It assumed that students face academic pressure, often social isolation, and mental stress that may contribute such tragedies. In contrast, suicidal hanging was found predominant among service holders.[11,15]

Among ligature materials, ropes were used most (44%), followed by different types of clothing materials. Our findings are comparable with several previous findings.[11,12,16,18,20,21] In this study, the ligature mark was most commonly located above the thyroid cartilage (89.8%), regardless of whether the hanging was complete or partial. Similar findings were observed in other studies.[11,13,14,19,20] This may be explained by the frequent use of slip knots, where the final tightening of the ligature typically occurs once the noose settles at the upper part of the neck.[14] Analysis of ligature mark morphology revealed that 86% of cases exhibited grooving, which is more or less similar to the previous findings.[11,19] In contrast, another study reported that only 54% of cases had grooving.[20] Internal study of sternocleidomastoid (neck muscle) fibres revealed injury/damage in 78.3% cases – most likely due to compression or traction from the ligature, which is similar to previous studies.[11,19] On the contrary, some other evidence showed very low incidence of damaged sternocleidomastoid fibers in suicidal hanging.[4,6,21] Our study also revealed that the thyroid and hyoid bones were affected in 16% and 30% of the victims respectively, which is relatively high. Similar findings were reported by another study.[11] In contrast, several studies showed no or low incidence of such fractures.[4,13,19,21] This discrepancy is likely due to the fact that the majority of his victims were in the fourth and fifth decades of life, when ossification increases the likelihood of fracture, whereas in the present study most victims were between 21 and 30 years. Parchmentization, a typical feature of hanging, was observed in 53.5% in our series. However, previous studies reported much higher incidence.[4,6,9,11]

The leading suspected cause behind suicidal hanging was familial disharmony, followed by financial crisis other contributing factors, which is consistent with findings from studies conducted in several

countries.[13,16,18,19] Moreover, the relatively high proportion among married individuals (72%) suggests that marital discord is an important contributor to suicidal hanging, which is consistent with the research findings from both home and abroad.[11,14,18,19]

Although this cross-sectional, descriptive study provides valuable information, its single-center setting at a tertiary care hospital limits the applicability of the findings to the wider population of the country. However, the study has substantial sample size and detailed autopsy assessments offer a comprehensive perspective on suicidal hanging in Bangladesh.

CONCLUSION

Our study provides an in-depth insight into suicidal hanging in Bangladesh, highlighting common patterns and associated risk factors. Promoting education, empathy, and reducing excessive stress on young people can play a crucial role in lowering youth suicide rates. By preventing self-harm among this economically active segment of the population, a developing country like Bangladesh can also enhance its economic growth and productivity. Future research should explore the long-term impact of suicidal hanging on families and communities, as well as assess the effectiveness of various preventive strategies. Social, legal and psychiatric interventions are required to prevent suicide.

Conflict of Interest: None declared by the authors.

Funding Source: Self-funded.

Ethical Approval: The study was approved by the Ethical Review Committee of Shaheed Suhrawardy Medical College, Dhaka, Bangladesh.

Authors' Contribution: Concept and design of the study: N Sultana, MZR Khan, FJ Bari; Data collection, compilation and analysis: N Sultana, MZR Khan, FJ Bari, M Biswas, MT Sultan; Manuscript preparation: N Sultana, FJ Bari, M Biswas, MT Sultan; Critical review and editing: MZR Khan, S Alam, MS Hossain. All authors approved the final version of the manuscript for submission.

REFERENCES

1. World Health Organization (WHO). Suicide world wide in 2021: global health estimates. Geneva: WHO; 2025.
2. Reddy KSN, Murty OP. The Essentials of Forensic Medicine & Toxicology. 34th ed. New Delhi: Jaypee Borthers; 2017.
3. Ambade VN, Tumram N, Meshram S, Borkar J. Ligature material in hanging deaths: the neglected area in forensic examination. Egypt J Forensic Sci. 2015;5(3):109-13.
4. Datta M, Banik SK, Datta M, Rahman KGM, Ara M, Islam M. Distinguishing suicidal hanging from homicidal ligature strangulation – a diagnostic accuracy study of autopsy and scene findings. Insight. 2025;8(2):432-8.
5. Sharma BR, Harish D, Sharma A, Sharma S, Singh H. Injuries to neck structures in deaths due to constriction of neck, with a special reference to hanging. J Forensic Leg Med. 2008;15(5):298-305.
6. Suárez-Peñaranda JM, Alvarez T, Miguéns X, Rodríguez-Calvo MS, de Abajo BL, Cortesão M, et al. Characterization of lesions in hanging deaths. J Forensic Sci. 2008;53(3):720-3.
7. Saternus KS, Maxeiner H, Kernbach-Wighton G, Koebke J. Traumatology of the superior thyroid horns in suicidal hanging – an injury analysis. Leg Med (Tokyo). 2013;15(3):134-9.
8. Moinuddin SK, Basha VC. Hanging deaths at tertiary care teaching hospital. Indian J Forensic Med Toxicol. 2021;15(2):1142-7.
9. Alam MS, Islam MS, Uddin NM, Hasan MR, Nurunnabi M. Suicidal hanging deaths in Sylhet: autopsy analysis of 208 cases. Shaheed Syed Nazrul Islam Med Coll J. 2021;6(2):171-6.
10. Sultan MT, Nurunnabi ASM, Jahan Z, Mozaffor M. Socio-demographic profile of unnatural deaths: an autopsy study at a tertiary hospital in Dhaka city. Barind Med Coll J. 2025;11(2):30-3.
11. Siddiqi MM, Jabin N, Bari FJ, Mazumder MAK, Ferdous J, Suraiya R. Autopsy findings in suicidal hanging cases. J Armed Forces Med Coll Bangladesh. 2024;20(2):33-6.
12. Hossain M, Rahman Z, Akhter S. Suicidal death autopsy analysis at Dhaka Medical College. Bangladesh Med J. 2011;40(1):18-21.
13. Datta M, Banik SK, Zoha RB, Syeed S, Rahman R, Keya AT, et al. Autopsy-based indicators of suicidal hanging – a study of ligature marks, salivary signs, and parchmentization. Insight. 2025;8(3):623-9.
14. Ali E, Maksud M, Zubyra S, Hossain MS, Debnath PR, Alam A, et al. Suicide by hanging: a study of 334 cases. Bangladesh Med J. 2014;43(2):90-3.

15. Ahmed T, Ferdous J, Sultana SF, Hossain DI, Dey S, Jeba TR. Analysis of autopsy finding in suicidal death. Planet. 2024;8(1):212-6.

16. Mahesar RA, Raza Ul Mustafa A, Latif M, Azeema N, Rao MA, et al. Suicidal hanging in Pakistan: an exploratory two-year content analysis study. Int Rev Psychiatry. 2024;36(4-5):480-6.

17. Abd-Elwahab Hassan D, Ghaleb SS, Kotb H, Agamy M, Kharoshah M. Suicidal hanging in Kuwait: retrospective analysis of cases from 2010 to 2012. J Forensic Leg Med. 2013;20(8):1118-21.

18. Taktak S, Kumral B, Unsal A, Ozdes T, Buyuk Y, Celik S. Suicidal hanging in Istanbul, Turkey: 1979–2012 autopsy results. J Forensic Leg Med. 2015;33: 44-9.

19. Rao d. An autopsy study of death due to suicidal hanging – 264 cases. Egypt J Forensic Sci. 2016;6(3):248-54.

20. Ambade VN, Tumram N, Meshram S, Borkar J. Ligature material in hanging deaths: the neglected area in forensic examination. Egypt J Forensic Sci. 2015;5(3):109-13.

21. Jayaprakash S, Sreekumari K. Pattern of injuries to neck structures in hanging – an autopsy study. Am J Forensic Med Pathol. 2012;33(4):395-9.

Original Article

Serum Troponin-I Levels Facilitate Early Prediction of Cardiac Toxicity among High-Risk Patients Under Chemotherapy with Doxorubicin

Asaduzzaman M[1], Khatun N[2], Asaduzzaman M[3], Islam MR[4], Alam MJ[5]

ABSTRACT

A quasi-experimental study was conducted in the Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh, between September 2021 to August 2022, to evaluate troponin-I level as a biomarker to detect early-onset of cardiotoxicity among patients under chemotherapy with doxorubicin. We included patients having any malignancy (histopathologically confirmed) and receiving a dose of doxorubicin 45–75 mg/m² BSA 3 weekly in each cycle of chemotherapy. Exclusion criteria were: patients aged <18 years or >70 years, having pre-treatment level of troponin-I >0.08 ng/ml, any pre-existing cardiac disease detected through echocardiography, any significant change in ECG before treatment except sinus tachycardia, known case of hypertension, diabetes mellitus, chronic renal failure, chronic liver disease, obesity (BMI ≥25), previous exposure to chemotherapy or radiotherapy and WHO performance status 3 to 4. However, a non-probability, convenient and purposive sampling technique was adopted. A total of 71 patients were finally enrolled in this study. Multiple assessment were done at baseline and after 3 and 6 cycles of chemotherapy, which included systemic examination, laboratory investigations including complete blood count (CBC), serum troponin-I level, chest radiograph, ECG, echocardiography, ultrasonogram of the whole abdomen and CT scan/MRI, if needed. The mean age of the patients was 32.97±14.1 years. Most of the patients were in the 18–30 years age group (49.4%), followed by 31–40 years age group (22.5%) and 41–50 years age group (15.5%). A male predominance was observed; male-female ratio was 1.63:1. Cardiac toxicity was present in 21(29.6%) patients and absent in 50(70.4%) patients (403.71±42.358 mg/m² BSA vs. 368.36±44.53 mg/m² BSA of mean cumulative dose of doxorubicin; p<0.01). The mean serum troponin-I level at baseline was 0.035±0.025 ng/ml, which raised after three cycles of chemotherapy to 0.061±0.098 ng/ml (p<0.05) and further raised after six cycles to 0.248±0.395 ng/ml (p<0.001). The mean left ventricular ejection fraction (LVEF) at baseline was 64.46±3.749%; after three and six cycles of chemotherapy LVEF decreased to 62.87±3.902% and 60.14±7.112% respectively (p<0.001). Therefore, detection of increased levels of troponin-I facilitate early prediction of cardiac toxicity among high-risk patients under chemotherapy. Our study suggests the necessity of policy adjustment to incorporate routine cardiac screening in clinical practice for cancer patients.

Keywords: *Anthracycline, doxorubicin, cardiac toxicity, troponin-I, malignancy, chemotherapy.*

Mugda Med Coll J. 2026; 9(1): 43-47
DOI: https://doi.org/10.3329/mumcj.v9i1.90817

1. Dr. Mohammad Asaduzzaman, Assistant Registrar, Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka-1212. Email: asaddr32@gmail.com (Corresponding author).
2. Prof. Nazrina Khatun, Professor & Head, Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka-1212.
3. Dr. Mohammad Asaduzzaman, Associate Professor, Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka-1212.
4. Dr. Muhammad Rafiqul Islam, Assistant Professor, Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka-1212.
5. Dr. Mohammed Jahangir Alam, Medical Officer, Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka-1212.

INTRODUCTION

Cancer chemotherapy has made remarkable advances in the treatment of both solid and hematologic malignancies, allowing in many patients the hope for a cure of their cancer. However, these therapies are not without their complications. Cancer treatment-associated cardiotoxicity (CTAC) is becoming an increasing health burden, as the number of cancer survivors increases due to early screening and modern anticancer treatment.[1,2] However, cardiotoxicity is a feared adverse effect that may limit the use of anthracyclines (e.g., doxorubicin) and affect the quality of life and the survival of patients with cancer regardless of oncological prognosis.[1-4] Therefore, clinicians must identify adverse events early and take suitable measures before permanent or irreversible dysfunction.

Anthracyclines either used alone, or in combination with other chemotherapy agents, are widely used agents for the treatment of cancer.[2,4] Anthracyclines e.g., doxorubicin, initiate cardiotoxicity in 5%–48% cases (dose-dependent) through ROS production, mitochondrial dysfunction, DNA damage, and activation of pro-apoptotic pathway leading to cardiomyocyte death.[3] Early detection of cardiotoxicity using biomarkers is critical to help prevent life-threatening cardiac events. The measurement of serum cardiac troponins is the gold standard for the diagnosis of acute myocardial events in humans and it has gained increasing recognition as a new tool for the assessment of cardiotoxicity in several previous studies.[4-7] Due to its unique high-definition technology, elevated serum cardiac troponin-I levels can be detected earlier with the ultrasensitive immunoassay technology.[4,5] Hence, any cardiotoxicity caused by anthracycline can be detected at preclinical phase or later. The role of biomarkers like troponin-I in identifying subclinical cardiotoxicity and its therapy with angiotensin-converting enzyme (ACE) inhibitor to prevent LVEF reduction is a recognized and effective supportive strategy for high-risk patients under chemotherapy.[4]

Following the standard guidelines, solid tumors like sarcomas are frequently treated with anthracyclines, e.g., doxorubicin, and many cancer survivors subsequently develop cardiotoxicity,[8,9] which is also true for Bangladeshi cancer patients.[10] There are ongoing searches for early detection of cardiotoxicity. Troponin-I may be an ideal biomarker to detect the early onset of cardiotoxicity, which is readily available, and inexpensive. Even in Bangladesh in any resource-strained settings, estimation of troponin-I in cancer patients may reduce morbidity and mortality from CTAC.[4,8,9] However, no such study has been conducted in our country to date. Therefore, we proposed this study to evaluate troponin-I level as a biomarker to detect early-onset of cardiotoxicity among patients under chemotherapy. It is expected that this study will play a significant role in the perspective of Bangladesh; in a resource-challenged country like Bangladesh, a simple blood test like troponin-I could be used for early-detection of chemotherapy-induced cardiotoxicity in cancer patients and help clinicians reduce further morbidity and mortality as well as treatment costs.

METHODS

This quasi-experimental study (before and after study) was conducted in the Department of Medical Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka, Bangladesh, between September 2021 to August 2022. Malignant patients who were admitted under the Department of Medical Oncology and had planned chemotherapy with anthracycline (e.g., doxorubicin) within the time frame were the study population. Samples were selected through inclusion and exclusion criteria from those patients (following Chu & DeVita).[11] We included patients having any malignancy (e.g., sarcoma) that was histopathologically confirmed and those who received a dose of doxorubicin 45-75 mg/m² BSA 3 weekly in each cycle of chemotherapy. Exclusion criteria were: patients aged <18 years and >70 years, having pre-treatment level of troponin-I >0.08 ng/ml, any pre-existing cardiac disease detected through echocardiography, significant changes in ECG before treatment except sinus tachycardia, known case of hypertension, diabetes mellitus, chronic renal failure, chronic liver disease, obesity (BMI e"25), previous exposure to chemotherapy or radiotherapy and WHO performance status 3 to 4. A non-probability, convenient and purposive sampling technique was adopted.

The baseline evaluation included demographic characteristics, physical examinations and laboratory investigations, including complete blood count, diabetes panel, lipid profile, renal and hepatic function tests, serum troponin-I level (troponin was

considered positive for values e"0.08 ng/mL, according to Cardinale et al.),[12] ECG and echocardiography (2D, M-mode) report was done by cardiologist, chest x-ray postero-anterior (P/A) view, ultrasonography of the whole abdomen and other imaging modalities, immunohistochemistry, if needed, cytology and biopsy made the diagnosis of malignancies with histopathology (along with immunohistochemistry). Similar assessments were done following treatment (after 3 and 6 cycles of chemotherapy) including clinical response by systemic examination, WHO performance status, complete blood count (CBC), serum troponin-I level, chest x-ray P/A view, ultrasonogram of the whole abdomen, ECG, echocardiography, and CT scan/ MRI, if needed.

Data was recorded in the patient data sheet and after scrutinizing, cleaning and editing, relevant data was compiled in a master sheet in the computer. Statistical analysis was done by using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). Categorical data was expressed as frequency and percentage, while continuous data was expressed as mean±SD. Categorical variables were compared by using paired sample t-test and independent sample t-test where applicable. For all analyses, the significance level was set at 0.05, and a p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 32.97±14.1 years. Most the patients were in the 18–30 years age group (49.4%), followed by 31–40 years age group (22.5%), 41–50 years age group (15.5%), 51–60 years age group (7%) and 61–70 years age group (5.6%). A male predominance was observed (62% were male and 38% were female); male-female ratio was 1.63:1 (Table-I). At baseline no patient had troponin-I level >0.08 ng/ ml. However, after completion of three cycles of chemotherapy with doxorubicin 5(7.0%) patients showed positive troponin-I levels (i.e., (>0.08 ng/ml) and after six cycles, a total of 21(29.6%) showed such positive results (Table-II). The mean serum troponin-I level at baseline, day after three and six cycles of chemotherapy were estimated 0.035±0.025 ng/ml, 0.061±0.098 ng/ml and 0.248±0.395 ng/ml respectively indicating a gradual rise over time. The differences were statistically significant (p<0.001) (Table-III). The mean left ventricular ejection fraction (LVEF) at baseline, after three and six cycles of chemotherapy were 64.46±3.749%, 62.87±3.902% and 60.14±7.112% respectively indicating a gradual decrease over time. The differences were statistically significant (p<0.001) (Table-IV). No cardiac toxicity was found in 50 patients and their mean cumulative dose of doxorubicin was 368.36±44.53 mg/m^2 BSA. In contrast, cardiac toxicity was observed in 21 patients and their mean cumulative dose of doxorubicin was 403.71±42.358 mg/m^2 BSA. This difference was statistically highly significant (p<0.01) (Table-V).

Table-I: *Age and gender distribution of the chemotherapy patients (N=71)*

Variables	Frequency (Percentage)
Age group (in years)	
18–30	35 (49.4)
31–40	16 (22.5)
41–50	11 (15.5)
51–60	5 (7.0)
61–70	4 (5.6)
Gender	
Male	44 (62.0)
Female	27 (38.0)

Table-II: *Distribution of troponin-I positive cases among chemotherapy patients (N=71)*

Serum Troponin-I (>0.08 ng/ml)	Frequency	Percentage
At baseline	0	0
After 3 cycles	5	7.0
After 6 cycles	21	29.6

Table-III: *Troponin-I at baseline, day after completion of 3 and 6 cycles of chemotherapy*

Serum Troponin-I (ng/ml)	Mean±SD	t-value	p-value
Baseline	0.035±0.025	-2.142	<0.05
After 3 cycles	0.061±0.098		
Baseline	0.035±0.025	-4.558	<0.001
After 6 cycles	0.248±0.395		
After 3 cycles	0.061±0.098	-4.432	<0.001
After 6 cycles	0.248±0.395		

Paired t-test was applied to reach p-value.

Table-IV: *Left ventricular ejection fraction (LVEF) at baseline, after 3 and 6 cycles of chemotherapy*

LVEF (%)	Mean±SD	t-value	p-value
Baseline	64.46±3.749	3.984	<0.001
After 3 cycles	62.87±3.902		
Baseline	64.46±3.749	4.011	<0.001
After 6 cycles	60.14±7.112		
After 3 cycles	62.87±3.902	5.421	<0.001
After 6 cycles	60.14±7.112		

Paired t-test was applied to reach p-value.

Table-V: *Association between cumulative dose of doxorubicin and cardiac toxicity*

Cardiac toxicity	Cumulative dose of doxorubicin (mg/m² BSA) Mean±SD	t-value	p-value
Absent (n=50)	368.36±44.53	-3.161	<0.01
Present (n=21)	403.71±42.358		

Independent-sample t-test was applied to reach p-value.

DISCUSSION

In the present study, 71 cancer patients were enrolled based on selection criteria. The mean age of the patients was 32.97±14.1 years. In similar studies, Sandri et al.[13] reported that the mean age of the participants was 47±11 years, while Sawaya et al.[14] reported average age 48 years and Cardinale et al.[7] found the mean age 50±13 years. Our result is comparatively lower than their study population. The underlying causes of such discrepancies might be due to inclusion of more patients of Ewing sarcoma. Besides, age reporting in our culture is still questionable as age verification is absent our healthcare settings, which might contribute to our finding.

In this study, at baseline no patient had troponin-I level >0.08 ng/ml. However, after completion of three cycles of chemotherapy with doxorubicin 5(7.0%) patients showed positive troponin-I levels (i.e., (>0.08 ng/ml) and after six cycles, a total of 21(29.6%) showed such positive results. In previous studies, Cardinale et al.[6] and Sandri et al.[13] observed similar proportion of troponin-I positive patients (30% and 32% respectively), which are comparable to our finding.

The mean serum troponin-I level at baseline, day after three and six cycles of chemotherapy were estimated 0.035±0.025 ng/ml, 0.061±0.098 ng/ml and 0.248±0.395 ng/ml respectively indicating a gradual rise over time. The differences were statistically significant (p<0.001). Cardinale et al.[12] studied on 703 patients using the same cut-off value of troponin-I (0.08 ng/ml) and reported 0.16±0.24 ng/ml as the mean troponin-I value after treatment completion, which is lower than the current study finding. The huge difference in sample size might be attributable to such different results. In contrast, Sandri et al.[13] reported a higher mean troponin-I value after treatment (0.63±0.54 ng/ml). Michel et al.[15] compared post-treatment and pre-treatment troponin levels described in 42 studies. Post-treatment troponins were significantly higher compared to pre-treatment troponins (OR 14.3, 95% CI 6.0-34.1; n=3049). Additionally, analysis of absolute serum troponins revealed increased post-treatment compared to pre-treatment values (SMD 1.0; 95% CI 0.6 to 1.3; n=811). Post-treatment troponins were elevated in 22.4% of patients. Those findings are in congruence with our results.

For cardiac functions, we compared the mean left ventricular ejection fraction (LVEF); at baseline, after three and six cycles of chemotherapy, LVEF were were 64.46±3.749%, 62.87±3.902% and 60.14±7.112% respectively indicating a gradual decrease over time. The differences were statistically significant (p<0.001). Cardinale et al.[7] reported baseline LVEF in patients with cardiotoxicity as 61±3.6% and 63±3.7% in patients with no cardiotoxicity (p<0.001), at the end of chemotherapy LVEF in patients with cardiotoxicity 55±4.6% and patients with no cardiotoxicity 61±4% (p<0.001). Sandri et al.[13] reported an 18% reduction of LVEF in troponin-I positive patients, while only 3% reduction in troponin-I negative patients. Their findings are comparable to our results as well.

In our study, cardiac toxicity was not observed in 50 patients and their mean cumulative dose of doxorubicin was 368.36±44.53 mg/m² BSA. On the other hand, cardiac toxicity was found in 21 patients and their mean cumulative dose of doxorubicin was 403.71±42.358 mg/m² BSA. The difference was statistically significant (p<0.01). Cardinale et al.[7]

reported cumulative anthracycline dose in patients with cardiotoxicity as 359±172 mg/m² and in patients with no cardiotoxicity as 299±144 mg/m² ($p<0.001$). This finding is comparable to our study result.

Our study has several limitations. Single-centre design and small sample size may limit generalizability. Besides, we studied only troponin-I as biomarker; however, using other biomarkers like troponin-T, topoisomerase 2β, myeloperoxidase, NT-proBNP could be employed to get comparable and better results. More follow-up visits were needed to precisely evaluate cumulative dose-related cardiotoxicity. These factors need to be addressed in future research.

CONCLUSION

Our data suggests that serum troponin-I levels increase with the cumulative dose of doxorubicin. Besides, increased dose of doxorubicin is associated with decreased level of left ventricular functions of the heart. Therefore, evaluating biochemical parameter like troponin-I can aid in diagnosing sub-clinical cardiac damage. Detection of increased concentrations of troponin-I can facilitate early prediction of cardiac toxicity among high-risk patients under chemotherapy.

Conflict of Interest: No potential conflict of interest was reported by the authors.

Funding Source: Self-funded.

Ethical Approval: Ethical approval for this study was obtained from the Ethics Committee of National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh (Ref. No. NICRH/Ethics/2022/44).

Authors' Contribution: Concept and design: M Asaduzzaman, N Khatun; Patient selection, data collection, compilation, and analysis: M Asaduzzaman, MJ Alam; Manuscript preparation, editing and final submission: M Asaduzzaman, N Khatun, M Asaduzzaman, MR Islam, MJ Alam.

REFERENCES

1. Volkova M, Russell R 3rd. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Curr Cardiol Rev. 2011;7(4):214-20.
2. Bhagat A, Kleinerman ES. Anthracycline-induced cardiotoxicity: causes, mechanisms, and prevention. Adv Exp Med Biol. 2020;1257:181-92.
3. Narezkina A, Narayan HK, Zemljic-Harpf AE. Molecular mechanisms of anthracycline cardiovascular toxicity. Clin Sci (Lond). 2021; 135(10):1311-32.
4. Ananthan K, Lyon AR. The role of biomarkers in cardio-oncology. J Cardiovasc Transl Res. 2020;13(3):431-50.
5. Wu AH, Lu QA, Todd J, Moecks J, Wians F. Short- and long-term biological variation in cardiac troponin I measured with a high-sensitivity assay: implications for clinical practice. Clin Chem. 2009;55(1):52-8.
6. Cardinale D, Sandri MT, Martinoni A, Tricca A, Civelli M, Lamantia G, et al. Left ventricular dysfunction predicted by early troponin I release after high-dose chemotherapy. J Am Coll Cardiol. 2000;36(2):517-22.
7. Cardinale D, Colombo A, Bacchiani G, Tedeschi I, Meroni CA, Veglia F, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation. 2015;131(22):1981-8.
8. Khouri MG, Klein MR, Velazquez EJ, Jones LW. Current and emerging modalities for detection of cardiotoxicity in cardio-oncology. Future Cardiol. 2015;11(4):471-84.
9. Cardinale D, Cipolla CM. Chemotherapy-induced cardiotoxicity: importance of early detection. Expert Rev Cardiovasc Ther. 2016;14(12):1297-9.
10. Islam MR, Siddiqua SM, Islam R, Hossain A, Al Ayub SB, Islam MS, et al. Lung cancer in Bangladesh. J Thorac Oncol. 2023;18(8):972-80.
11. Chu E, DeVita Jr. VT. Physician's Cancer Chemotherapy Drug Manual 2021. Burlington, MA; Jones & Bartlett Learning; 2022.
12. Cardinale D, Sandri MT, Colombo A, Colombo N, Boeri M, Lamantia G, et al. Prognostic value of troponin I in cardiac risk stratification of cancer patients undergoing high-dose chemotherapy. Circulation. 2004;109(22):2749-54.
13. Sandri MT, Cardinale D, Zorzino L, Passerini R, Lentati P, Martinoni A, et al. Minor increases in plasma troponin I predict decreased left ventricular ejection fraction after high-dose chemotherapy. Clin Chem. 2003;49(2):248-52.
14. Sawaya H, Sebag IA, Plana JC, Januzzi JL, Ky B, Cohen V, et al. Early detection and prediction of cardiotoxicity in chemotherapy-treated patients. Am J Cardiol. 2011;107(9):1375-80.
15. Michel L, Mincu RI, Mahabadi AA, Settelmeier S, Al-Rashid F, Rassaf T, Totzeck M. Troponins and brain natriuretic peptides for the prediction of cardiotoxicity in cancer patients: a meta-analysis. Eur J Heart Fail. 2020;22(2):350-61.

Original Article

Supracostal Punctures for Percutaneous Nephrolithotomy: Factors that Predict Safety, Success, and Stone-Free Rate in Patients with Renal Stone

Rahman KMA[1], Hasan MM[2], Rashid MM[3], Alam MM[4], Khan SI[5], Arafuzzaman K[6], Alam MA[7], Amin MA[8]

ABSTRACT

Percutaneous nephrolithotomy (PCNL) is the standard treatment for large or complex renal stones. Supracostal puncture offers an alternative access route when infra-costal access is challenging, but it carries potential risks. A cross-sectional, observational study was conducted in the Department of Urology, Mugda Medical College Hospital, Dhaka, Bangladesh, between January 2022 and December 2024, to evaluate the safety, success, and stone-free rates of supracostal PCNL and identify factors predicting outcomes in patients with renal stones. A total of of 70 patients (40 males and 30 females) undergoing PCNL via supracostal puncture were included in this study. Stone characteristics, puncture levels, operative details, complications, and stone-free rates were analyzed. The mean age of the patients was 29.6±8.4 years. Stone-free rate (SFR) was 89.4%. Complications occurred in 14.3% of the patients including intraoperative haemorrhage (5.7%), hydrothorax (4.3 pneumothorax (2.9%), and delayed haemorrhage (1.4%). Multivariate logistic regression analysis showed that stone size (OR=0.65, 95% CI 0.48–0.89, p<0.01), stone type (staghorn vs non-staghorn; OR=0.42, 95% CI 0.18–0.98, p<0.05), and degree of hydronephrosis (OR=1.34, 95% CI 1.01–1.78, p<0.05) are independent predictors of stone-free status. However, gender, puncture level, and number of tracts were not significant predictors (p>0.05) Supracostal PCNL is a safe and effective approach for complex renal stones when infra-costal access is not feasible. Careful patient selection and surgical expertise are critical to maximizing stone-free rates and minimizing complications.

Keywords: *Supracostal percutaneous nephrolithotomy, renal calculi, staghorn stone, operative outcome, minimally invasive urology*

Mugda Med Coll J. 2026; 9(1): 48-52
DOI: https://doi.org/10.3329/mumcj.v9i1.90821

INTRODUCTION

Renal stone disease is a common urological condition, with an increasing incidence worldwide due to dietary changes, obesity, and metabolic disorders.[1] Large or complex renal calculi, particularly staghorn stones, pose significant challenges to effective management and are associated with increased morbidity if left untreated.[2] Percutaneous nephrolithotomy (PCNL) has emerged as the standard treatment modality for stones larger than 2 cm, offering high stone clearance rates with relatively low complication rates.[3]

The success of PCNL depends largely on optimal access to the collecting system. Traditionally,

1. Dr. K M Arifur Rahman, Assistant Registrar, Department of Urology, Mugda Medical College Hospital, Dhaka-1214. Email: arifrpmch@gmail.com (Corresponding author)
2. Dr. Md. Mahmud Hasan, Associate Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.
3. Dr. Mohammod Mamunur Rashid, Associate Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.
4. Dr. Muhammad Mahmud Alam, Associate Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.
5. Dr. Shariful Islam Khan, Senior Consultant, Department of Urology, Mugda Medical College Hospital, Dhaka-1214.
6. Dr. Khondaker Arafuzzaman, Assistant Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.
7. Dr. Md. Akter Alam, Assistant Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.
8. Dr. Mohammad Al Amin, Assistant Professor, Department of Urology, Mugda Medical College & Hospital, Dhaka-1214.

infracostal punctures below the 12th rib are preferred due to the reduced risk of thoracic complications.[4] However, in certain cases, particularly when stones are located in the upper pole or calyces with complex anatomy, supracostal punctures – accessing the kidney above the 12th or 11th rib – may be necessary to achieve direct tract alignment and facilitate complete stone clearance.[5,6] Despite its advantages in providing a straight tract to the upper pole, supracostal access has been associated with increased risk of complications, including pneumothorax, hydrothorax, and pleural injury.[7,8] Previous studies have evaluated the safety and efficacy of supracostal PCNL, reporting variable complication rates and stone-free outcomes. For instance, studies have demonstrated stone-free rates ranging from 80% to 95%, with major thoracic complications occurring in 2–10% of cases.[9,10] Factors influencing the success of PCNL include stone size, composition, location, degree of hydronephrosis, and surgeon experience.[11] Understanding these predictors is crucial to optimize patient selection, minimize complications, and improve outcomes.

Despite the growing body of literature, data from single-center experiences, particularly in developing countries, remain limited. Local anatomical variations, differences in patient demographics, and variations in surgical expertise may influence outcomes, underscoring the need for institution-specific analyses.[12] Evaluating supracostal PCNL in such contexts provides insights into its applicability, safety, and effectiveness in routine clinical practice. Therefore, the present study aims to assess the outcomes of supracostal PCNL in patients with renal stones, focusing on stone-free rates, safety profile, and factors predicting successful clearance. By analyzing perioperative parameters, complications, and predictive factors, this study seeks to contribute to the evidence base guiding the selection and optimization of supracostal access in renal stone management.

METHODS

This cross-sectional, observational study was conducted in the Department of Urology, Mugda Medical College Hospital, Dhaka, Bangladesh, between January 2022 and December 2024. The study included patients with renal stones requiring percutaneous nephrolithotomy (PCNL) via a supracostal approach. A total of 70 patients (comprising 40 males and 30 females) were enrolled in the study. Inclusion criteria were patients with renal stones larger than 2 cm, complex staghorn calculi, impacted stones at pelvi-ureteric junction, or stones located in the upper pole calyces requiring supracostal access. Our exclusion criteria included patients with radiolucent stone, uncorrected coagulopathy, untreated urinary tract infection, or severe cardiopulmonary comorbidities precluding general anaesthesia.

All patients underwent a detailed history and physical examination. Laboratory investigations included complete blood count, renal function tests, coagulation profile, and urine culture. Imaging studies consisted of non-contrast computed tomography (NCCT) of the kidneys, ureters, and bladder to assess stone size, number, location, and anatomy of the collecting system. Hydronephrosis grading was noted for each patient.[4,5]

PCNL was performed under general anaesthesia with the patient in the prone position. Supracostal puncture was achieved either above the 12th rib or, in selected cases, above the 11th rib, depending on stone location and collecting system anatomy. Fluoroscopy guidance was used to localize the calyx for puncture. After successful puncture, a guidewire was introduced into the collecting system, followed by tract dilation using serial Alken dilators up to 24–30 Fr. Nephroscopy was introduced, and stones were fragmented using a pneumatic or ultrasonic lithotripter.[6,7]

A nephrostomy tube and D-J stent were placed at the conclusion of the procedure in all patients. Postoperative analgesia and antibiotics were administered as per standard protocol. Hemoglobin levels and vital parameters were monitored, and patients were assessed for complications including bleeding, pneumothorax, hydrothorax, and sepsis.[8]

The primary outcome was the stone-free rate (SFR), defined as the absence of residual fragments >4 mm on postoperative imaging (x-ray of KUB region) within 7 days as residual stone <4 mm is considered clinically insignificant residual fragment. Secondary outcomes included perioperative complications, duration of surgery, number of access tracts required, and hospital stay. Complications were graded using the Clavien-Dindo classification.[9,10]

Data was scrutinized, compiled and coded. Data analysis was done using IBM SPSS Statistics for

Windows, version 23 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±SD (standard deviation), while categorical variables were expressed as frequencies and percentages. Then, univariate and multivariate logistic regression analyses were performed. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 70 patients underwent supracostal PCNL. The mean age was 29.6±8.4 years (ranging between 18 and 55 years). There were 40 males (57.1%) and 30 females (42.9%). Right kidney stones were present in 42 patients (60%) and left kidney stones in 28 patients (40%). Staghorn stones were present in 31 patients (44.3%), while non-staghorn stones were seen in 39 patients (55.7%). The mean stone size was 28.4±9.6 mm. Supracostal puncture above the 12th rib was performed in 50 cases (71.4%) and above the 11th rib in 20 cases (28.6%). Single-tract PCNL was achieved in 62 patients (88.6%), while multiple tracts were required in 8 patients (11.4%). The mean duration of operation was 85±20 minutes. (Table-I). The overall stone-free rate (SFR) was 89.4% (63/70). Complete clearance was achieved in 100% of stones <2 cm, 93.3% in stones 2–3 cm, and 77.4% in staghorn stones. Patients with severe hydronephrosis had 100% SFR, while moderate hydronephrosis was associated with 87.1% SFR (Fig. 1). Overall, 14.3% (10/70) of patients experienced complications. Intraoperative hemorrhage occurred in 4 patients (5.7%), hydrothorax in 3 patients (4.3%), pneumothorax in 2 patients (2.9%), and delayed haemorrhage in 1 patient (1.4%). None of patients required thoracostomy (Table-II). Multivariate logistic regression identified stone size (OR 0.65, 95% CI 0.48–0.89, p<0.01), stone type (staghorn vs non-staghorn; OR 0.42, 95% CI 0.18–0.98, p<0.05), and degree of hydronephrosis (OR 1.34, 95% CI 1.01–1.78, p<0.05) as independent predictors of stone-free status. Gender, puncture level, and number of tracts were not significant predictors (p>0.05) (Table-III).

Table-I: *Demographic and clinical characteristics of the patients (N=70)*

Variables	Frequency	Percentage
Gender		
Male	40	57.1
Female	30	42.9
Affected kidney		
Right	42	60.0
Left	28	40.0
Stone types		
Staghorn	31	44.3
Non-staghorn	39	55.7
Puncture level		
Supra-12th rib	50	71.4
Supra-11th rib	20	28.6
Number of tracts		
Single	62	88.6
Multiple	8	11.4

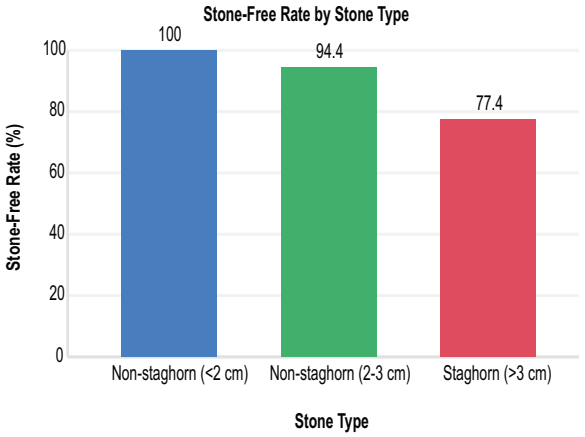

Fig. 1: *Bar diagram showing stone-free rate by stone types.*

Table-II: *Complications (Clavien-Dindo Classification) (N=10)*

Complications	Frequency	Percentage	Clavien-Dindo Grade
Intraoperative haemorrhage	4	5.7	II
Hydrothorax	3	4.3	II
Pneumothorax	2	2.9	IIIa
Delayed haemorrhage	1	1.4	II

Table-III: *Univariate and multivariate logistic regression analyses*

Prediction factors	Univariate **analysis** (p-value)	Multivariate **analysis** (OR)	95% CI	Multivariate **analysis** (p-value)
Stone size	0.01*	0.65	0.48–0.89	0.01*
Stone type (staghorn vs. non-staghorn)	0.02*	0.42	0.18–0.98	0.04*
Degree of hydronephrosis	0.03*	1.34	1.01–1.78	0.03*
Gender	0.88	-	-	0.91
Puncture level (11th vs. 12th)	0.45	-	-	0.52
Number of tracts	0.12	-	-	0.08

*=Statistically significant; OR=Odds Ratio, CI=Confidence Interval.

DISCUSSION

The mean age of the patients was 29.6±8.4 years, with a slight male predominance (57.1%), which aligns with previous reports indicating a higher prevalence of urolithiasis among young adult males.[1,2] Right-sided stones were more common (60%), consistent with the anatomical predilection described in prior studies.[3,4] The mean stone size was 28.4±9.6 mm, with nearly half of the patients presenting with staghorn stones (44.3%). This reflects a challenging patient population, as staghorn stones are typically associated with lower stone-free rates (SFR) and higher procedural complexity.[4]

Supracostal access was predominantly performed above the 12th rib (71.4%), with a minority requiring supra-11th rib puncture. Single-tract PCNL was feasible in 88.6% of cases, and the mean operative time was 85±20 minutes. These findings corroborate prior literature reporting that single supracostal tracts can provide adequate access for most renal stones, minimizing invasiveness while maintaining high clearance rates.[5,6] Multiple tracts were required only in complex or staghorn stones, which is consistent with established practice that more extensive stone burdens necessitate additional access points to achieve complete clearance.[7]

The overall SFR in our study was 89.4%, comparable to previously published series of supracostal PCNL reporting SFRs between 85–95%.[8,9] Stratification by stone type and size showed that small non-staghorn stones (<2 cm) were completely cleared in all patients (100%), medium stones (2–3 cm) in 94.4%, and staghorn stones in 77.4% with only 7 (10.6%) patients may needs ancillary therapy. These results highlight that stone complexity remains the primary determinant of clearance. Notably, patients with severe hydronephrosis achieved 100% SFR, possibly due to the dilated collecting system facilitating easier access and manipulation of calculi.[10] Multivariate analysis confirmed that stone size and staghorn morphology were independent predictors of incomplete clearance, while hydronephrosis positively influenced stone-free outcomes. Puncture level, number of tracts, and gender did not significantly impact SFR, suggesting that procedural technique and patient anatomy are secondary to stone characteristics in determining success.

The overall complication rate was 14.3%, with most events being minor (Clavien-Dindo grade II) including intraoperative haemorrhage (5.7%), hydrothorax (4.3%) and delayed haemorrhage in 1 patient (1.4%). Pneumothorax occurred in 2 patients (2.9%), which was classified as grade IIIa; however, none of patients required thoracostomy. These findings are in line with the reported risk profile of supracostal PCNL, where pleural complications occur in 2–5% of cases, and hemorrhage is the most frequent adverse event.[11-14] The relatively low complication rate in our cohort may be attributed to careful imaging guidance, limited tract number, and adherence to standard surgical protocols. Overall, our results reinforce that supracostal PCNL is a safe and effective option for managing renal stones, including complex staghorn calculi, especially when performed with a single tract whenever feasible.

Our study has some limitations that are comprised with small sample size from a single center with short follow up period. Large sample with multicenter long follow up period is recommended. The study also underscores the importance of preoperative assessment of stone size, morphology, and hydronephrosis in predicting procedural success. Surgeons should anticipate lower clearance rates for

staghorn and larger stones and counsel patients accordingly, while minor complications can generally be managed conservatively.

CONCLUSION

To conclude, supracostal PCNL offers high SFR with acceptable morbidity, with stone size, type, and degree of hydronephrosis being the main determinants of outcome. These findings support its continued use as a first-line approach for complex renal calculi, provided careful planning and technique are employed.

Conflict of interest: None declared.

Funding statement: No funding received.

Ethical approval: The study was approved by the Institutional Review Board (IRB) of Mugda Medical College, Dhaka, Bangladesh.

Authors' contribution: Conceptualization and design of the study: KMA Rahman, MM Hasan, MM Rashid; Patient selection, data collection, compilation and analysis: KMA Rahman, MM Hasan, MM Rashid, MM Alam, SI Khan, K Arafuzzaman, MA Alam, MA Amin; Manuscript preparation, editing and final submission: KMA Rahman, MM Hasan, MM Rashid, MM Alam, SI Khan, K Arafuzzaman, MA Alam, MA Amin.

REFERENCES

1. Türk C, Petøík A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU Guidelines on Interventional Treatment for Urolithiasis. Eur Urol. 2016;69(3):475-82.
2. Scales CD Jr, Smith AC, Hanley JM, Saigal CS. Prevalence of kidney stones in the United States. Eur Urol. 2012;62(3):160-5.
3. Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: urolithiasis. J Urol. 2005;173(5):848-57.
4. Smith AD, Preminger GM, Assimos DG, Dretler SP, Krambeck AE, Miller NL, et al. AUA guideline: management of staghorn calculi: diagnosis and treatment recommendations. J Urol. 2016;195(3): 1154-61.
5. Al-Kandari AM, Ibrahim HM, Shaaban HS, El-Sherbiny M, El-Nahas AR. Role of ureteral stenting after uncomplicated ureteroscopy for distal ureteral stones: a randomized, controlled trial. Urolithiasis. 2018;46(2):145-152.
6. Desai MR, Shah K, Desai M, Ganpule A, Sabnis RB. Percutaneous nephrolithotomy for complex pediatric renal calculus disease. J Endourol. 2009;23(8):1221-6.
7. Akman T, Binbay M, Sari E, Yuruk E, Tepeler A, Akcay M, et al. Factors affecting bleeding during percutaneous nephrolithotomy: single surgeon experience. J Endourol. 2011;25(4):489-94.
8. Michel MS, Trojan L, Rassweiler J. PCNL: current status and future directions. World J Urol. 2007;25(3):331-8.
9. Kumar A, Agarwal MM, Gupta NP. Percutaneous nephrolithotomy: a review of 1000 cases. Indian J Urol. 2020;36(3):215-222.
10. Turna B, Tefekli A, Akman T, Binbay M, Sari E, Tepeler A, et al. Comparison of percutaneous nephrolithotomy and retrograde intrarenal surgery for the treatment of renal calculi: a prospective, randomized trial. Urology. 2007;69(1):34-8.
11. Ganpule AP, Desai MR. Mini-percutaneous nephrolithotomy: technique and outcomes. Indian J Urol. 2010;26(3):168-73.
12. Sakly A, Khaldi S, Touati A, Dimassi E, Zakhama W, Binous Y. Outcomes and complications of percutaneous nephrolithotomy as primary versus secondary procedure for kidney stones: a prospective cohort study. Ann Med Surg (Lond). 2024;86(10):5711-5.
13. Akman T, Binbay M, Tekinarslan E, Ozkuvanci U, Kezer C, Erbin A, et al. Outcomes of percutaneous nephrolithotomy in patients with solitary kidneys: a single-center experience. Urology. 2011;78(2): 272-6.
14. Shi X, Peng Y, Li L, Li X, Wang Q, Zhang W, et al. Renal function changes after percutaneous nephrolithotomy in patients with renal calculi with a solitary kidney compared to bilateral kidneys. BJU Int. 2018;122(4):633-8.

Original Article

Effectiveness of Bedside Leucodepletion Filter in Multi-Transfuse Thalassemia Patients

Urmi AA[1], Khatun A[2], Akter UM[3], Rahman AHMS[4], Chakrabarty T[5], Yasmin R[6], Appolo AM[7], Alam MM[8]

ABSTRACT

Multi-transfused thalassemia patients are prone to transfusion-related complications. Febrile nonhemolytic transfusion reactions (FNHTR) are a relatively common complication associated with allogenic transfusions. As leucocytes have been implicated in the mechanism of FNHTR, it has been proposed that the transfusion of leucodepleted RBCs should be associated with a decreased incidence of FNHTR. Currently, the best leucodepletion can be achieved using leucodepletion filter. A quasi-experimental study was carried out between March 2019 and August 2021 in the Department of Transfusion Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, to evaluate the effectiveness of bedside leucodepletion filter in decreasing febrile nonhemolytic transfusion reactions (FNHTR) in multi-transfused thalassemia patients. We adopted a purposive sampling method. A total of 84 transfusion dependent thalassemia patients were included in this study according to inclusion and exclusion criteria and divided equally into two groups – intervention group and comparison group. Allocation of intervention was performed by non-randomized alternate assignment. The intervention group received packed red blood cells using leucodepletion filters, while the comparison group received packed red blood cells with conventional blood transfusion filters. The incidence of FNHTR was evaluated between these two groups. The mean age was 19.11±16.54 years in the intervention group and 15.79±10.83 years in the comparison group. Females were predominant in both groups, i.e., 59.5% and 54.8% in intervention group and comparison group respectively. Among adverse reactions, 21(25%) of the patients experienced chills and rigors – 2(4.8%) in the intervention group and 19(45.2%) in the comparison group. Other symptoms were only observed in the comparison group such as fever (38.1%), vomiting (4.8%), myalgia (7.1%), hypotension (2.4%) and skin rash (2.4%). Only 2(4.8%) patients had FNHTR in intervention group, while 25(59.5%) in comparison group experienced FNHTR. FNHTR was observed significantly lower (OR=29.4; CI=5.72–100) in the intervention group ($p<0.05$). To conclude, use of bedside leucodepletion filter significantly decreased the febrile nonhemolytic transfusion reactions in multi-transfused thalassemia patients.

Keywords: *Thalassemia, Blood transfusion, Transfusion reaction, FNHTR, Leucodepletion filter.*

Mugda Med Coll J. 2026; 9(1): 53-58
DOI: https://doi.org/10.3329/mumcj.v9i1.90826

1. Dr. Aklima Akther Urmi, Assistant Professor, Department of Transfusion Medicine, Dhaka Medical College Hospital, Dhaka-1000. Email: aklima0191@gmail.com (Corresponding author).
2. Prof. Ayesha Khatun, Professor and Head, Department of Transfusion Medicine, Bangladesh Medical University (BMU), Dhaka-1000.
3. Dr. Umme Mezbah Akter, Assistant Professor, Department of Transfusion Medicine, Khulna City Medical College Hospital, Khulna-9100.
4. Dr. A.H.M. Saik Rahman, Assistant Professor, Department of Transfusion Medicine, Ad-din Barrister Rafiq-Ul-Huq Hospital, Postogola, Dhaka-1211.
5. Dr. Tonusree Chakrabarty, Assistant Professor, Department of Transfusion Medicine, Dhaka Medical College Hospital, Dhaka-1000.
6. Dr. Rumana Yasmin, Associate Professor, Department of Transfusion Medicine, Universal Medical College Hospital, Dhaka-1215.
7. Dr. Al Mahmood Appolo, Resident Physician, National Gastroliver Institute & Hospital (NGIH), Dhaka-1212.
8. Dr. Md. Mahbubul Alam, Junior Consultant (Medicine), National Gastroliver Institute & Hospital (NGIH), Dhaka-1212.

INTRODUCTION

Thalassemia is a blood disorder in which an abnormal form of hemoglobin is made due to genetic aberration.[1] Approximately 5000 children are born with thalassemia each year in Bangladesh.[2] Blood transfusion is the prime therapy for thalassemia major but is a double-edged sword with substantial cumulative risks including transfusion reactions, allo immunization, and transfusion transmitted infections.[3] Now-a-days thalassemia is a major health care challenge in Bangladesh and the largest consumer of its transfusion services. It is reported that 3% of the total blood is collected is spent on thalassemia patients.[2] Blood is an expensive and limited resource. Since it can save lives, it also leads to a number of adverse reactions in the recipients. Adverse reactions are an undesirable effect in a patient linked with the administration of blood or blood products.[3] Half a century ago only whole blood was used for transfusion. However, now-a-days, whole blood has been separated into its various components such as RBCs, platelets and plasma.[4] The average amount of leucocytes present in donated human blood is estimated to be 109/unit.[1] Until recently, little attention had been paid to the leucocytes present in various blood components. However, it has been shown that removal of leucocytes can minimize the risk associated with these contaminating leucocytes such as febrile nonhemolytic transfusion reactions (FNHTR), HLA alloimmunization, platelet refractoriness.[1,5-7]

Thalassemia major patients are dependent on regular transfusion to sustain life. Multi transfuse thalassemia patients are prone to transfusion related complications. A common adverse effect of chronic transfusion in these patients is FNHTR with an occurrence rate of about 0.5-6.8% of all units transfused.[5] The FNHTR occur due to immune reaction of the recipient's against donor leucocytes. FNHTR typically occur during transfusion but may arise within 4 to 6 hours after the transfusion has been completely administered. Most FNHTR are self-limited; characterized by fever (>100.4ºF or 38°C), chills and rigors. Nausea, vomiting, dyspnoea, and hypotension may accompany these reactions.[3,5,6] These reactions are generally not life threatening, but they are expensive in their management, evaluation, associated blood product wastage.[5] FNHTR are results from leucocytes in transfused blood, destroyed by antibodies in the recipient, generating pyrogen in vivo or by pyrogenic cytokines such as IL-6, IL-8, TNF-α, which are released during storage by contaminating leucocytes and platelets. In a multivalent analysis, the storage duration of RBCs before transfusion was identified as a more significant factor associated with FNHTR than leucocyte contamination.[6,7] However, the ideal product for transfusion in thalassemia is packed red cells, preferably leucodepleted. According to the guidelines, the total amount of leucocyte present in a blood unit should be <5×106/unit.[2] Leucodepletion is a process of removing leucocytes from the donated blood either during collection, processing or at the bedside.[1] There are several methods of leucodepletion of blood such as manual and automated cell washing, freezing and de-glycerolization of red cells, centrifugation and buffy coat removal, at bed side through leucocyte filters and blood component collection through apheresis technology. Currently the best leucoreduction can be achieved with the help of 3rd and 4th generation filters.[7] Evidence showed that leucoreduction reduces the incidence of FNHTR and associated clinical costs significantly.[5] Moreover, it is the prime responsibility of the physicians and the hospitals to offer their patients adequate and uninterrupted supply of the safest possible blood for transfusion when needed.[8] Initially transfusion was given to these children only as a life saving measure but the patients suffered due to poor quality of life and remain incapacitated.[9] With the availability of better transfusion regimen, iron chelation therapy, proper management complications and good supportive care, it is now possible for thalassemic child to have a near normal life span with a good quality of life.[10] Hence, in this study, we tried to compare adverse outcomes between two groups of thalassemia patients – transfused with packed red blood cells through conventional blood filter vs. transfused with leucodepleted blood using leucodepletion filter.

METHODS

This quasi-experimental study was carried out in the Department of Transfusion Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between March 2019 and August 2021. A total of 84 diagnosed and transfusion dependent thalassemia patients were included in this study after fulfilling the eligibility criteria. They were equally divided into intervention and comparison group.

Inclusion criteria:

1. Thalassemia patient who are transfusion dependent; and
2. Patients who had subsequent two episodes of fever of at least 38°C or onset of chills and rigors within 24 hours of transfusion in a previously afebrile child (based on patient's history).

Exclusion criteria:

1. Multi-transfuse patients other than thalassemia and chronic anaemia;
2. Thalassemia patients suspicious of hemolytic transfusion reactions (based on clinical history and Coombs test report); and
3. Thalassemia patients suspicious of transfusion-associated sepsis (based on clinical history and physical examination).

We adopted a purposive sampling method. Selected patients were transfused by packed red blood cells and divided into two groups according to the status of leucodepletion method. Allocation of interventions were done by non-randomized alternate assignment. In this study, odd-numbered patients were transfused with packed red blood cells using leucodepleted filter (intervention group). On the other hand, the even numbered thalassemia patients were transfused with packed red blood cells with conventional blood transfusion filter (comparison group). Intervention and comparison groups were matched according to age, number of total transfusions, and previous history of febrile reactions. The temperature, pulse, blood pressure, and presence of any skin rash were recorded carefully before, during and after transfusions (within 1 hour). A semi-structured questionnaire was used to collect sociodemographic data, clinical history, investigations and transfusion related information of the participants. Data was also collected over mobile phone from those who developed reactions after being discharged from the hospital.

Data was collected, coded and compiled into the computer. Statistical Package for Social Sciences (SPSS) version 22.0 for Windows was used for statistical analysis. Unpaired Student's t-test was used to compare numerical data, while Chi-square test was used to compare categorical data. The level of significance was set at 5% and p-value <0.05 was considered statistically significant. Odds ratio with 95% CI were calculated for risk factor analysis.

RESULTS

The mean age was 19.11±16.54 years in intervention group and 15.79±10.83 years in comparison group. More than half (59.5%) of the patients were female in the intervention group and 23(54.8%) in the comparison group. More than one third (40.5%) of the patients were male in the intervention group and 19(45.2%) in the comparison group. Mean age was almost similar between two groups (p>0.05) (Table-I). Among adverse reactions, 21(25%) of the patients experienced chills and rigors – 2(4.8%) in the intervention group and 19(45.2%) in the comparison group. Other symptoms were only observed in the comparison group such as fever (38.1%), vomiting (4.8%), myalgia (7.1%), hypotension (2.4%) and skin rash (2.4%) (Table-II). Only 2(4.8%) patients had FNHTR in intervention group, while 25(59.5%) in comparison group experienced FNHTR. FNHTR was observed significantly lower (OR=29.4; CI=5.72–100) in the intervention group (p<0.05) (Table-III). We observed that only 1(50%) and 19(76%) patients had onset of reaction within 2 hours of transfusion in the intervention group and comparison group respectively. However, only 1(50%) and 6(24%) patients had onset of reaction after 2 hours of transfusion in the intervention group and comparison group respectively. The mean onset of reaction was 3.00±1.41 hours in intervention group and 3.07±2.62 hours in comparison group. The mean onset of reaction was similar between two groups (p>0.05) (Table-IV).

Table-I: *Age and gender distribution of the study participants (N=84)*

Variables	Intervention group (n=42)	Comparison Group (n=42)	p-value
Age group (in years)			
≤10	17 (40.5%)	15 (35.7%)	>0.05^{NS}
11–20	14 (33.3%)	19 (45.2%)	
21–30	4 (9.5%)	3 (7.2%)	
>30	7 (16.7%)	5 (11.9%)	
MeanSD (Range)	19.11±16.54 (4–64)	15.79±10.83 (4–60)	>0.05^{NS}
Gender			
Male	17 (40.5%)	19 (45.2%)	>0.05^{NS}
Female	25 (59.5%)	23 (54.8%)	

Unpaired Student's t-test and Chi-square test were applied respectively; NS=not significant .

Table-II: *Transfusion related adverse reactions among the study participants (N=84)*

Variables	Intervention Group (n=42)	Comparison group (n=42)
Fever	-	16 (38.1%)
Chills and rigors	2 (4.8%)	19 (45.2%)
Vomiting	-	2 (4.8%)
Myalgia	-	3 (7.1%)
Hypotension	-	1 (2.4%)
Skin rash	-	1 (2.4%)

Table-III: *Comparison of febrile nonhemolytic transfusion reactions (FNHTR) between groups (N=84)*

FNHTR	Intervention group (n=42)	Comparison Group (n=42)	Test statistics
Yes	2 (4.8%)	25 (59.5%)	$p<0.05^S$
No	40 (95.2%)	17 (40.5%)	OR=29.4; CI=5.72–100

Chi-square test was applied; S=significant.

Table-IV: *Comparison of the onset of reaction between groups (N=27)*

Onset of reaction	Intervention group (n=2)	Comparison Group (n=25)	p-value
≤2 hours	1 (50.0%)	19 (76.0%)	
>2 hours	1 (50.0%)	6 (24.0%)	
Mean±SD	3.00±1.41	3.07±2.62	$>0.05^{NS}$
(Range)	(1–4)	(1–10)	

Unpaired Student's t-test was applied; NS=not significant.

DISCUSSION

Febrile non hemolytic transfusion reactions (FNHTR) are the most common transfusion reaction among multi-transfuse thalassemia patient which is due to leukocytes contaminations in blood components. Though FNHTR is not life-threatening but it hampers their quality of life greatly. Sometimes transfusions have to be discontinued due to severity of febrile reactions with chills and rigors.[7,9] In this study, we evaluated the effectiveness of using bedside leucodepletion filter for blood transfusion among thalassemia patient in reducing FNHTR.

In this present study, it was observed that 40.5% of patients belonged to age d"10 years in intervention group and 45.2% patients belonged to age 11–20 years in comparison group. The mean age was 19.11±16.54 years (ranged between 4 and 64 years) in intervention group and 15.79±10.83 years (ranged between 4.3 and 60 years) in comparison group. The mean age were almost similar between two groups. Tan et al. reported that the median age of the patients was 8 years, as they enrolled 26 multi-transfused thalassemic children aged between 9 months and 13 years, which is much less than that of our study because they they took only younger, pediatric patients in their study.[9] In our study, females were predominant in both groups, i.e., 59.5% and 54.8% in intervention group and comparison group respectively. However, gender distribution was similar between two groups. Abdulqader et al. studied on 204 thalassemia major patients where 52% were male and 48% were female; no significant association was observed with gender, which is in congruence with the present study.[11]

In the present study, 21(25%) of the patients experienced chills and rigors; 2(4.8%) in the intervention group and 19(45.2%) in the comparison group. Other symptoms were only observed in the comparison group such as fever (38.1%), vomiting (4.8%), myalgia (7.1%), hypotension (2.4%) and skin rash (2.4%). Waheed et al. observed febrile non hemolytic transfusion reaction (FNHTR) in 13.08% patients in the intervention groups. The clinical signs and symptoms of FNHTR were chills (51.1%), rigors (47.0%), fever (33.3%), hypotension (11.4%), vomiting (8.41%), myalgia (4.71%) and cough (3.0%).[3] Abdulqader et al. observed 28% of patients had FNHTR manifested as fever and chills.[11] Most of the FNHTRs are self-limiting in nature; they are characterized by fever with or without chills and rigors. Nausea, vomiting, dyspnea, and hypotension may accompany these reactions.[12-14] According to King et al., patients with a history of FNHTR are at a 15% risk of recurrence of such adverse reactions during subsequent transfusion.[5] Tan et al. also reported that severe reactions (e.g., hemolytic transfusion reactions) were rare in their study, however, mild reactions (e.g., fever, urticaria and petechial rash) were common.[9]

In this study, we observed that 4.8% of patients had FNHTR in intervention group and 59.5% in comparison group. In a study done by Nasir et al.

study, reaction rate declined to 0%, when bedside filter was used and no FNTHR was documented on cases which had earlier reported high incidence of FNHTR.[1] On the other hand, use of non-leucoreduced blood resulted in the occurrence of febrile non-haemolytic transfusion reactions in 100% cases. Therefore, a remarkable reduction of FNTHR happened when a bedside filter leucoreduced blood is used compared to non-leucoreduced blood.[1] Devi & Gaikhonlungpou reported that transfusion reaction rate was observed 0.22% when leucoreduced blood was used and 0.58% when non-leucoreduced blood was used.[14] However, Dutt et al. reported only 1 patient (0.8%) had such adverse event while receiving bedside filtered PRBCs, which is comparable to our study finding.[15] In present study, in patients with bedside leucodepletion filters FNHTR significantly decreased 29.4 times compared to patients without leucodepletion filter ($p<0.05$). Similarly, several previous studies reported that transfusion reactions were significantly reduced in the group receiving filtered blood.[5,9,14-16] Comparing our study with the above mentioned studies, all got a similar domino effect highlighting that bedside leucodepletion filter is beneficial in reducing the incidence of FNHTRs. Anecdotal evidence may claim that bedside filter has no effect on reducing the rates of FNHTR; however, that could invariably happen in those centers, where filters used are invariable of sub-standard. Overall, leucoreduction using leucodepletion filter in thalassaemia patients helps us prevent transfusion reactions.

In this study, only 1(50%) patient had onset of adverse reaction d"2 hours in intervention group and 76% in comparison group. The mean onset of reaction was 3±1.41 hours in intervention group and 3.07±2.62 hours in comparison group. The mean onset of reaction was similar between two groups. Tan et al. showed the median onset was 2 hours (ranged between 10 minutes and 18 hours), which is comparable with the current study.[9]

Our study had a relatively small sample and was done in a single hospital in Dhaka city due to time and budget constraint. Further studies can be undertaken with a large number of patients from diferent hospitals across the country under a randomized controlled trial.

CONCLUSION

It can be concluded that febrile non hemolytic transfusion reactions (FNHTR) were significantly reduced among those thalassemia patients who were transfused with packed red blood cells using leucodepletion filters. Adoption of this newer technology in multi-transfuse patients like thalassemia can facilitate in minimizing the sufferings and thereby improving the quality of life. However, standard policy should be developed by the health authority to provide low-cost leukocyte free red cells in prospective recipients of multiple transfusions.

Conflict of interest: None declared.

Funding source: Self-funded.

Ethical approval: Ethical approval was obtained from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Authors' contribution: Conceptualization and design of the study: AA Urmi, A Khatun; patient selection, data collection and compilation: AA Urmi, UM Akter, AHMS Rahman, T Chakrabarty, R Yasmin; data analysis: AA Urmi, AM Appolo, MM Alam; supervision of the study: A Khatun; manuscript preparation, editing and final submission: AA Urmi, A Khatun, UM Akter, AHMS Rahman, T Chakrabarty, R Yasmin, AM Appolo, MM Alam.

REFERENCES

1. Nasir K, Waheed U, Tahir S, Zaheer HA. Leucodepletion in thalassaemia major patients in Pakistan. J Islamabad Med Dent Coll. 2018;7(3): 157-8.
2. Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare, Government of the People's Republic of Bangladesh. National Guidelines on Thalassaemia Management for Physician. Dhaka: DGHS; 2019.
3. Waheed U, Wazeer A, Qasim Z, Iqbal Z, Zaheer, HA. Surveillance of adverse transfusion reactions in multi-transfused thalassaemia patients in Mirpur, Azad Jammu and Kashmir, Pakistan. Ann Pak Inst Med Sci. 2016;12(1):27-30.
4. Sharma JD. Management practices of thalassemia in Bangladesh. J Chittagong Med Coll Teach Assoc. 2024;35(1):1-3.
5. King KE, Shirey RS, Thoman SK, Bensen Kennedy D, Tanz WS, Ness PM. Universal leukoreduction decreases the incidence of febrile nonhemolytic

transfusion reactions to RBCs. Transfusion. 2004;44(1):25-9.

6. Bilgin YM, van de Watering LM, Brand A. Clinical effects of leucoreduction of blood transfusions. Neth J Med. 2011;69(10):441-50.
7. Sharma RR, Marwaha N. Leukoreduced blood components: advantages and strategies for its implementation in developing countries. Asian J Transfus Sci. 2010;4(1):3-8.
8. Nurunnabi A, Jahan M, Alam M, Hoque M. Safe blood transfusion and ethical issue in transfusion medicine. J Dhaka Med Coll. 2010;19(2):144-9.
9. Tan KK, Lee WS, Liaw LC, Oh A. A prospective study on the use of leucocyte-filters in reducing blood transfusion reactions in multi-transfused thalassemic children. Singapore Med J. 1993;34(2): 109-11.
10. Dubey AP, Parakh A, Dublish S. Current trends in the management of beta thalassemia. Indian J Pediatr. 2008;75(7):739-43.
11. Abdulqader AMR, Mohammed AI, Mohammed NI. Red cell alloimmunization and autoimmunization in multi-transfused thalassemia patients in Sulaymaniyah province-Iraq. Korean J Clin Lab Sci. 2020;52(2):98-104.
12. Perrotta PL, Snyder EL. Non-infectious complications of transfusion therapy. Blood Rev. 2001;15(2):69-83.
13. Contreras M, Mollison PL. ABC of transfusion. Immunological complications of transfusion. BMJ. 1990;300(6718):173-6.
14. Devi AS, Gaikhonlungpou KG. Leukodepletion status of blood products and transfusion reactions in thalassemic patients. J Appl Hematol. 2014;5(1):29-31.
15. Dutt N, Sidhu M, Sharma S, Parihar R, Kumar D. Effectiveness of buffy coat leucoreduced packed red blood cells in decreasing febrile non hemolytic transfusion reactions in thalassemic patients.Int J Res Med Sci. 2017;5(5):1756-9.
16. Jamal R, Mazeni NR, Hussin H. Evaluation of two types of leukocyte removal filters on transfusion dependent thalassaemics. Malays J Pathol. 2000; 22(2):79-83.

Original Article

Prevalence of Stress, Anxiety and Depression among Intern Doctors during Hospital Ward Rotations: A Multicentre Experience from Bangladesh

Ahsan K[1], Zaher A[2], Roy S[3], Nurunnabi ASM[4], Sera TM[5]

ABSTRACT

Stress is a common response to demanding situations and can adversely affect emotional, physical, and cognitive functioning. Intern doctors working in different medical college hospitals are particularly vulnerable due to heavy workloads, night duties and continuous exposure to critically ill patients. In Bangladesh, an extremely low doctor–patient ratio and overcrowded public hospitals further intensify their burden. A cross-sectional, descriptive study was conducted, between September 2024 and August 2025, to assess psychological distress among 118 purposively selected intern doctors from four government medical college hospitals in Dhaka city, Bangladesh. We used a pre-tested, structured questionnaire for data collection. Level of stress was measured using Kessler 10 Psychological Distress (K10), while anxiety level was determined using the General Anxiety Disorder 7 (GAD 7) scale and depression level by using Patient Health Questionnaire 9 (PHQ-9). The mean age of the participants was 25.3±0.83 years; most of the participants belonged to the 25–26 years age group. Male-female ratio was 1:1.5. The prevalence of stress, anxiety, and depression were found high at 68%, 76%, and 77% respectively. Logistic regression analysis showed that female and unmarried interns had markedly higher odds of stress (OR=26.6), while high workload increased anxiety risk (OR=6.11). Severe sleep disturbance strongly predicted all three conditions. Interns in the 9–12-month duration group had significantly higher odds of depression (OR=21.7). Overall findings highlight substantial psychological distress among intern doctors, closely linked to gender, workload, sleep quality, workplace stress, and internship duration. Improved working conditions and targeted mental health support are urgently needed to protect wellbeing of the intern doctors working at different medical college hospitals across the country.

Keywords: *Stress, anxiety, depression, intern doctors, medical education, Bangladesh*

Mugda Med Coll J. 2026; 9(1): 59-66
DOI: https://doi.org/10.3329/mumcj.v9i1.90828

INTRODUCTION

Stress is a feeling of emotional pressure resulting from the body's reaction to life events.[1] Stress and its psychological manifestations are inherent in human life. These are a major source of concern in the modern day society. Stress affects daily life activities and sleep qualities. Stress in individuals disrupts the normal person's physical or mental wellbeing.[2] Stress has been found to be associated with anxiety and depression interpersonal conflict, sleep problems, and lower academic and clinical performance.[2] Stress has negative effects on attention, memory, decision making and performance.[3] Stress can be positive or negative. Positive stress is called eustress and negative

1. Prof. Kamrul Ahsan, Professor, Department of Paediatrics, Mugda Medical College & Hospital, Dhaka-1214, Bangladesh. Email: kamrul.hersmile@gmail.com (Corresponding author)
2. Dr. Arifa Zaher, Senior Consultant, Department of Obstetrics & Gynaecology, Sarkari Karmachari Hospital, Dhaka-1000, Bangladesh.
3. Dr. Subrata Roy, Senior Consultant, Department of Paediatrics, Mugda Medical College Hospital, Dhaka-1214, Bangladesh.
4. Dr. Abu Sadat Mohammad Nurunnabi, Graduate Student, Mitch and Leslie Frazer Faculty of Education, Ontario Tech University, Oshawa, ON, Canada.
5. Tushnad Mahzabeen Sera, MBBS Student, Mugda Medical College, Dhaka-1214, Bangladesh.

stress distress. Eustress triggers the body alarm, and enhances attention, performance and creativity. It has temporary effects only. Distress has negative effects on the body. Stress represents the wear and tear of the body. Chronic stress can have serious effects on human health and behavior.[2]

Undergraduate medical education is one of the most academically and emotionally demanding programmes in Bangladesh. After completion of MBBS programme, the mandatory one-year internship training adds to the already high level of stress associated with undergraduate medical education.[1,4] Intern doctors working in different medical college hospitals encounter various challenges in their work place, including academic demands, peer competition, limited leisure time, and frequent exposure to patients' suffering. Work place stress can negatively affects quality of work place performance, daily activities of life and sleep qualities. These challenges make the training more stressful. High levels of stress harm physical and mental health.[1]

Bangladesh is one of the most populous country of the world with the population of 18 billion. Doctor patient ratio is a major concern in health care delivery system. The current doctor-patient ratio in Bangladesh is only 5.26 per 10,000 population.[5] Bangladesh is one of the countries experiencing a significant shortage of healthcare workers.[6] As tertiary care facilities and referral centres, our medical college hospitals are overburdened.[6,7] High workload and not having personal free time are sources of dissatisfaction with work.[7] Medical practice is a stressful job by its nature. Dealing with noncompliant and recalcitrant patients, patient not responding to treatment or caring for dying patient are stressful job.[8] On the other hand, night shift resulting negative effects on hours of sleep and daytime sleepiness and fatigue, decrease the performance and increase the risk of accidents.[9]

The Diagnostic and Statistical Manual (DSM-5) specifically describes anxiety as excessive worry and apprehensive expectations, occurring more days than not for at least 6 months, about a number of events or activities, such as work or school performance, while depression (major depressive disorder) is individual must be experiencing depressed mood or loss of interest or pleasure like symptoms during the same 2-week period.[10] These conditions can damage both personal and professional reputations. Negative consequences may include decreased commitment, substance abuse, suicidal ideation, clinical incompetence, medical mistakes, and poor job performance. These adverse effects can ultimately diminish the quality of patient care.[1,7-9] Evidence showed that the prevalence of anxiety among house officers in Malaysia was observed between 60.7% and 63.7%, while depression was found in 42.9%, and stress in 57.1% of the study participants.[11]

Many studies have investigated the prevalence of anxiety, depression, and stress among medical interns/residents in different countries across the globe. However, there is insufficient information about such study in a developing country like Bangladesh. Therefore, this study was propsed to investigate the rate of anxiety and depression among intern doctors of Bangladesh. We conducted the survey among intern doctors working in four public medical college hospitals in Dhaka city, Bangladesh. Dhaka is the most populous city in Bangladesh and those government hospitals catchment area is substantially large, and hence the workload is fairly significant.

METHODS

This cross-sectional, descriptive study was conducted, between September 2024 and August 2025, on 118 purposively selected intern doctors from four government medical college hospitals in Dhaka city, Bangladesh. Intern doctors from Dhaka Medical College Hospital, Shaheed Suhrawardy Medical College Hospital, Sir Salimullah Medical College & Mitford Hospital, and Mugda Medical College Hospital were invited to take part in this study. We adopted a purposive sampling method. Intern doctors having completed at least four weeks of clinical rotation in different departments such as Medicine, Surgery, Paediatrics, Obstetrics & Gynaecology and experience of evening and night shift duties were enrolled in this study. Our exclusion criteria were: i) less than four weeks training period in total training period as intern, ii) having no experience of evening and night shift duties, and iii) declining consent to participate in the study. Our data collection tool was a pre-tested, structured questionnaire including demographic variables, stress indicators, and standardized scores for stress, anxiety and depression.

This self-report, pre-tested, structured questionnaire was used as tool having four parts. The first part collected sociodemographic data like age, gender, marital status, residence, duration of internship training and perception of stress. The second part measured the level of stress using Kessler 10 Psychological Distress (K10), while the third part measureed anxiety level using the General Anxiety Disorder 7 (GAD 7) scale and the fourth part measured depression level using Patient Health Questionnaire 9 (PHQ-9).

In this study, Kessler 10 Psychological Distress (K10) instrument was employed to measure stress levels. The K10 instrument has been widely used in population based epidemiological studies to measure current (4 weeks) distress, and is available in several languages. The K10 works without any substantial bias with respect to sex and educational level. The instrument has been designed to measure the severity and level of distress associated with psychological symptoms in population surveys. The K10 questionnaire consists of ten questions in the form of "how often in the past month did you feel" and offers specific symptoms such as "tired out for no good reason", "nervous", and "sad or depressed". The five possible responses to each question range from "none of the time" to "all of the time" and are scored from 1–5, respectively. The scores for all questions are summed to obtain a total score. The total scores are interpreted as follows: a score 20 is considered to represent no stress of any level; a score of 20–24 represents mild stress; a score of 25–29 represents moderate stress; and a score of 30–50 represents severe stress.[3]

To assess anxiety levels, we used the 7-item Generalized Anxiety Disorder-7 (GAD-7) scale. The GAD-7 scale comprises of seven highly relevant questions selected from 13 items (nine questions from the Diagnostic and Statistical Manual of Mental Disorder, 4th Edition, and four questions from the Anxiety Symptom Scale). The answers were scored as follows: 0 point for not at all, 1 point for several days, 2 points for more than half of the days, and 3 points for nearly every day. The score was scaled from 0–21 (0–4: without anxiety symptoms, 5–9: with mild anxiety symptoms, 10–14: with moderate anxiety symptoms, and 15–21: with severe anxiety symptoms).[12]

We used the 9-item Patient Health Questionnaire-9 (PHQ-9) to assess the level of depression. The participants were instructed to answer the questions in order to evaluate the frequency of the particular symptoms they felt during the duration of internship training through rotation. The answers were scored as follows: 0 point for not at all, 1 point for several days, 2 points for more than half of the days, and 3 points for nearly every day. The score was scaled from 0–27 (0–4: without depression symptoms, 5–9: with mild depression symptoms, 10–14: with moderate depression symptoms, 15–19: with moderate to severe depression symptoms, and 20–27: with severe depression symptoms).[13]

It may be mentioned that the participating intern doctors were informed that their participation would be voluntary, and in no way it would affect their performance in internship training. Besides, due to the sensitive nature of some questions, existing mental health support was provided to them including consultation with the psychiatrist, if needed. Moreover, as being vulnerable group of study participants as well as posing risks of suicidal ideation/thoughts, their anonymity, confidentiality and effective care during and after study were strictly ensured.[14]

After collection, data was scrutinized, cleaned, and coded. Then data analysis was done using R Statistical Software version 4.4.1 for Windows; R Core Team 2024 (R Foundation for Statistical Computing, Vienna, Austria). Data was expressed in the form of frequencies and percentages. Associations between variables was assessed using Chi-square (χ^2) test. Statistical significance was set at a two tailed p-value of <0.05. Logistic regression analysis was also done.

RESULTS

A total of 118 intern doctors were included in this study. The mean age was 25.3±0.83 years; most of them were in the 25–26 years age group. Male-female ratio was 1:1.5. The prevalences of stress, anxiety and depression among interns were found 68%, 76% and 77% respectively (Table-I). Anxiety levels differed significantly by gender (p=0.027); female interns showed higher rates of severe stress (39% vs. 19%) and severe anxiety (25% vs. 6%) (Table-II). Regarding workload, self-perceived workplace stress of the interns was significantly associated with measured

stress (p=0.034) and anxiety (p=0.028) (Table-III). Among male interns, training duration was significantly associated with stress (p=0.018) and anxiety (p=0.042), most notable in the 9–12-month group of intern doctors (Table-IV). Logistic regression analysis showed that female and unmarried interns had markedly higher odds of stress (OR=26.6). Heavy workload increased anxiety risk (OR=6.11). Severe sleep disturbance strongly predicted all three conditions. Interns in the 9–12-month duration group had significantly higher odds of depression (OR=21.7) (Table-V).

Table-I: *Prevalence of stress, anxiety and depression among intern doctors (N=118)*

Variables	Frequency
Stress Prevalence	
No	38 (32%)
Yes	80 (68%)
Anxiety Prevalence	
No	28 (24%)
Yes	90 (76%)
Depression Prevalence	
No	27 (23%)
Yes	91 (77%)

Table-II: *Gender related difference in stress and anxiety levels (N=118)*

Variables	Male n=47	Female n=71	p-value	Test Statistics
Stress				
No stress	19 (40%)	19 (27%)	0.106	χ^2=6.13, df=3
Mild stress	10 (21%)	15 (21%)		
Moderate stress	9 (19%)	9 (13%)		
Severe stress	9 (19%)	28 (39%)		
Anxiety				
No anxiety symptoms	15 (32%)	13 (18%)	0.027	χ^2=6.13, df=3
Mild stress	10 (21%)	15 (21%)		χ^2=9.16, df=3
Mild anxiety	13 (28%)	23 (32%)		
Moderate anxiety	16 (34%)	17 (24%)		
Severe anxiety	3 (6.4%)	18 (25%)		

Table-III: *Associations of stress, anxiety and depression levels with perceived stress at workplace (N=118)*

Variables	Feel stressed at workplace		p-value	Test Statistics
	Yes n=93	No n=25		
Stress				
No stress	26 (28%)	12 (48%)	0.034	χ^2=8.68, df=3
Mild stress	18 (19%)	7 (28%)		
Moderate stress	14 (15%)	4 (16%)		
Severe stress	35 (38%)	2 (8.0%)		
Depression				
No depression symptoms	18 (19%)	9 (36%)	0.213	χ^2=5.82, df=4
Mild depression	15 (16%)	6 (24%)		
Moderate depression	25 (27%)	3 (12%)		
Moderate to severe depression	20 (22%)	3 (12%)		
Severe depression	15 (16%)	4 (16%)		
Anxiety				
No anxiety symptoms	17 (18%)	11 (44%)	0.028	χ^2=9.13, df=3
Mild anxiety	29 (31%)	7 (28%)		
Moderate anxiety	27 (29%)	6 (24%)		
Severe anxiety	20 (22%)	1 (4.0%)		

Table-IV: *Prevalence of stress and duration of internship training (N=118)*

Variables	Duration of internship training				
	1–4 months n=29	5–8 months n=41	9–12 months n=48	p-value	Test Statistics
Stress prevalence among male					
No	3 (30%)	10 (71%)	6 (26%)	0.018	χ^2=8, df=2
Yes	7 (70%)	4 (29%)	17 (74%)		
Stress prevalence among female					
No	7 (37%)	9 (33%)	3 (12%)	0.113	χ^2=4.36, df=2
Yes	12 (63%)	18 (67%)	22 (88%)		

Table-V: *Logistic Regression Analysis*

Variables	Stress		Anxiety		Depression	
	OR	p-value	OR	p-value	OR	p-value
Age	0.50	0.078	0.43	0.040	0.45	0.066
Gender						
Male	—		—		—	
Female	0.03	0.011	0.05	0.034	0.00	<0.001
Workload						
No	—		—		—	
Yes	1.74	0.525	6.11	0.046	1.85	0.524
Sleep qualities						
No	—		—		—	
To some extent	1.83	0.624	8.96	0.098	1.15	0.915
Mostly	9.24	0.088	22.2	0.026	3.91	0.344
Badly	17.2	0.033	40.2	0.009	8.84	0.138
Marital status						
Married	—		—		—	
Unmarried/Divorced	0.15	0.038	0.19	0.086	0.26	0.190
Institution						
Mugda Medical College Hospital	—		—		—	
Shuhrawardy Medical College Hospital	1.03	0.972	5.30	0.137	4.08	0.216
Dhaka Medical College Hospital	0.81	0.795	0.58	0.522	5.77	0.070
Sir Salimullah Medical College & Mitford Hospital	0.59	0.507	0.52	0.453	0.77	0.780
Duration of training						
1–4 months	—		—		—	
5–8 months	0.75	0.716	2.30	0.332	2.58	0.325
9–12 months	4.37	0.076	4.88	0.073	21.7	0.005
Gender * Workload						
Female * Yes	5.36	0.154	2.36	0.486	52.7	0.008
Gender * Marital status						
Female * Unmarried/divorced	26.6	0.006	45.1	0.003	120	0.002

DISCUSSION

This study assessed the prevalence and determinants of stress, anxiety, and depression among intern doctors working in different government medical college hospitals in Dhaka city, Bangladesh. The findings reveal a high burden of psychological distress among medical interns, with 68% experiencing stress, 76% anxiety, and 77% depression. These rates are consistent with earlier studies from South Asian countries that have documented similarly high levels of mental health symptoms among medical trainees due to demanding workloads, inadequate rest, and limited institutional support.[7,15-18] Evidence showed that the prevalence of depression among medical students and young doctors ranged between 25% and 80% highlighting the global nature of this issue.[19]

The substantial proportion of interns with moderate-to-severe symptoms (31% severe stress, 43% moderate-to-severe anxiety, and 35% moderate-to-severe depression) indicates a clinically significant problem. Comparable findings are observed in studies done in tertiary hospitals in Bangladesh, India, Pakistan, and Nepal, where intense clinical responsibilities and extended duty hours contribute to emotional exhaustion and psychological morbidity.[7,15-18] The high psychological burden among interns in the present study underscores the urgent need for structured well-being programmes, stress-relief interventions, and routine mental health screening in Bangladeshi internship training programmes.

In our study, female intern doctors experienced higher levels of severe stress (39% vs 19%) and severe anxiety (25% vs 6%), and gender differences in anxiety were statistically significant (p=0.027). This gender trend has been consistently reported in medical literature. Several previous studies also reported that female medical trainees more frequently experience anxiety and depressive symptoms, attributed to social expectations, workplace pressures, and gender-linked psychosocial stressors.[15,17,18] Neurobiological and hormonal factors may play an important role here. Therefore, gender-responsive mental health strategies are needed, including supportive peer networks and access to counseling services tailored for female trainees.[20]

Workload emerged as a major contributor to psychological distress, anxiety and depression. Besides, disruption of daily life, sleep disturbance and reduced work performance illustrate the toll of demanding clinical duties. Overloaded with clinical duties and sleep disturbance were widely recognized as a strong risk factor for stress, anxiety, depressive illness, and burnout among interns, as per study reports from several countries.[7,11.15-18,20-23] In this study, association between workplace stress and measured stress (p=0.034) and anxiety (p=0.028) aligns with the 'Job Demand–Control model',[24] which predicts that high demands combined with low control enhance psychological strain in our hospitals. Considering the mandatory nature of internship duties in Bangladesh, revisiting duty hours, ensuring adequate rest, and implementing structured shift schedules may help reduce these adverse outcomes.

In the present study, training duration was significantly associated with stress (p=0.018) and anxiety (p=0.042) among male interns, particularly in the 9–12-month group. This pattern may reflect cumulative burnout, increasing patient-care responsibilities, and prolonged exposure to emotionally challenging situations. Similar findings have been documented internationally, where psychological symptoms intensify during later phases of internship due to fatigue, repeated night shifts, and increased expectations.[7,11,15,21-23] These results highlight the importance of periodic well-being assessments throughout the internship year rather than a one-time final evaluation.

The findings from this study highlight a concerning mental health burden among intern doctors and reinforce the need for systemic reforms in internship training in Bangladesh, which include but not limited to ensuring reasonable duty hours and adequate rest, integrating stress-management and self-care training into internship orientation programs, implementing structured mental health support services, offering inclusive and gender-sensitive psychological support, providing counseling and peer support especially for unmarried or socially isolated interns.[25-27]

Strengths of the study include the focus on multiple teaching hospitals in Dhaka city and the use of validated psychological scales with regression analysis to identify predictors. However, the present study has certain limitations. Because it followed a cross-sectional design, it was not possible to determine any cause-and-effect relationships between the variables. Self-reporting nature of the

questionnaire could be a potential for recall bias or concerns about the stigma attached. Exclusion of intern doctors working in different private medical college hospitals may limit generalizability of the study findings.

CONCLUSION

Our study revealed a high prevalence of stress (68%), anxiety (76%) and depression (77%) among intern doctors of Bangladesh. Female gender, heavy workload, and poor sleep quality were major contributing factors. Feeling stressed at workplace strongly aligned with measured stress/anxiety. Interaction effects (female × unmarried) were strong predictors across all models. Internship duration (9–12 months) associated with greater depression risk. Medical interns are at a critical stage of their professional development and this is the transitioning from theoretical learning to hands-on patient care. During this time, they face the challenges of hospital ward rotations, which often involve high patient loads, long duty hours and need for quick decision making. These conditions expose them to substantial workplace stress, anxiety and depression that effects on health care performance and qualities of daily life. This study will help us understand the extent and impact of these mental health issues in the context of patient care, professional development, workplace culture, efficiency of the health system, sustainability, and societal expectations. It will also help to mitigate challenges faced by the medical interns during ward rotations, providing insights that can lead to better support system, improved training environments and achieving required competences in medical training.

Conflict of interest: The authors have declared that no financial or personal competing interests exist.

Funding source: This study has received no external funding from any group, organization or institution.

Ethical clearance: This study was approved by the Institutional Review Board (IRB) of Mugda Medical College, Dhaka, Bangladesh.

Authors' contribution: Conceptualization and design of the study: K Ahsan; Questionnaire formulation: K Ahsan, A Zaher, Data collection and compilation: K Ahsan, A Zaher, S Roy, TM Sera; Data analysis: K Ahsan, ASM Nurunnabi; Manuscript preparation, editing and final submission: K Ahsan, A Zaher, S Roy, ASM Nurunnabi, TM Sera.

REFERENCES

1. Muhammad DG, Gbonjubola YT, Jamiu MO, Abiodun AO. Rate of depression, anxiety and stress among interns/house officers in Nigeria. J Health Allied Sci NU. 2024;14(S1):S123-8.
2. Sani M, Mahfouz MS, Bani I, Alsomily AH, Alagi D, Alsomily NY, et al. Prevalence of stress among medical students in Jizan University, Kingdom of Saudi Arabia. Gulf Med J. 2012;1(1):19-25.
3. LeBlanc VR. The effects of acute stress on performance: implications for health professions education. Acad Med. 2009;84(10 Suppl):S25-33.
4. Sanzana L, Cooke A, Parvin S, Ahmed S, Nurunnabi ASM. Gender differences in anxiety and depression amongst Bangladeshi medical students. Int J Hum Health Sci (IJHHS). 2025;9(3):180-4.
5. Ahmed SM, Hossain MA, Rajachowdhury AM, Bhuiya AU. The health workforce crisis in Bangladesh: shortage, inappropriate skill-mix and inequitable distribution. Hum Resour Health. 2011;9:3.
6. Mozaffor M, Nurunnabi ASM, Haseen F, Sultan MT, Saha S. Transforming health professions education for universal health coverage: challenges and recommendations for low-resource countries. Mugda Med Coll J. 2022;5(2):98-103.
7. Dey S, Khan MH, Rahman MS, Hossain I, Kairi TK. Prevalence of stress and its associated factors among intern physicians in Bangladesh: a cross-sectional study. BMJ Open. 2025;15(8):e093211.
8. Linn LS. Health status, job satisfaction, job stress and life satisfaction among academic and clinical faculty. JAMA. 1985;254:2775-82.
9. Attia F, Attia M. Effect of shift rotation on sleep quality and associated health problems among nurses at Asser Hospital, KSA. Int J Nurs Sci. 2016;6(2):58-65.
10. American Psychiatric Association, DSM-5 Task Force. Diagnostic and Statistical Manual of Mental Disorders: DSM-5®. 5th ed. Washington, DC: American Psychiatric Publishing; 2013.
11. Shahruddin SA, Saseedaran P, Salleh AD, Azmi CA, Alfaisal NH, Fuad MD, et al. Prevalence and risk factors of stress, anxiety and depression among house officers in Kota Kinabalu, Sabah. Educ Med J. 2016;8(1):31-40.
12. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-7.

13. Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. Psychiatr Ann. 2002;32(9):509-15.

14. Mozaffor M, Nurunnabi A, Shahriah S. Ethical issues in suicide research. J Psychiatr Assoc Nepal (JPAN). 2020;9(1):5-9.

15. Chakraborty A, Jha A, Banerjee A, Banerjee N, Saha D, Das A. Depression, anxiety, and stress levels among medical students and interns in a medical college of Kolkata: a cross-sectional study. J Compr Health. 2024;12(2):89-93.

16. Nihal GN, Challuri P, Reddy MPK, Babu RS. Stress and anxiety among medical interns and doctors deputed in COVID duties: a cross-sectional study. Telangana J Psychiatr. 2021;7(2):122-7.

17. Arif A, Iram M, Nofal S, Sohail A, Riaz B, Ahmed S. Prevalence of depression, anxiety and stress in medical students, interns and residents in Pakistan. Pak J Med Health Sci. 2021;15(9):2333-6.

18. Pokhrel NB, Khadayat R, Tulachan P. Depression, anxiety, and burnout among medical students and residents of a medical school in Nepal: a cross-sectional study. BMC Psychiatry. 2020;20(1):298.

19. Rotenstein LS, Ramos MA, Torre M, Segal JB, Peluso MJ, Guille C, et al. Prevalence of depression, depressive symptoms, and suicidal ideation among medical students: a systematic review and meta-analysis. JAMA. 2016;316(21):2214-26.

20. Binti Mohd Sabri NR, Binti Nikmat AW, Mohamed SB, Abdullah NB. Psychological inflexibility and anxiety among house officers in a hospital in Selangor, Malaysia. East Asian Arch Psychiatry. 2024;34(4):128-33.

20. Mata DA, Ramos MA, Kim MM, Guille C, Sen S. In their own words: an analysis of the experiences of medical interns participating in a prospective cohort study of depression. Acad Med. 2016; 91(9):1244-50.

21. Abdulghani HM, Irshad M, Al Zunitan MA, Al Sulihem AA, Al Dehaim MA, Al Esefir WA, et al. Prevalence of stress in junior doctors during their internship training: a cross-sectional study of three Saudi medical colleges' hospitals. Neuropsychiatr Dis Treat. 2014;10:1879-86.

22. Zolhavarieh SM, Rezaei M, Roshanaei G, et al. Survey of job stress among interns of Hamadan University of Medical Sciences, Hamadan, Iran, in 2018. Avicenna J Clin Med. 2018;27(1):61-7.

23. Hsieh YH, Hsu CY, Liu CY, Huang TL. The levels of stress and depression among interns and clerks in three medical centers in Taiwan – a cross-sectional study. Chang Gung Med J. 2011;34(3):278-85.

24. Kain J, Jex S. Karasek's (1979) job demands-control model: a summary of current issues and recommendations for future research. In: Perrewé PL, Ganster DC. eds. New Developments in Theoretical and Conceptual Approaches to Job Stress. Leeds, UK: Emerald Publishing Ltd.; 2010.

25. Beresin EV, Milligan TA, Balon R, Coverdale JH, Louie AK, Roberts LW. Physician wellbeing: a critical deficiency in resilience education and training. Acad Psychiatry. 2016;40(1):9-12.

26. Styra R, Hawryluck L, McGeer A, Dimas M, Lam E, Giacobbe P, et al. Support for psychological distress in health care workers: thinking about now and beyond the COVID-19 pandemic. Health Promot Chronic Dis Prev Can. 2022;42(10):421-30.

27. Obeagu EI. Strategies to safeguard mental health among medical and allied health trainees: a narrative review. Adv Med Educ Pract. 2025;16: 2219-27.

Original Article

Immunohistochemistry for Mismatch Repair (MMR) Proteins in Endometrial Cancer

Alamgir SN[1], Ferdous J[2], Faika MJ[3], Farhana K[4], Rahman KT[5], Rashid FB[6], Asaduzzaman M[7]

ABSTRACT

A cross-sectional study was conducted in the Department of Gynaecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between January and December of 2023, to evaluate the immunohistochemistry findings for mismatch repair (MMR) proteins in endometrial cancer. A total of 54 endometrial carcinoma patients diagnosed by fractional curettage or diagnostic curettage admitted into the BSMMU Hospital were enrolled in this study. Patient's history (including age, BMI, family history, parity, menstrual pattern, comorbidities, clinical complaints, investigations and operation notes) was recorded in data collection sheet. After surgery, blocks were made from pathological specimens for histopathological examination. After regular histopathological examination, assessment of the MMR status of each patient's tumour was determined by immunohistochemistry by using monoclonal mouse antibodies against MMR proteins (MLH1, MSH2, MSH6, and PMS2) following the Dako EnVision method according to manufacturer protocol (in the Department of Pathology of the same institution). Immunohistochemistry findings revealed that two-thirds (63%) of the patients had intact expression of all MMR protein (MMRp), while 37% had a loss of expression of any of the proteins, which is known as mismatch repair deficiency (dMMR) state. Among them, the most common MMR defect identified was combined loss of MLH1/PMS2 in 9(16.67%) cases, followed by isolated PMS2 loss or isolated MSH2 loss in 6(11.11%) cases, combined MSH2/MSH6 loss in 4(7.4%) cases, while loss of all four proteins was observed in only 1(1.85%) case (Table-III). Deeper myometrial invasion (e"50%) was more evident in MMRp tumours compared to dMMR tumours ($p<0.01$). Cervical extension was also found more frequent in MMRp tumours ($p<0.05$). In contrast, dMMR tumours were found more frequently having lower tumour grade and lower FIGO stage compared to MMRp tumours ($p<0.05$). However, no differences were observed in tumour type, size, adnexal involvement, lymphovascular space invasion (LVSI), and lymph node involvement ($p>0.05$)

Keywords: *Endometrial cancer, histopathology, immunohistochemistry, mismatch repair protein.*

Mugda Med Coll J. 2026; 9(1): 67-72
DOI: https://doi.org/10.3329/mumcj.v9i1.90829

1. Dr. Sadia Nusrat Alamgir, Assistant Professor, Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka-1212. Email: sadianusrat77@yahoo.com (Corresponding author).
2. Prof. Jannatul Ferdous, Chairman, Department of Gynaecological Oncology, Bangladesh Medical University (BMU), Dhaka-1000.
3. Dr. Mst. Jakanta Faika, Assistant Professor, Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka-1212.
4. Dr. Kaniz Farhana, Assistant Professor, Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka-1212.
5. Dr. Khandker Tafriha Rahman, Assistant Professor, Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka-1212.
6. Dr. Farhana Binty Rashid, Assistant Professor, Department of Obstetrics & Gynaecology, Dhaka Medical College & Hospital, Dhaka-1000.
7. Dr. Mohammad Asaduzzaman, Assistant Registrar, Department of Medical Oncology, National Institute of Cancer Research and Hospital (NICRH), Dhaka-1212.

INTRODUCTION

Endometrial cancer has emerged as a significant gynaecological malignancy in low- and middle-income countries (LMICs) like Bangladesh, frequently ranked as the second most common female genital tract malignancy after cervical cancer.[1,2] Recent advancement in genetic studies revealed that about 20–40% of endometrial cancer cases exhibit a mismatch repair deficiency (dMMR) phenotype. dMMR is caused by genetic or epigenetic alterations of any of the mismatch repair genes (*MLH1, MSH2, MSH6, PMS2*).[3,4] The MMR system is crucial for maintaining genomic stability by correcting DNA replication errors, which are more common in genome regions with short repetitive DNA sequences. The most relevant MMR proteins in humans are *MLH1, MSH2, MSH6, and PMS2*, which are coded by the corresponding genes. These genes are *MLH1* (mutL homolog 1), *MSH2* (mutS homolog 2), *MSH6* (mutS homolog 6), and *PMS2* (PMS1 homolog 2, mismatch repair system component), located in chromosomes 3, 2, 2, and 7, respectively.[5]

Detection of deficient mismatch repair function is used diagnostically, predictively, and prognostically in endometial cancer.[4] Immunohistochemistry (IHC) assay of MMR proteins has emerged as a widely employed method for detecting the dMMR phenotype in endometrial cancer. It serves as a molecular classification,[6,7] a companion diagnostic for immunotherapy,[6,8-10] a secondary screening for Lynch syndrome.[6,7,9] Regarding molecular classification, various guidelines, and the recently published FIGO 2023 staging encourage its implementation for all endometrial cancers, explicitly highlighting the requirement for dMMR assessment through IHC.[7] In immunotherapy applicability, MMR IHC is preferred over PCR-based microsatellite instability (MSI) testing for endometrial cancer.[8] As we mentioned earlier, universal screening for Lynch syndrome through immunohistochemistry of MMR protiens and mutations in all endometrial cancer cases is also suggested by certain guidelines.[6,7,9] Under the circumstances, the significance of the MMR-IHC assay in patients with endometrial cancer has become increasingly evident even in low-resource settings like Bangladesh. Hence, we propsed the present study to evaluate the immunohistochemistry findings for mismatch repair (MMR) proteins in endometrial cancer (tumours removed by surgery) in a tertiary level specialized hospital in Dhaka, Bangladesh.

METHODS

This cross-sectional study was conducted in the Department of Gynaecological Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between January and December of 2023. Sample selection was done following purposive sampling technique. A total of 54 endometrial carcinoma patients diagnosed by fractional curettage or diagnostic curettage admitted into the BSMMU Hospital were enrolled in this study. At the time of their entry into the study a complete personal and family history was taken and recorded. Their age, BMI, parity, menstrual pattern, comorbidities, clinical complaints were noted in the data collection sheet. Preoperative investigations included some imaging modalities like transvaginal sonography (TVS) and magnetic resonance imaging (MRI) scans. All of the enrolled patients were treated by hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic and para aortic lymphadenectomy and/omentectomy as per staging. Paroperative findings and the findings of the cut section of the uterus (myometrial invasion, cervical extension, tumour size, ascites, omental metastasis) were noted.

After surgery was done, pathological specimens were routinely fixed with formalin and embedded in paraffin; then blocks were prepared for histopathological examination. After that, for immunohistochemistry evaluation, from paraffin embedded blocks 4 micrometer thick sections were cut, deparaffinized with xylene and rehydrated through a graded series of alcohol. Assessment of the MMR status of each patient's tumour was determined by immunohistochemistry (*MLH1, MSH2, MSH6,* and *PMS2*) by using monoclonal mouse antibodies against MMR proteins following the Dako EnVision method according to manufacturer protocol. Antibodies, source, clone and localisation for mismatch repair (MMR) proteins are shown in Table-I.

Table-I: *Antibodies used, source, clone and localization for mismatch repair (MMR) proteins (Dako EnVision by Agilent Technologies, Inc., Santa Clara, CA, USA)*

Antibodies	Source	Clone	Localisation
MLH1	Mouse monoclonal	ES05	Nuclear
PMS2	Rabbit monoclonal	EP51	Nuclear
MSH2	Mouse monoclonal	FE11	Nuclear
MSH6	Rabbit monoclonal	EP49	Nuclear

Any nuclear staining even patchy was taken as "no loss of expression" for MMR protein and was reported as MMR proficient. On the other hand, only absolute absence of nuclear staining was considered as "loss of expression", according to the College of American Pathologists (CAP) guideline.[8] Molecular expressions are shown in Fig. 1–4. Both regular histopathological examination and immunohistochemistry were done in the Department of Pathology of the same institution. The analysis of immunoreactivity was done by the Consultant Pathologist. All were recorded in the data sheet.

After collection, data was checked for omission, inadequacy and inconsistency. Omission was corrected by re-taking history or re-examining the patient. Irrelevant and inconsistent data was discarded. Categorical variables was presented as frequency and percentage. Associations between molecular expression and clinicopathological factors was assessed using Pearson's chi-square test. Statistical significance was set at a two tailed p-value of <0.05. Data analysis was done using STATA software version 14 (StataCorp LLC, College Station, Texas, USA).

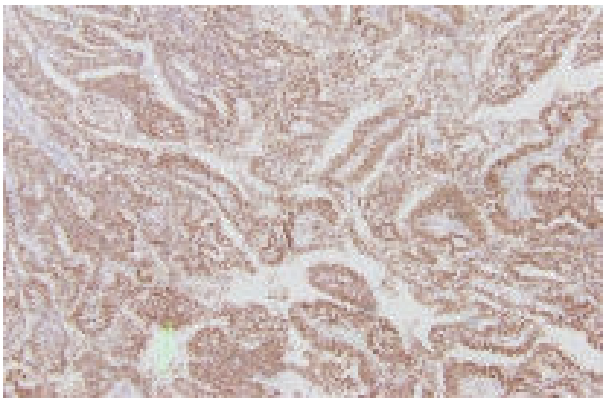

Fig. 1: *Photomicrograph showing intact expression of MLH1 in tumour cells (×100 magnification).*

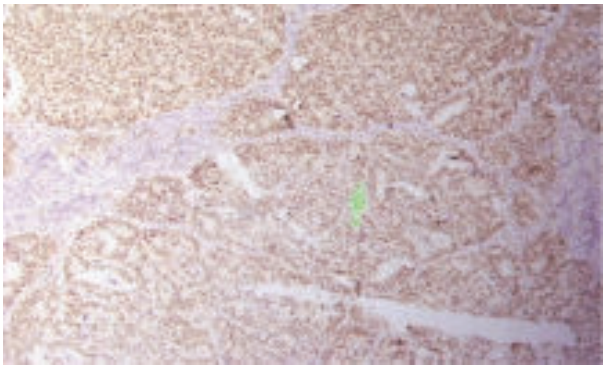

Fig. 2: *Photomicrograph showing intact expression of PMS2 in tumour cells (×100 magnification).*

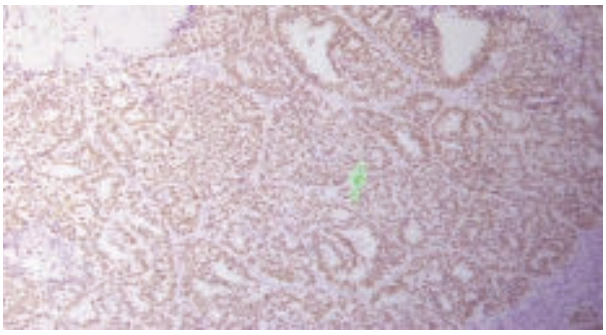

Fig. 3: *Photomicrograph showing intact expression of MSH2 in tumour cells (×100 magnification).*

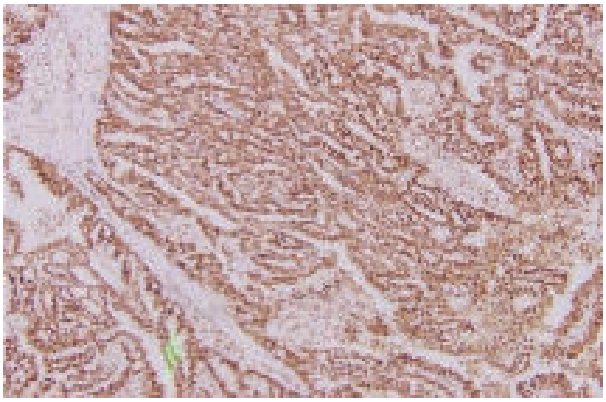

Fig. 4: *Photomicrograph showing intact expression of MSH6 in tumour cells (×100 magnification).*

RESULTS

Out of 54 patients, more than two-thirds (68.5%) were in the ≥60 years age group. Estimated BMI <25 was predominant (57.4%). The majority of the women were postmenopausal (79.6%), while most of them (61.1%) had both hypertension and diabetes mellitus as comorbidities. A positive family history of cancer was found in 20.4% cases (Table-II). Immunohistochemistry findings revealed that two-thirds (63%) of the patients had intact expression of all MMR

protein (MMRp), while 37% had a loss of expression of any of the proteins, which is known as mismatch repair deficiency (dMMR) state. Among them, the most common MMR defect identified was combined loss of *MLH1/PMS2* in 9(16.67%) cases, followed by isolated *PMS2* loss or isolated *MSH2* loss in 6(11.11%) cases, combined *MSH2/MSH6* loss in 4(7.4%) cases, while loss of all four proteins was observed in only 1(1.85%) case (Table-III). The majority of dMMR tumours (85%) and MMRp tumours (70.6%) were of endometroid variety; however, the difference was not significant ($p>0.05$). MMRp tumours were mostly larger in size, the difference was not significant though ($p>0.05$). Deeper myometrial invasion (≥50%) was more evident in MMRp tumours compared to dMMR tumours ($p<0.01$). Cervical extension was also found more frequent in MMRp tumours ($p<0.05$). In contrast, dMMR tumours were found more frequently having lower tumour grade and lower FIGO stage compared to MMRp tumours ($p<0.05$). However, no differences were observed in adnexal involvement, lymphovascular space invasion (LVSI), and lymph node involvement ($p>0.05$) (Table-IV).

Table-II: *Demographic characteristics of the patients (N=54)*

Variables	Frequency	Percentage
Age group (in years)		
<60	17	31.5
≥60	37	68.5
BMI (kg/m^2)		
≥25	23	42.6
<25	31	57.4
Menopausal history		
Premenopausal	11	20.4
Postmenopusal	43	79.6
Comorbidities		
HTN and DM	33	61.1
HTN	6	11.1
DM	6	11.1
Others	9	16.7
Family history of cancer		
Yes	11	20.4
No	43	79.6

Table-III: *Distribution of the MMR protein expression (N=54)*

Variables	Frequency	Percentage
Intact expression of all proteins/ MMR proficient	34	62.96
Loss of expression of one or more protein/ MMR deficient	20	37.04
i) Combined loss of *MLH1* & *PMS2*	9	16.67
ii) Isolated *PMS2* or *MSH2* loss	6	11.11
iii) Combined loss of *MSH2* & *MSH6*	4	7.41
iv) Loss of all proteins	1	1.85

Table-IV: *Comparison of clinicopathological factors between groups (N=54)*

Variables	dMMR (n=20) Frequency (Percentage)	MMRp (n=34) Frequency (Percentage)	p-value
Histological type			
Endometroid	17 (85.0)	24 (70.6)	0.232^{NS}
Non-endometroid	3 (15.0)	10 (29.4)	
Size of tumour (cm)			
<2	7 (35.0)	4 (11.8)	0.121^{NS}
2–4	6 (30.0)	13 (38.2)	
>4	7 (35.0)	17 (50.0)	
Myometrial invasion			
<50%	15 (75.0)	8 (23.5)	0.004^{S}
≥50%	5 (25.0)	26 (76.5)	
Cervical extension			
Yes	2 (10.0)	13 (38.2)	0.025^{S}
No	18 (90.0)	21 (61.8)	
Adnexal involvement			
Yes	2 (10.0)	9 (26.5)	0.147^{NS}
No	18 (90.0)	25 (73.5)	
Lymphovascular space invasion (LVSI)			
Yes	13 (65.0)	6 (17.6)	0.387^{NS}
No	7 (35.0)	28 (82.3)	
Lymph node involvement			
Yes	2 (10.0)	10 (29.4)	0.098^{NS}
No	18 (90.0)	24 (70.6)	
Grade			
Grade I	9 (45.0)	11 (32.3)	0.047^{S}
Grade II	9 (45.0)	9 (26.5)	
Grade III	2 (10.0)	14 (41.2)	
FIGO stage			
Stage I	13 (65.0)	10 (29.4)	0.033^{S}
Stage II	6 (30.0)	12 (35.3)	
Stage III	1 (5.0)	10 (29.4)	
Stage IV	-	2 (5.9)	

Chi-square test was applied to reach p-value; S=significant, NS=not significant.

DISCUSSION

We tried to adopt the molecular classification of endometrial carcinoma applied by the cancer genome atlas (TCGA), which has already been proved as more reproducible; valuable prognostic and predictive information can be obtained through this classification. For evaluation of the molecular status for patients with endometrial cancer genetic testing is required. In the present study, for detection of status of MMR protein, imunohistochemistry assay was used; its effectiveness was shown in several previous studies.[11-13] The four MMR proteins assessed are *MLH1, MSH2, MSH6, and PMS2*. These proteins form two heterodimers, which are *MLH1-PMS2* and *MSH2-MSH6*. When *MLH1* or *MSH2* are lost, there is a consequent loss of *PMS2* or *MSH6*, respectively. On the other hand, a loss of *MSH6* or *PMS2* expression can occur as an isolated event.[14] That is why IHC assessment of only *MSH6* and *PMS2* has been suggested to have the same accuracy as the full MMR panel in identifying dMMR cases. Moreover, IHC using antibodies against the four MMR proteins (*MSH2, MSH6, MLH1, and PMS2)* represents a relatively widely available, affordable, and easy to perform technique, compared to MSI testing.[13]

We observed a relatively high prevalence of abnormal expression of MMR proteins in our study population (37%). This finding was in congruence with the findings of several previous studies (25-37%).[11,15-17] However, other studies showed much lower incidence of dMMR tumours (17-20%).[18,19]

Concerning the relationship of MMR proteins and other clinicopathological features, we observed that the dMMR endometrial tumours presented with less aggressive endometrioid histology at lower tumour stages and grades compared to MMR-proficient tumours. Hashmi et al. reported that dMMR was related to high FIGO stage; any relation with tumour grade was not established.[20] However, Tangjitgamol et al. found that early stage, more endometrioid histology, and lower grade tumour were associated with MMR deficiency.[21]

The lymphovascular space invasion (LVSI) is a marker of metastatic potential in cancer patients. In the present study, LVSI was observed in 65% of endometrial cancers with dMMR suggesting that metastasis was more likely in dMMR cases.[22] However, dMMR endometrial cancers have more favourable prognosis compared to their MMR-proficient counterparts. Microsatellite instability (MSI) phenotype or dMMR endometrial tumours have a protective immunephenotype and positively correlate with high immune infiltration. In theory, this protective immune phenotype can counteract the poor clinicopathological parameters that co-exist in dMMR tumours.[22]

Last but not the least, our study has several limitations. The study population was selected from one selected hospital in Dhaka city; hence, the results of the study may not reflect the exact picture of the country. A small sample size was another limitation, which was due to time and budget constraint. Further studies are recommended with large sample size and involving multicentre from different regions of the country.

CONCLUSION

In this study, two-thirds of the study patients (EC) had intact expression of all MMR proteins and the rest had a loss of expression of any of the proteins, i.e., mismatch repair deficiency (dMMR). MMR deficiency is common in EC, between 20–40%, and impacts the screening for Lynch syndrome (LS), therapeutic decision-making, risk stratification, and inclusion in clinical trials. With the increasing emphasis on molecular classification in EC, accurate and reproducible testing is paramount to improving patient outcomes.

Conflict of interest: None declared.

Funding source: Self-funding.

Ethical approval: This study was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh (BSMMU/2022/9561-IRB Reg. No. 3956).

Authors' contribution: Conceptualization and design of the study: SN Alamgir, J Ferdous; patient selection, data collection and compilation: SN Alamgir, J Ferdous, MJ Faika, K Farhana, KT Rahman, FB Rashid; data analysis: SN Alamgir, M Asaduzzaman; supervision of the study: J Ferdous; manuscript preparation, editing and final submission: SN Alamgir, J Ferdous, MJ Faika, K Farhana, KT Rahman, FB Rashid, M Asaduzzaman.

REFERENCES

1. Hossain N, Banu F, Anwar R, Afroz M, Ara N. Pattern of gynecological malignancies in Bangladesh: five years' experience at National Institute of Cancer Research & Hospital (NICRH). Cancer J Bangladesh. 2021;2(1):15-8.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49.
3. Deshpande M, Romanski PA, Rosenwaks Z, Gerhardt J. Gynecological cancers caused by deficient mismatch repair and microsatellite instability. Cancers (Basel). 2020;12(11):3319.
4. Ramsoekh D, Wagner A, van Leerdam ME, Dooijes D, Tops CM, Steyerberg EW, et al. Cancer risk in MLH1, MSH2 and MSH6 mutation carriers; different risk profiles may influence clinical management. Hered Cancer Clin Pract. 2009;7(1):17.
5. Human Genome Organization (HUGO) Gene Nomenclature Committee. The Resource for Approved Human Gene Nomenclature. Available at: https://www.genenames.org/ (accessed January 10, 2023).
6. Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. Virchows Arch. 2021;478(2):153-90.
7. Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023;162(2):383-94.
8. Bartley AN, Mills AM, Konnick E, Overman M, Ventura CB, Souter L, et al. Mismatch repair and microsatellite instability testing for immune checkpoint inhibitor therapy: guideline from the College of American Pathologists in collaboration with the Association for Molecular Pathology and Fight Colorectal Cancer. Arch Pathol Lab Med. 2022;146(10):1194-1210.
9. Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, et al. Endometrial cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(9):860-77.
10. Vikas P, Messersmith H, Compton C, Sholl L, Broaddus RR, Davis A, et al. Mismatch repair and microsatellite instability testing for immune checkpoint inhibitor therapy: ASCO endorsement of College of American Pathologists guideline. J Clin Oncol. 2023;41(10):1943-8.
11. Riedinger CJ, Esnakula A, Haight PJ, Suarez AA, Chen W, Gillespie J, et al. Characterization of mismatch-repair/microsatellite instability-discordant endometrial cancers. Cancer. 2024;130(3): 385-99.
12. Mills AM, Bullock TN, Ring KL. Targeting immune checkpoints in gynecologic cancer: updates & perspectives for pathologists. Mod Pathol. 2022;35(2):142-51.
13. Raffone A, Travaglino A, Cerbone M, Gencarelli A, Mollo A, Insabato L, et al. Diagnostic accuracy of immunohistochemistry for mismatch repair proteins as surrogate of microsatellite instability molecular testing in endometrial cancer. Pathol Oncol Res. 2020;26(3):1417-27.
14. Arciuolo D, Travaglino A, Raffone A, Raimondo D, Santoro A, Russo D, et al. TCGA molecular prognostic groups of endometrial carcinoma: current knowledge and future perspectives. Int J Mol Sci. 2022;23(19):11684.
15. de Freitas D, Aguiar FN, Anton C, de Almeida DC, Bacchi CE, Carvalho JP, et al. Clinicopathological characteristics of endometrial carcinomas according to DNA mismatch repair protein status. Heliyon. 2023;9(6):e17495.
16. Ruscelli M, Maloberti T, Corradini AG, Rosini F, Querzoli G, Grillini M, et al. Prognostic impact of pathologic features in molecular subgroups of endometrial carcinoma. J Pers Med. 2023;13(5):723.
17. Da Cruz Paula A, DeLair DF, Ferrando L, Fix DJ, Soslow RA, Park KJ, et al. Genetic and molecular subtype heterogeneity in newly diagnosed early- and advanced-stage endometrial cancer. Gynecol Oncol. 2021;161(2):535-44.
18. Black D, Soslow RA, Levine DA, Tornos C, Chen SC, Hummer AJ, et al. Clinicopathologic significance of defective DNA mismatch repair in endometrial carcinoma. J Clin Oncol. 2006; 24(11):1745-53.
19. Yamamoto A, Yamaguchi T, Suzuki O, Ito T, Chika N, Kamae N, Tamaru JI, Nagai T, Seki H, Arai T, Tachikawa T, Akagi K, Eguchi H, Okazaki Y, Ishida H. Prevalence and molecular characteristics of DNA mismatch repair deficient endometrial cancer in a Japanese hospital-based population. Jpn J Clin Oncol. 2021;51(1):60-9.
20. Hashmi AA, Mudassir G, Hashmi RN, Irfan M, Asif H, Khan EY, et al. Microsatellite instability in endometrial carcinoma by immunohistochemistry, association with clinical and histopathologic parameters. Asian Pac J Cancer Prev. 2019;20(9): 2601-6.
21. Tangjitgamol S, Kittisiam T, Tanvanich S. Prevalence and prognostic role of mismatch repair gene defect in endometrial cancer patients. Tumour Biol. 2017;39(9):1010428317725834.
22. Jumaah AS, Al-Haddad HS, Salem MM, McAllister KA, Yasseen AA. Mismatch repair deficiency and clinicopathological characteristics in endometrial carcinoma: a systematic review and meta-analysis. J Pathol Transl Med. 2021;55(3):202-11.

Review Article

A Mosquito's Tale: Navigating Dengue Challenges in Bangladesh

Anzoom J[1], Huq H[2], Tasnim J[3], Begum M[4], Sultana K[5]

ABSTRACT

Dengue is a significant public health concern in numerous tropical and subtropical nations like Bangladesh, especially in industrial and semi-urban regions, which have witnessed the majority of outbreaks. An estimated 50 million dengue infections occur worldwide annually and it has been included among the top ten global health hazards by the World Health Organization. Humans are among the only known hosts for the dengue virus, which is spread by the Aedes mosquito. In Bangladesh, the prevalence of dengue has experienced a substantial rise over the past 35 years, with growing urbanization, modernization, and global warming being widely regarded as the primary drivers. Factors like rapid urbanization, unchecked population growth, failing waste management systems, and absence of effective vector control contributed to the rise and spread of dengue infection in the country. This review paper aims to thoroughly examine the dynamics of dengue infection, with a focus on the interrelated impacts of climate, urbanization, and public health preparedness in Bangladesh. The approach entails analyzing past viewpoints, changes in population, and factors that influence society, while also evaluating government policies, ethical concerns, and initiatives sponsored by the community. The review will try to discover effective techniques for dengue prevention and control by examining successful community development initiatives and behaviour change models.

Keywords: *Dengue, public health, prevention and control, climate change, urbanization, Bangladesh*

Mugda Med Coll J. 2026; 9(1): 73-80
DOI: https://doi.org/10.3329/mumcj.v9i1.90830

INTRODUCTION

Dengue is a significant public health concern in numerous tropical and subtropical nations, especially in industrial and semi-urban regions, which have witnessed the majority of outbreaks.[1] An estimated 50 million dengue infections occur worldwide annually and it is included among the top 10 global health hazards by the World Health Organization (WHO).[2] Bangladesh is located in the tropical and subtropical regions, similar to other Southeast Asian countries. Consequently, it has become an ideal breeding ground for the dengue vector and the subsequent rise in its spread.[3] Humans are among the only known hosts for the dengue virus, which is spread by the Aedes mosquito.[2] The prevalence of dengue has experienced a substantial rise over the past 35 years, with growing urbanization, modernization, and global warming being widely regarded as the primary drivers.[4] A number of factors, including rapid urbanization, unchecked population growth, failing waste management systems, and an absence of effective vector control, contribute to the occurrence and spread of dengue.[5] However, this review paper aims to thoroughly examine the dynamics of dengue infection, with a focus on the interrelated impacts of climate, urbanization, and

1. Dr. Jarin Anzoom, Graduate Student, School of Allied and Public Health, University of Chester, Wheeler Campus, Chester, UK. Email: drjarinanzoomrpmc@gmail.com (Corresponding author)
2. Dr. Hiya Huq, Graduate Student, School of Psychology, Social Work and Public Health, Oxford Brookes University, Headington Campus, Oxford, UK.
3. Dr. Jarin Tasnim, Graduate Student, School of Allied and Public Health, University of Chester, Wheeler Campus, Chester, UK.
4. Dr. Munira Begum, Assistant Professor, Department of Community Medicine, Rangpur Medical College, Rangpur-5400, Bangladesh.
5. Dr. Khadiza Sultana, Surveillance Medical Officer, National Malaria Elimination & Aedes Transmitted Disease Control Program, Directorate General of Health Services (DGHS), Dhaka-1212, Bangladesh.

public health focusing on Bangladesh. The approach entails analyzing past viewpoints, changes in population, and factors that influence society, while also evaluating government policies, ethical concerns, and initiatives sponsored by the community. The review will try to discover effective techniques for dengue prevention and add to the debate on public health improvement by examining successful community development initiatives and behavior change models.

HISTORICAL PERSPECTIVE OF DENGUE IN BANGLADESH

In the 1780s, there was a dengue outbreak that was recorded in North America, Africa, and Asia nearly at the same time.[6] Dengue fever, formerly known as 'Dacca fever',[7] was initially documented in the 1960s in Bangladesh (formerly East Pakistan). Until 1965, there were only a few isolated reports of dengue cases in Bangladesh, leading people to believe that the country was free from the disease.[8] However, it was not until the 21st century that the disease became epidemic and eventually endemic due to metropolitan cycles and the establishment of the "domesticated" insect vector Aedes aegypti.[9,10]

The earliest dengue outbreak in Bangladesh was documented in 2000, with a total of 5551 cases and 93 fatalities registered.[11] Afterwards, dengue has established itself as a prevalent and recurring occurrence in Bangladesh.[1] For instance, using data from 200 inpatients, Islam et al. examined a dengue epidemic that hit Bangladesh in 2002.[12] Viral isolation and molecular characterisation were among the laboratory approaches used to confirm dengue cases. Phylogenetic analysis of the eight Dengue Virus Type-3 (DEN-3) strains found in the study showed that they are closely related to isolates found in Thailand in the 1990s. The results indicated that the circulating DEN-3 viruses were most likely brought to Bangladesh from nearby nations.[12] This epidemic brought to light the fact that dengue has been a major issue in Bangladeshi public health since the year 2000. From 2000 to 2003, all four serotypes (DEN-1–4) were identified in Dhaka metropolis, with a higher incidence of the DEN-3 serotype.[13] The incidence of dengue decreased significantly in subsequent years, reaching a minimum of 375 cases in 2014. Nevertheless, in the year 2016, approximately 6100 instances of dengue have been documented in Bangladesh.[14]

The reemergence of DENV-3 was detected in 2017, leading to a significant increase in dengue infections starting from the onset of the monsoon season in 2018.[15] The number of newly reported dengue infections surpassed 10,000 in 2018. In 2019, there were 101,354 dengue cases and 164 dengue-related deaths reported in Bangladesh, making it one of the worst dengue epidemics in the country's history.[1] According to the Directorate General of Health Services (DGHS) of Bangladesh, a total of 100,201 confirmed dengue cases got admitted into hospitals in 2019 – 51,179 were reported in Dhaka city and 49,022 were reported in other parts of Bangladesh. This indicated a tenfold surge in the number of hospitalized cases compared to the most significant outbreak prior to 2019.[10] In 2020, Bangladesh recorded a total of 1405 cases of dengue, with just three deaths confirmed to be directly caused by dengue.[16] However, the number of dengue cases in 2021 was 28,429, with 105 deaths attributable to the disease.[1] During the COVID-19 pandemic, concurrent dengue and COVID-19 infections compounded and heightened problems were observed in the healthcare system due to unreadiness, inadequate facilities, and insufficient funding. As a result, country's greatest death toll of 81 cases documented in 2022.[17] Besides, a disturbing spike in dengue incidence and deaths in Bangladesh (110,224 cases of DENV infections and 528 deaths between January and August of 2023) was reported, which was very different from previous patterns; probable factors behind were the arrival of a new strain of dengue virus (DENV-4) and the delayed start of the rainy season.[17] The situation was further complicated by a concurrent outbreak reported at the Rohingya refugee camps in Cox's Bazar district in 2022.[18] Since then dengue cases and fatalities reached a record-breaking high in the country, with numbers still remain on an upward trajectory (as shown in Fig. 1).

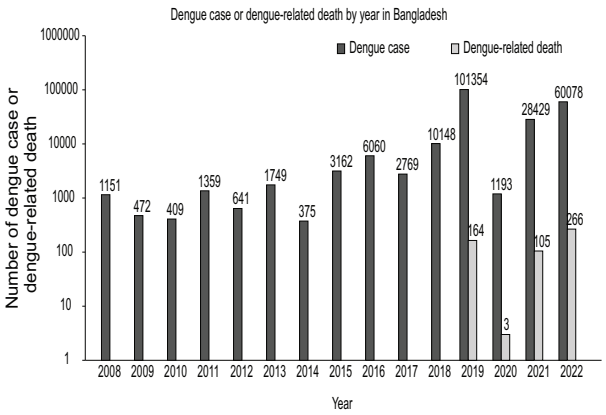

Fig. 1. *Dengue cases and deaths connected to dengue fever reported in Bangladesh between 2008 and 2022 (Source: Kayesh et al.)*[1]

SOCIODEMOGRAHIC TAPESTRY OF DENGUE

Dengue fever was found positively associated with low socioeconomic position, low income, poor education, ignorance about dengue, unemployment, overcrowding in the home, substandard housing (including inadequate sewage and garbage disposal), and the kind of dwelling, as based on several research.[19-24] In addition, evidence showed that during dengue epidemics, men were more likely to get infected with the virus, while women were more likely to experience severe cases of the disease.[25] Another report on dengue in Bangladesh revealed that 73.33% of cases were between 18 and 40 years, affecting mostly young and economically active people. Only 15.24% and 9.52% of cases were found in the 41–60 years and <18 years age group respectively. Patients >60 years had the lowest percentage (1.90%). Dengue cases were similar across age groups, although more men were infected, suggesting a gender-related susceptibility. In addition, urban areas had a higher infection rate (54.35%) than rural areas.[26]

MAPPING THE GEOGRAPHICAL DISTRIBUTION OF DENGUE

Urban regions of Bangladesh are prone to dengue epidemics due to a combination of factors, including a dense population, unplanned development, lack of surveillance, and a lack of attention to dengue prevention measures. This problem is further worsened by climate change. As a result of better trade and communication, more people, including dengue patients, are able to travel, increasing the nationwide prevalence of dengue.[18] In 2019, the Dhaka division had the largest number of dengue cases, followed by the Khulna, Chattogram, Barishal, Rajshahi, Mymensingh, Rangpur, and Sylhet division. The Dhaka Division had the largest number of dengue cases in 2022, followed by Chattogram, Khulna, Barishal, Rajshahi, Mymensingh, Rangpur, and Sylhet. This indicates that the Dhaka Division, especially Dhaka city, was the epicentre of the outbreak[1] (as shown in Fig. 2).

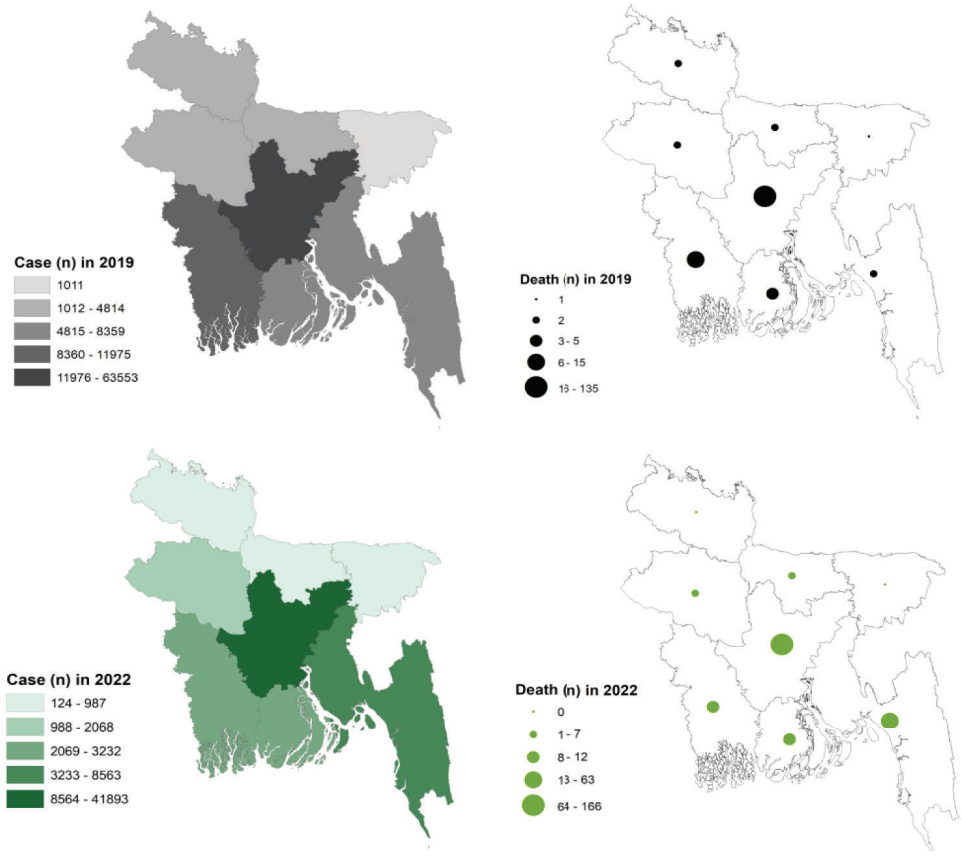

Fig. 2: *Dengue infection and fatalities associated with dengue documented in various regions of Bangladesh in the years 2019 and 2022 (Source: Kayesh et al.)*[1]

DENGUE SEROTYPE DYNAMICS AND DISEASE PATTERN

The four different serotypes of dengue fever (DENV-1 through DENV-4) are all found in tropical and subtropical areas worldwide.[27,28] The 2000 outbreak in Bangladesh saw the presence of all four serotypes of the dengue virus, with DEN-3 being the most prevalent.[28] In order to identify the dengue virus serotypes that were circulating, Another study, done between 2013 and 2016, showed that Dhaka contained both DEN2 and DEN1, while Chittagong and Khulna exhibited a predominance of DEN2. 2014 marked the expansion of DEN1 outside of Dhaka. Both DEN1 and DEN2 were circulating in 2015; however, by 2016, DEN2 had taken over as the most common strain in all three cities.[15] However, DEN-1 and 2 were the most common strain in the outbreaks between 2013 and 2016, whereas DEN-3 has isolated the outbreaks prior to 2002.[15,28-30] In 2017, the DEN-3 was observed to reappear, and in the recent past, DEN-3 and DEN-4 were more frequently observed.[30] The most common symptoms of dengue fever during the initial outbreak in 2000 were fever (100%), headache (91%), and joint pain (85%). In 2019, the dengue epidemic that was the worst occurred in Bangladesh. In addition to fever, gastrointestinal symptoms, particularly nausea and vomiting (69.2% of cases) and abdominal pain (84.6%), were the most common presentation.[12,13,15,30] In addition, around 25% of individuals in the 2019 outbreak had hypotension, which is a symptom of plasma leakage and imminent shock. However, a research that tracked paediatric patients from 2006 to 2008 found that shock symptoms were present in just 11% of events.[31] Hence, it is clear that dengue is likely experiencing an epidemiological change in Bangladesh, with a focus on more severe cases (dengue shock syndrome rather than dengue haemorrahic fever). This shift may have been prompted by the recent comeback of the DENV-3 serotype.[13,15,30] In addition, A major public health concern for Bangladesh could arise from secondary infections caused by the resurgence of the DENV-4 serotype, which has been absent for over 20 years.[13]

SEASONAL VARIATION, CLIMATE CHANGE AND URBANIZATION

The Aedes mosquito is a vector that is affected by climate change; spread of dengue in tropical and subtropical regions typically displays a seasonal pattern. This pattern is a result of the impact of climate on the disease's propagation cycle.[32,33] Moreover, changes in average temperature and temperature fluctuations have a significant impact on the viability and population growth of the Aedes mosquito. They thrive during the day and are most effective in transmitting dengue fever when the diurnal temperature range (DTR) is near zero, which is around 29.3°C.[21,34] Because Aedes mosquitoes prefer to lay their eggs in man-made containers, which are more abundant in urban environments, rainfall and human population density are also relevant factors.[35,36] All of these are true for Bangladesh being situated in the South-East Asia region. Data showed a strong correlation between monthly humidity and dengue incidence, with the strongest impacts shown two months after the fact. Based on the study's projections, a significant increase in dengue incidence by 2100 could be caused by a rise in global temperatures.[36] Evidence on the influence of climate change through assessing vectorial capacity (VC) of Aedes aegypti mosquitoes under several climate scenarios demonstrated that despite a projected drop in yearly VC by the end of the century, the risk of possible dengue epidemic transmission remains high in all regions. The decrease in VC obscures notable fluctuations in monthly VC indicating a possible elongation of the dengue season throughout the entire year.[34] Evidence also showed that rising and fluctuating temperatures, uncontrolled and fast urbanisation, a high rate of population growth, and Bangladesh's weak medical infrastructure all contribute to the intensity and frequency of dengue outbreaks in the last couple of decades.[10,21,30,34,36,37]

Such risks of further outbreaks highlight the necessity of flexible public health planning, as climate change modifies the timing and geographical distribution of dengue risk in Bangladesh. This calls for the implementation of enhanced monitoring and control strategies to minimise the impact of future outbreaks.

HEALTH BELIEF MODEL FOR DENGUE PREVENTION

The influence of information, values, and practices on dengue prevention and control is clearly apparent. The Health Belief Model (HBM) is widely utilized and consists of several key components: risk susceptibility, risk severity, benefits to action, barriers to action, self-efficacy, and cues to action.[38] Regarding dengue, the Health Belief Model (HBM) offers a framework for comprehending how to efficiently organize communications and impact behavioural

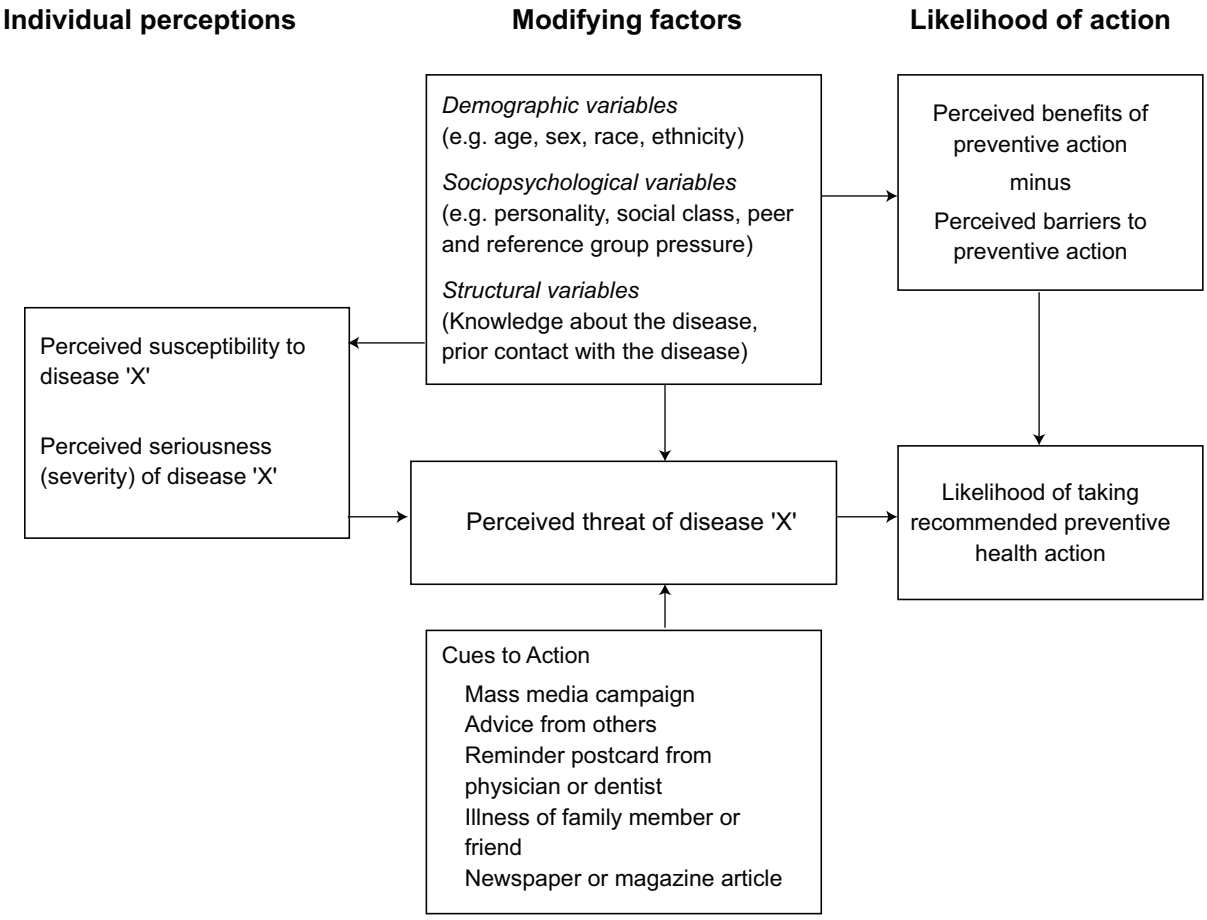

Fig. 3: *Health Belief Model (Source: Roden)*[40]

modification.[39] The HBM framework emphasises the necessity for focused interventions by highlighting a variety of beliefs. The HBM is supported by the positive association between knowledge/practices and attitude/practices, which suggests that raising awareness has a beneficial effect on preventative behaviours. It is imperative to tackle information gaps and psychological obstacles in order to customise Dengue prevention tactics and encourage a more all-encompassing community reaction.[39,40]

Since there is no vaccine for dengue fever is available in Bangladesh, adopting healthy habits such as acquiring accurate knowledge, maintaining a positive mindset, and consistently following safe practices can contribute to the elimination of dengue fever.[2,41]

INTERVENTION AND STRATEGIES

The mitigation of dengue issues in Bangladesh involves a synergistic approach that combines governmental endeavors with collaborative strategies. Moreover, possible measures to be implemented consist of implementing statewide event-based dengue surveillance coupled with environmental management, conducting research on ecological, environmental, and entomological markers of infection, and creating geospatial and risk mapping to identify sensitive areas.[41] Unfortunately, even though dengue research is making great strides globally, it remains a significant challenge to provide effective treatment and prevention alternatives, making dengue management and prevention a pressing issue in Bangladesh today.[5]

Dengue outbreak prevention continues to rely primarily on vector control.[1] In Bangladesh, the city corporations/municipalities are in charge of mosquito management as part of its current vector-control mission. The main component of the programme is the use of insecticidal chemicals to kill adult mosquitoes. This is particularly important during the months of August and September, when hospitals often see a high number of dengue cases.[42-

[44] Despite the implementation of vector control measures in the past decades, namely targeting mosquitoes and their breeding grounds, dengue remains a significant public health issue in Bangladesh. This might be due to a confluence of circumstances, such as the availability of vulnerable human hosts during the start of transmission seasons and favourable weather conditions (rainfall that coincides with higher temperatures). Base on previous evidence, it is recommended that the vector-control programmes need to be initiated in the month of April.[44] Nevertheless, it is believed that a mix of vector control schemes yields better results than any one method alone.[42] According to World Health Organization (WHO), a continuous engagement of the community is crucial in order to significantly enhance vector control endeavours.[2] Several evidence suggested that dengue cases may be significantly reduced with the implementation of community-based environmental management strategies, such as water container covers and house screening.[45,46]

Effective dengue prevention and control can be accomplished through the use of appropriate preventative measures, including the utilisation of mosquito nets, repellent spray, and mosquito coils; elimination of stagnant water; and avoidance of the accumulation of rubbish in and around residences to deter mosquito reproduction. In addition, community surveillance and enhance awareness impact significantly in prevention and control of dengue related morbidity and mortality in the community. It affects people's understanding of dengue, their perception of its severity and susceptibility, as well as their habits and beliefs.[41,47,48]

Finally, we recommend that emphasizing health education on dengue should be a priority for dengue management programmes focusing on healthy living, vector control, importance of early diagnosis and treatment and those will be run by local government and non-government organizations (NGOs) both in rural and urban densely-populated areas.

CONCLUSION

Our analysis of dengue related issues in Bangladesh uncovers a complex public health problem that requires a thorough and subtle strategy. Comprehending the development of healthcare systems and interventions is crucial, as emphasized by the historical perspectives and models of public health. Demographic views provide insights into changes in population size and disease trends, highlighting the importance of implementing focused measures for protection and screening. An in-depth analysis of the values that shape policy making is required in order to address the ethical and ideological aspects of public health. Community development techniques and engagement tactics are seen as essential instruments, highlighting the significance of community involvement in enhancing health. Looking ahead, it is crucial to improve public health in response to the difficulties posed by dengue. Suggested measures involve enhancing community-based initiatives, incorporating behavioral change models into public health interventions, and promoting interdisciplinary collaboration. Furthermore, allocating resources towards conducting research to comprehend the specific circumstances of the region and applying enduring strategies can greatly enhance efforts to prevent and manage dengue in Bangladesh. By prioritizing these principles, organizations may work together to build a strong public health framework that is better equipped to handle Dengue problems and enhance the well-being of the community.

Conflict of Interest: None declared by the authors.

Funding Source: None.

Ethical Approval: Not applicable.

Authors' Contribution: The first author was involved in conceptualization and design of the narrative review. All authors were equally involved in literature search and review, data collection and compilation as well as manuscript writing, editing and final submission.

REFERENCES

1. Kayesh MEH, Khalil I, Kohara M, Tsukiyama-Kohara K. Increasing dengue burden and severe dengue risk in Bangladesh: an overview. Trop Med Infect Dis. 2023;8(1):32.
2. World Health Organization (WHO). Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition. New Delhi, India: WHO; 2011.
3. Mutsuddy P, Jhora ST, Shamsuzzaman AKM, Kaisar SMG, Khan MNA. Dengue situation in Bangladesh: an epidemiological shift in terms of morbidity and mortality. Can J Infect Dis Med Microbiol. 2019; 2019:3516284.

4. Gubler DJ. Dengue, urbanization and globalization: the unholy trinity of the 21(st) century. Trop Med Health. 2011;39(4 Suppl):3-11.

5. Hossain MI, Alam NE, Akter S, Suriea U, Aktar S, Shifat SK, et al. Knowledge, awareness and preventive practices of dengue outbreak in Bangladesh: a countrywide study. PLoS One. 2021;16(6):e0252852.

6. Mamun MA, Misti JM, Griffiths MD, Gozal D. The dengue epidemic in Bangladesh: risk factors and actionable items. Lancet. 2019;394(10215):2149-50.

7. Russell PK, Buescher EL, McCown JM, Ordõnez J. Recovery of dengue viruses from patients during epidemics in Puerto Rico and East Pakistan. Am J Trop Med Hyg. 1966;15(4):573-9.

8. Aziz MA, Gorham R, Gregg MB. 'Dacca fever'. *Pak J Med Res.* 1967;6:83-92.

9. Dhar-Chowdhury P, Haque CE, Driedger SM. Dengue disease risk mental models in the city of Dhaka, Bangladesh: juxtapositions and gaps between the public and experts. Risk Anal. 2016;36(5):874-91.

10. Hossain MS, Siddiqee MH, Siddiqi UR, Raheem E, Akter R, Hu W. Dengue in a crowded megacity: Lessons learnt from 2019 outbreak in Dhaka, Bangladesh. PLoS Negl Trop Dis. 2020;14(8): e0008349.

11. Yunus EB, Bangali AM, Mahmood MAH, Rahman MM, Chowdhury AR, Talukder KR. Dengue outbreak 2000 in Bangladesh: from speculation to reality and exercises. Dengue Bull. 2001;25:15-20.

12. Islam MA, Ahmed MU, Begum N, Chowdhury NA, Khan AH, Parquet Mdel C, et al. Molecular characterization and clinical evaluation of dengue outbreak in 2002 in Bangladesh. Jpn J Infect Dis. 2006;59(2):85-91.

13. Hossain MS, Noman AA, Mamun SMAA, Mosabbir AA. Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks. Trop Med Health. 2023;51(1):37.

14. Tabassum T, Taylor-Robinson AW. Dengue serotypes in Bangladesh: whole genome sequencing and comparative genomics facilitates pathogenesis and epidemiology studies and informs improved disease control. Microbiol Infect Dis. 2019;3(1):1-5.

15. Shirin T, Muraduzzaman AKM, Alam AN, Sultana S, Siddiqua M, Khan MH, et al. Largest dengue outbreak of the decade with high fatality may be due to reemergence of DEN-3 serotype in Dhaka, Bangladesh, necessitating immediate public health attention. New Microbes New Infect. 2019;29:100511.

16. Hasan MM, Sahito AM, Muzzamil M, Mohanan P, Islam Z, Billah MM, et al. Devastating dengue outbreak amidst COVID-19 pandemic in Bangladesh: an alarming situation. Trop Med Health. 2022;50(1):11.

17. Haider N, Asaduzzaman M, Hasan MN, Rahman M, Sharif AR, Ashrafi SAA, et al. Bangladesh's 2023 Dengue outbreak – age/gender-related disparity in morbidity and mortality and geographic variability of epidemic burdens. Int J Infect Dis. 2023;136:1-4.

18. Bonna AS, Pavel SR, Mehjabin T, Ali M. Dengue in Bangladesh. Int J Infect Dis. 2023:S1201-9712(23)00644-6.

19. Hagenlocher M, Delmelle E, Casas I, Kienberger S. Assessing socioeconomic vulnerability to dengue fever in Cali, Colombia: statistical vs expert-based modeling. Int J Health Geogr. 2013;12:36.

20. Yang J, Mosabbir AA, Raheem E, Hu W, Hossain MS. Demographic characteristics, clinical symptoms, biochemical markers and probability of occurrence of severe dengue: a multicenter hospital-based study in Bangladesh. PLoS Negl Trop Dis. 2023;17(3):e0011161.

21. Paul KK, Dhar-Chowdhury P, Haque CE, Al-Amin HM, Goswami DR, Kafi MAH, et al. Risk factors for the presence of dengue vector mosquitoes, and determinants of their prevalence and larval site selection in Dhaka, Bangladesh. PLoS One. 2018;13(6):e0199457.

23. Islam S, Haque CE, Hossain S, Walker D. Association among ecological and behavioural attributes, dengue vector and disease control: a cross-sectional study of the city of Dhaka, Bangladesh. Int Health. 2020;12(5):444-54.

24. Abir T, Ekwudu O, Kalimullah NA, Nur-A Yazdani DM, Al Mamun A, Basak P, et al. Dengue in Dhaka, Bangladesh: hospital-based cross-sectional KAP assessment at Dhaka North and Dhaka South City Corporation area. PLoS One. 2021;16(3):e0249135.

25. Huy NT, Van Giang T, Thuy DH, Kikuchi M, Hien TT, Zamora J, et al. Factors associated with dengue shock syndrome: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2013;7(9):e2412.

26. Prattay KMR, Sarkar MR, Shafiullah AZM, Islam MS, Raihan SZ, Sharmin N. A retrospective study on the socio-demographic factors and clinical parameters of dengue disease and their effects on

the clinical course and recovery of the patients in a tertiary care hospital of Bangladesh. PLoS Negl Trop Dis. 2022;16(4):e0010297.

27. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, et al Dengue: a continuing global threat. Nat Rev Microbiol. 2010;8(12 Suppl):S7-16.

28. Pervin M, Tabassum S, Islam MN. Isolation and serotyping of dengue viruses by mosquito inoculation technique from clinically suspected cases of dengue fever. Bangladesh Med Res Counc Bull. 2002;28(3):104-11.

29. Muraduzzaman AKM, Alam AN, Sultana S, Siddiqua M, Khan MH, Akram A, et al. Circulating dengue virus serotypes in Bangladesh from 2013 to 2016. Virusdisease. 2018;29(3):303-7.

30. Hasan MJ, Tabassum T, Sharif M, Khan MAS, Bipasha AR, Basher A, et al. Clinico-epidemiologic characteristics of the 2019 dengue outbreak in Bangladesh. Trans R Soc Trop Med Hyg. 2021;115(7):733-40.

31. Alam ABMS, Sadat SA, Swapan Z, Ahmed AU, Karim MN, Paul HK, et al. Clinical profile of dengue fever in children. Bangladesh J Child Health. 2009;33(2):55-8.

32. Johansson MA, Dominici F, Glass GE. Local and global effects of climate on dengue transmission in Puerto Rico. PLoS Negl Trop Dis. 2009;3(2):e382.

33. Karim MN, Munshi SU, Anwar N, Alam MS. Climatic factors influencing dengue cases in Dhaka city: a model for dengue prediction. Indian J Med Res. 2012;136(1):32-9.

34. Paul KK, Macadam I, Green D, Regan DG, Gray RT. Dengue transmission risk in a changing climate: Bangladesh is likely to experience a longer dengue fever season in the future. Environ Res Lett. 2021;16(11):114003.

35. Islam S, Haque CE, Hossain S, Rochon K. Role of container type, behavioural, and ecological factors in Aedes pupal production in Dhaka, Bangladesh: an application of zero-inflated negative binomial model. Acta Trop. 2019;193:50-59.

36. Banu S, Hu W, Guo Y, Hurst C, Tong S. Projecting the impact of climate change on dengue transmission in Dhaka, Bangladesh. Environ Int. 2014;63:137-42.

37. Sharmin S, Glass K, Viennet E, Harley D. Interaction of mean temperature and daily fluctuation influences dengue incidence in Dhaka, Bangladesh. PLoS Negl Trop Dis. 2015;9(7):e0003901.

38. Champion V, Skinner CS. The Health Belief Model. In: Glanz K, Rimer B, Viswanath K. eds. Health Behavior and Health Education. 4th ed. San Francisco, CA: Jossey-Bass; 2008.

39. Lennon JL. The use of the health belief model in dengue health education. Dengue Bull. 2005;29:217-9.

40. Roden J. Revisiting the Health Belief Model: nurses applying it to young families and their health promotion needs. Nurs Health Sci. 2004;6(1):1-10.

41. Mone FH, Hossain S, Hasan MT, Tajkia G, Ahmed F. Sustainable actions needed to mitigate dengue outbreak in Bangladesh. Lancet Infect Dis. 2019;19(11):1166-7.

42. Lima EP, Goulart MO, Rolim Neto ML. Meta-analysis of studies on chemical, physical and biological agents in the control of Aedes aegypti. BMC Public Health. 2015;15:858.

43. Al-Amin HM, Johora FT, Irish SR, Hossainey MRH, Vizcaino L, Paul KK, et al. Insecticide resistance status of Aedes aegypti in Bangladesh. Parasit Vectors. 2020;13(1):622.

44. Haider N, Chang YM, Rahman M, Zumla A, Kock RA. Dengue outbreaks in Bangladesh: Historic epidemic patterns suggest earlier mosquito control intervention in the transmission season could reduce the monthly growth factor and extent of epidemics. Curr Res Parasitol Vector Borne Dis. 2021;1:100063.

45. Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence?: systematic review and meta-analysis. PLoS Negl Trop Dis. 2016;10(3):e0004551.

46. Che-Mendoza A, Medina-Barreiro A, Koyoc-Cardeña E, Uc-Puc V, Contreras-Perera Y, Herrera-Bojórquez J, et al. House screening with insecticide-treated netting provides sustained reductions in domestic populations of Aedes aegypti in Merida, Mexico. PLoS Negl Trop Dis. 2018;12(3):e0006283.

47. Ahsan A, Haider N, Kock R, Benfield C. Possible drivers of the 2019 dengue outbreak in Bangladesh: the need for a robust community-level surveillance system. J Med Entomol. 2021;58(1):37-9.

48. Hossain MJ, Das M, Islam MW, Shahjahan M, Ferdous J. Community engagement and social participation in dengue prevention: a cross-sectional study in Dhaka City. Health Sci Rep. 2024;7(4):e2022.

Review Article

Teaching Procedural Skills in Clinical Education Using Gagné's Instructional Design Model

Nurunnabi ASM[1], Nigar K[2], Alam MA[3], Khatun M[4], Sultana F[5], Hossain MA[6], Alam QS[7]

ABSTRACT

Competence in teaching procedural skills is required for faculty in all clinical specialties of a medical college. There exist several long-standing and widely accepted theories on psychomotor skill acquisition, which favour graduated learning and sequential teaching approach; Gagné's instructional design model is one of them. Gagné's instructional design model is based on the idea that learning is a process that involves the acquisition of knowledge and skills through a series of steps. Teaching procedural skills is crucial in medical education and evidence showed that Gagné's model delineates a sequence of specific instructional events that correlate with crucial conditions of learning, providing a framework that is able to maximally enhance the learning process, improve session flow and ensure that objectives are comprehensively addressed. This review paper aims to see how and to what extent Gagné's instructional design model supports teaching procedural skills to medical students.

Keywords: *Gagné's instructional design model, clinical education, medical education, procedural skills, teaching and learning.*

Mugda Med Coll J. 2026; 9(1): 81-86
DOI: https://doi.org/10.3329/mumcj.v9i1.90838

INTRODUCTION

In a resource-poor setting like Bangladesh, medical education often suffers from lack of rigorous and appropriate instructional designs;[1,2] however, in recent years situation has fortunately improved, and medical educators now have access to much higher quality medical education research through online resources to guide development of medical curriculum and instructional methods.[2,3]

Competence in teaching procedural skills is required for faculty in all clinical specialties of all medical colleges in Bangladesh. For our involvement in undergraduate medical education, all faculty members are likely be involved in teaching procedures to novice learners at some point, with the goal of having the learner achieve graduated independence and technical competence in different skill sets.[1] Teaching procedural skills to novices is complex because it requires not only teaching new cognitive tasks but motor skills as well. These newly found psychomotor or procedural skills must be retained so that physicians can access them at the bedside of the patients sometimes years after they were initially taught.[4,5] There exist several long-standing and widely accepted theories on psychomotor or procedural skill acquisition, which favour a graduated learning and sequential teaching approach;[6,7] Gagné's instructional design model is one of them.

Gagné's instructional design model is based on the idea that learning is a process that involves the acquisition of knowledge and skills through a series of steps. The conditions of learning, which were first postulated by Gagné in 1965[8] and elaborated upon in his later works done in 1985.[9] Gagné's nine events of instruction is a component of his 'Conditions of Learning Theory' (Fig. 1).

1. Dr. Abu Sadat Mohammad Nurunnabi, Graduate Student, Mitch and Leslie Frazer Faculty of Education, Ontario Tech University, Oshawa, ON, Canada. Email: shekhor19@ yahoo.com (Corresponding author)
2. Dr. Kawsar Nigar, Assistant Professor, Department of Obstetrics & Gynaecology, Mymensingh Medical College & Hospital, Mymensingh-2206, Bangladesh.
3. Dr. Mohammad Ashraful Alam, Assistant Professor, Department of Cardiology, Kushtia Medical College, Kushtia-7000, Bangladesh
4. Dr. Maksuda Khatun, Assistant Professor, Department of Medicine, Shaheed Suhrawardy Medical College & Hospital, Dhaka-1207, Bangladesh.
5. Dr. Farhana Sultana, Assistant Professor, Department of Radiology & Imaging, Shaheed Suhrawardy Medical College & Hospital, Dhaka-1207, Bangladesh.
6. Dr. Muhammad Anwar Hossain, Assistant Professor, Department of Surgery, Shaheed Suhrawardy Medical College & Hospital, Dhaka-1207, Bangladesh.
7. Dr. Quazi Shahid-ul Alam, Assistant Professor, Department of Paediatric Orthopaedic Surgery, Dhaka Medical College & Hospital, Dhaka-1000, Bangladesh.

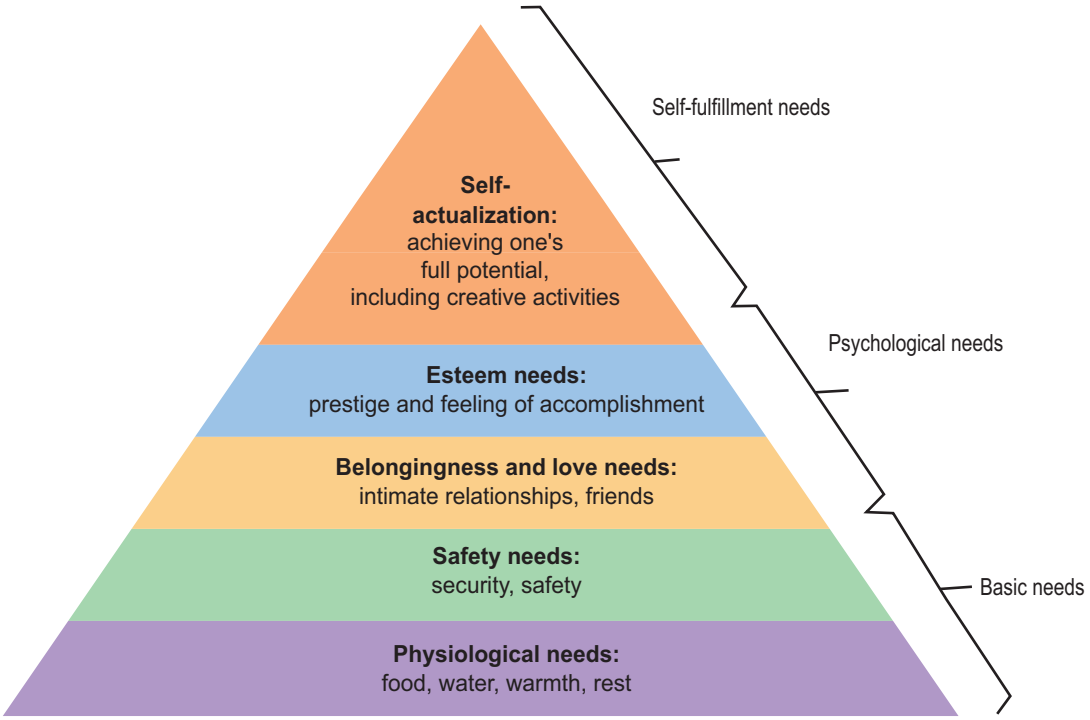

Fig. 1. *Conditions of Learning (Based on Gagné, 1965)*[8]

In this theory, he outlines nine specific steps that instructional designers should use when designing a program of instruction.[9] They are as follows: 1) gain attention: capture the learner's interest and motivate them to engage with the content; 2) inform learners of objectives: clearly state the goals and outcomes of the learning experience; 3) stimulate recall of prior learning: activate the learner's existing knowledge and build upon it. 4) present the content: deliver the information in a clear and organized manner; 5) provide learning guidance: offer support and guidance to help learners navigate the material; 6) elicit performance: encourage learners to practice and apply their knowledge and skills; 7) provide feedback: offer constructive feedback to help learners improve their performance; 8) assess performance: evaluate the learner's progress and mastery of the content; and 9) enhance retention and transfer: help learners transfer their knowledge and skills to real-world situations (Fig. 2).

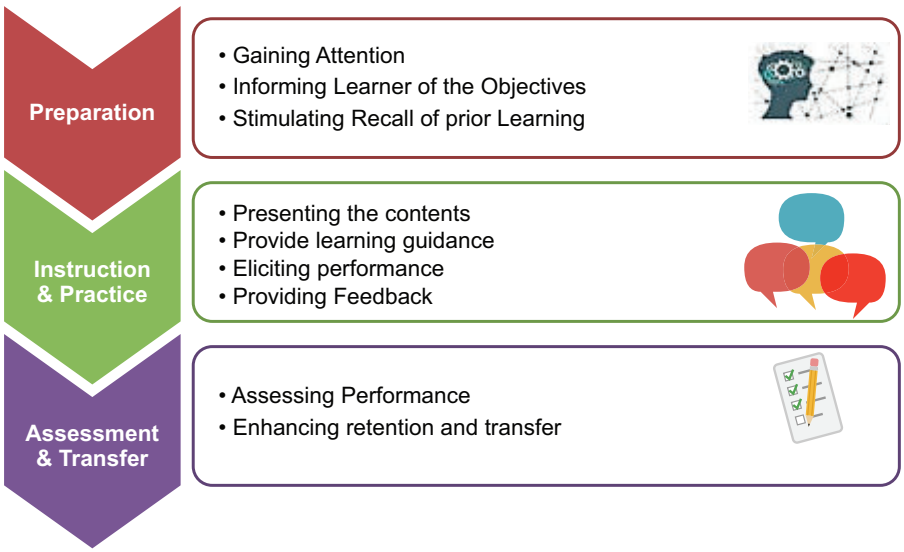

Fig. 2. *Nine Elements of Learning (Based on Gagné, 1985)*[9]

The steps or strategies require the instructional designer to address the possible conditions that would affect the learners' ability to understand and process new and prior knowledge. His theory is based on information processing models that focus on the cognitive events that happen when learners are presented with a stimulus.[9] Gagné's theory is used in the instructional technology field largely because of the theories ability to be adapted for all types of learning environments and learning modalities. Gagné's theory draws from both the behaviorist and cognitivism models of learning.[7,10,11] According to Gagné's theory the five kinds of learned capabilities are: intellectual skills, cognitive strategies, verbal information, attitudes, and motor skills.[9,12]

As medical educators, it is imperative that we use teaching techniques founded on evidence based medical education research as far as possible. Ineffective instruction risks producing poorly performing physicians in an era of increased accountability, with potentially harmful and costly consequences.[13] Teaching procedural skills is crucial in medical education and evidence showed that Gagne's model delineates a sequence of specific instructional events that correlate with crucial conditions of learning, providing a framework that is able to maximally enhance the learning process, improve session flow and ensure objectives are comprehensively addressed.[4,5,7,14,15] Therefore, this paper aims to see how and to what extent Gagné's instructional design model supports teaching procedural skills to medical students.

METHODS

The literature search was conducted using 'Google Scholar' and 'PubMed' and consisted of the search terms – "procedural skills," procedure skills," "procedural skills training," "procedure skills teaching," "clinical skills," "skills training," "undergraduate medical education," and "medical education." References were searched for additional articles. From those articles, we went through the abstracts and searched specifically for the papers that used "Gagné's instructional design model" in teaching "procedural skills." Non-medical articles were not excluded because we did not want to eliminate articles pertaining to coaching or deliberate practice that are pertinent to skills acquisition. We sought additional papers, even books on teaching methodology guidelines, if available. However, non English articles/papers were excluded. After primary sorting and reading the abstracts, only relevant papers were downloaded, and we did try to do an extensive review of those downloaded papers. After meticulous scrutiny, a total of 26 articles were finally selected and utilized to perform this review.

RESULTS

The selected 26 articles were sorted and found diverse in terms of teaching different clinical procedures. However, using Gagné's instructional design model to teach medical procedures, the papers' discussions were on Gagné's theory of instructional design, developing lesson plan, describing learning outcome, constructing, and tailoring the instructional events necessary to achieve this outcome. This model has been used to develop instructional plans to teach a variety of procedural and communication skills, which were also discussed by some of those papers. Conventionally, as we have observed, Gagné's theory of instructional design has five learning outcomes and nine events of instruction.[9,12]

DISCUSSION

Essential to Gagné's ideas of instruction are what he calls "conditions of learning": internal conditions deal with what the learner knows prior to the instruction, external conditions deal with the stimuli that are presented to the learner, e.g., instructions provided by the teacher.[7,8]

Using Gagné's model to teach psychomotor skills, several evidence revealed the same general approach and structure outlined herein which can be applied to multiple clinical skills across specialties. For example, Belfield showed how to teach chest x-ray interpretation,[13] while Buscombe used the example of teaching bone marrow aspiration.[14] The research explored and found that proposed activities, hints and tips, as included in the model, allowed educators to develop engaging lesson plans that systematically address key learning events in an ordered and evidenced manner[7,11,14-24] This model enables educators to design teaching plan with reliable checklists or rating scales to assure competence in the procedure as checklists assure that learning objectives are met and procedures are taught in a stepwise fashion, while rating scales allow for assessment of procedural skills acquisition;[7,11,14-24] however, they are not "as granular as checklists".[5] This framework has provision for positive constructive

feedback and suggestions for improvement to the learners, which ultimately helps them with the opportunities for focused and repetitive practice.[7,11,14-24] The whole process provides a psychologically safe environment for learners.[20,21,23-25]

Gagné's model follows a systematic instructional design process while ensuring flexibility to adjust according to specific situations in training. In fact, this is one of the most widely used instructional design models due to its suitability for online training.[26,27] This can be integrated in simulation based medical teaching as well.[18-20] However, the use of a dedicated clinical skills lab for such sessions allows a more structured and comprehensive teaching plan, and more conducive learning environment compared to that of done in the ward or outpatient department of the hospital or any outpatient clinic.[13,19-21] Gagne's instructional design does not only provide a platform for lecture-based lessons but can also be expanded to accommodate lesson planning for a wide range of skills, such as practical, communication, and interpersonal skills.[20,21,23,26] Another important observation is that this model avoids the common pitfall of teaching procedures as isolated entities, with procedural understanding instead embedded in real-life application and relevance, which is very essential for clinical education.[7,15,18] Moreover, evidence suggests that students specifically reported feeling enabled not only to perform the procedure but also to firmly understand indications and the interpretation of basic results, with this positively generating increased learner enthusiasm.[7,15,25] Thereby, it creates opportunities for co-creation of learning objectives, as well as assessment procedure/rubrics.[7,18,26] Besides, in this model of teaching, the transfer of knowledge constitutes applying their skills in a clinical setting, while initially being supervised. The session can be closed by reviewing the key points, answering the questions, and asking for learners' feedback.[7,22,26] This type of teaching strategy has great value to the trainees, it provided them with the opportunity to interact with other participants and learning from their previous experiences.[14-25] Overall, it enhances aids grater learner participation and collaboration.[15,23]

Gagné's instructional design model is a valuable tool for teaching procedural skills in clinical education. By incorporating the nine events of instruction into lesson planning and delivery, educators can create effective and engaging learning experiences that promote skill acquisition and mastery.[7,15,16,26] For students, they move their abilities into clinical practices when they are out for their clinical practicum or residency training as well as further individual practice.[13,19] However, in designing a session based on Gagne's model, several factors need to be considered. Including the nature of objectives, setting, time, available resources, institutional constraints, content, number of learners, their characteristics and their preferences.[7,22,26-31] For example, many studies applied this strategy and support its suitability only in small group teaching.[7,15,19,22,23] Table-I shows how Gagné's events of instruction and internal cognitive processes work. However, the events do not always occur in this exact order[12,26,28] and not all events must be present for learning to occur, as their purpose is to stimulate internal cognitive processes, not replace them.[12,26,28-30]

Table-I: *Gagné's events of instruction and internal cognitive processes*[28]

Instructional Event	Cognitive Process
1. Gain attention	Reception of pattern of neural impulses
2. Explain objectives	Activating the process of executive control
3. Stimulate recall	Retrieval of prior learning to working memory
4. Present content	Emphasizing features for selective perception
5. Provide guidance	Semantic encoding; cues for retrieval
6. Elicit performance	Activating response organization
7. Provide feedback	Establishing reinforcement
8. Assess performance	Activating retrieval; making reinforcement possible
9. Enhance retention	Providing cues and strategies for retrieval

In practice, one of the challenges identified is that there is no evidence of applying this model in large group teaching.[28-31] Small group teaching may not be feasible where there are fewer qualified faculty staff able to teach following this specialized model.[17,26,28-31] Another challenge is experimenting such model in low-resource settings like Bangladesh, which is often difficult in terms of money and manpower. The cost of consumables and related equipment for such training and practice may create a huge financial burden for many medical colleges in the country.[3] Besides, our medical teachers do not have proper training, they also lack time[3,30] and proper institutional guidelines[3,31] and most of them stick to traditional 'teacher-centric' instructional methods.[31]

CONCLUSION

Gagné's model is based on how humans process information; his principles refer to actions from both teachers and learners during the teaching process. In Gagné's theory of instructional design, the developer of the lesson plan must first pin down the type of outcome to be achieved; only after that should instructional events be tailored to achieve this outcome. Gagné's instructional design model can be effectively applied in clinical education to teach procedural skills to students. By following the nine events of instruction, educators can create engaging and interactive learning experiences that promote skill acquisition as well as retention. Besides, when needed, for online learning, those nine events of instruction can also be operationalized in both synchronous and asynchronously in medical teaching and learning.

Conflict of Interest: None declared by the authors.

Funding Statement: No external funding received.

Ethical Approval: Not applicable.

Authors' Contribution: ASM Nuruunabi was involved in concept and design of this review paper. All authors were equally involved in literature search, compilation, review and analysis as well as manuscript preparation, critical review, editing and final submission.

REFERENCES

1. Akhter N, Talukder MHK. Status of outpatient department based teaching-learning in undergraduate medical education of Bangladesh. Bangladesh J Med Educ. 2023;14(2):18-22.
2. Nurunnabi ASM, Rahim R, Alo D, Al Mamun A, Kaiser AM, Mohammad T, et al. Experiential learning in clinical education guided by the Kolb's experiential learning theory. Int J Hum Health Sci (IJHHS), 2022;6(2):155-60.
3. Nurunnabi ASM, Haroon K, Mohammad T, Hasan MM, Tripura KK, Sadeque SP, et al. Simulation based teaching and learning in clinical education. Bangladesh J Neurosurgery. 2023;13(1):24-8.
4. Kovacs G. Procedural skills in medicine: linking theory to practice. J Emerg Med. 1997;15(3):387-91.
5. Quinn A, Falvo L, Ford T, Kennedy S, Kaminsky J, Messman A. Curated collections for educators: Six key papers on teaching procedural skills. AEM Educ Train. 2021;5(4):e10692.
6. Taylor DC, Hamdy H. Adult learning theories: implications for learning and teaching in medical education: AMEE Guide No. 83. Med Teach. 2013;35(11):e1561-72.
7. Khadjooi K, Rostami K, Ishaq S. How to use Gagne's model of instructional design in teaching psychomotor skills. Gastroenterol Hepatol Bed Bench. 2011;4(3):116-9.
8. Gagné RM. The conditions of learning. 1st ed. New York, NY: Holt, Rinehart & Winston; 1965.
9. Gagné RM. The conditions of learning and theory of instruction. 4th ed. New York, NY: Holt, Rinehart & Winston; 1985.
10. Kantak SS, Winstein CJ. Learning-performance distinction and memory processes for motor skills: a focused review and perspective. Behav Brain Res. 2012;228(1):219-31.
11. Berger-Estilita J, Greif R. Using Gagné's "Instructional Design" to teach clinically applicable knowledge in small groups. Trends Anaesth Crit Care. 2020;35:11-5.
12. Gagné RM. Mastery learning and instructional design. Perform Improv Quart. 1988;1(1):7-18.
13. Wearne S. Teaching procedural skills in general practice. Aust Fam Physician. 2011;40(1-2):63-7.
14. Belfield J. Using Gagne's theory to teach chest x-ray interpretation. Clin Teach. 2010;7(1):5-8.
15. Buscombe C. Using Gagne's theory to teach procedural skills. Clin Teach. 2013;10(5):302-7.
16. Bashir K, Rauf L, Yousuf A, Anjum S, Bashir MT, Elmoheen A. Teaching benign paroxysmal positional vertigo to emergency medicine residents by using Gagne's nine steps of instructional design. Adv Med Educ Pract. 2021;12:1223-7.

17. Cheung L. Using an instructional design model to teach medical procedures. Med Sci Educ. 2016;26: 175-180.

18. Woo WH. Using Gagne's instructional model in phlebotomy education. Adv Med Educ Pract. 2016;7:511-6.

19. Khan DA, Wahid I, Zeb S. Step by step instructions to utilize Gagne's model of instructional outline in educating psychomotor aptitudes. Inrt J Pathol. 2017;15(4):189-93.

20. Torbatinezhad H, Amani H. Computer-assisted instruction (CAI), virtual patients (VP), and human patient simulation (HPS) in medical education based on Gagne's educational design pattern. Jorjani Biomed J. 2018;6(2):1-20.

21. Lo WL, Hsieh MC. Teaching communication skills: using Gagne's model as an illustration. Tzu-chi Med J. 2019;32(1):19-25.

22. Masrur A, Tayyab A, Khan SA, Mansoor M, Khan FA, Shah SS. The impact of utilizing Gagne's instructional strategy for teaching A-scan biometry to undergraduate medical students. Multicult Educ. 2021;7(12):1.

23. Owaidah AY. Using Gagne's instructional design to teach communication skills in phlebotomy education through role-play. F1000 Res. 2022;11:46.

24. Ng JY. Combining Peyton's four-step approach and Gagne's instructional model in teaching slit-lamp examination. Perspect Med Educ. 2014;3(6):480-5.

25. Ali S, Ali L. Efficacy of Gagne's nine events of instructions in improving the performance of undergraduate medical students. Adv Health Prof Educ. 2015;1(2):65-8.

26. Ullah H, Rehman AU, Bibi S. Gagné's 9 events of instruction – a time tested way to improve teaching. Pak Armed Forces J. 2015; 65(4):535-9.

27. Azar AJ, Khamis AH, Naidoo N, Lindsbro M, Boukhaled JH, Gonuguntla S, et al. Design, implementation and evaluation of a distance learning framework to expedite medical education during COVID-19 pandemic: a proof-of-concept study. J Med Educ Curric Dev. 2021;8:238212-05211000349.

28. McNeill L, Fitch D. Microlearning through the lens of Gagne's nine events of instruction: a qualitative study. TechTrends. 2023;67:521-33.

29. Al-Eraky MM. Robert Gagné's nine events of instruction, revisited. Acad Med. 2012;87(5):677.

30. Reigeluth CM. ed. Design theories and models: an overview of their current status. Hillsdale, NJ: Lawrence Erlbaum Associates; 1983.

31. Seels B, Glasgow Z. Exercises in instructional design. Columbus, OH: Merrill Publishing Co.; 1990.

Case Report

Hangman's Fracture – A Case Report and Review of Literature

Alam MS[1], Haroon K[2]

ABSTRACT

Hangman's fractures are bilateral fractures of the C2 pars interarticularis produced during hyperextension injuries. C2 fractures are the most common form of cervical spine injury. A patient was admitted with the complaints of weakness of the left upper and lower limb following a road traffic accident. His face was spared. CT scan of the cervical spine showed bilateral pars fracture with a broken fragment. He was treated by anterior cervical fusion with tricortical bone graft and fixation between C2 and C3 with plate and screws, in the third day following trauma. The patient had immediate improvement following surgery. His weakness completely recovered and he came to follow up after one month walking without support. The anterior approach to the Hangman's fracture is a very effective and easy procedure. Autologous tricortical bone graft gives strength as well as good fusion to the spinal column. However, careful patient selection is necessary for this. The outcome is very much rewarding to the patient.

Keywords: *Hangman's fracture, anterior approach, C2 body fracture, Goel's classification*

Mugda Med Coll J. 2026; 9(1): 87-91
DOI: https://doi.org/10.3329/mumcj.v9i1.90839

INTRODUCTION

Hangman's fractures are bilateral fractures of the C2 pars interarticularis produced during hyperextension injuries.[1] C2 fractures are the most common form of cervical spine injury. C2 fractures can be roughly divided into three categories: fractures of the dens, Hangman's fracture involving both pedicles, and atypical fractures.[2] In 1965, Schneider et al. coined the term 'Hangman's fracture', which is the second most common fracture of the second cervical vertebra.[1,3,4] It accounts for 4%–7% of spinal fractures and about 1/5 of cervical vertebral fractures.[5] Hangman's fracture occurs most commonly due to anatomical features, mechanical susceptibility, embryological attributes etc.[4,5] Hangman fracture is classified according to Levine & Edwards (Table-I, Fig. 1). It is widely and mostly used classification.[4] However, a new classification system was presented by Goel et al. (Table-II), taking into account the atlanto-axial instability.

Table-I: *Hangman's fracture classification by Levine & Edwards (1985)[6]*

Type	Description
Type I	<3 mm displacement, no angulation
Type II	>3 mm displacement, significant angulation
Type IIA	The most striking modification, significant angulation without translation due to hinging of the anterior longitudinal ligament (ALL)
Type III	Angulated anterior fragment with facet joint dislocation

1. Prof. Md. Shafiul Alam, Professor and Head, Department of Gamma Knife, National Institute of Neurosciences & Hospital, Dhaka-1207. Email: drchapal1970@gmail.com (Corresponding author)
2. Dr. Kaisar Haroon, Associate Professor, Department of Clinical Neurosurgery, National Institute of Neurosciences & Hospital, Dhaka-1207.

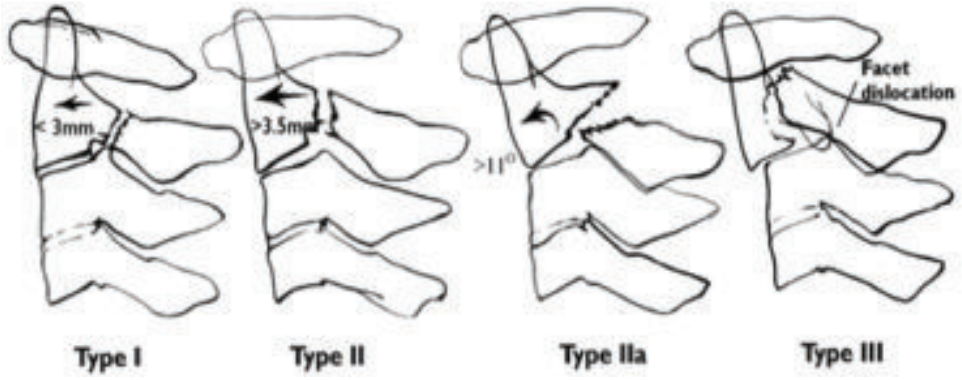

Fig. 1: *Hangman's fracture classification by Levine & Edwards (1985)*[6]

Table-II: Classification of hangman's fracture by Goel et al. (2022)[7]

Type	Description
Type 1	No atlantoaxial or C2–3 instability
Type 2	Presence of C2–3 instability and no atlantoaxial instability
Type 3	Presence of atlantoaxial instability and no C2–3 instability
Type 4	Presence of both atlantoaxial and C2–3 instability

Other classification of Hangman's fracture include Williams, Seljeskog & Chou, Pepin & Hawkin, Francis & Fielding, Effendi et al., Levine & Rhyne.[8] Li, Zhong & Wang described another classification for atypical Hangman fractures.[9]

The mechanism of injury are usually four types: motor vehicle accident, falling from a height, falling on a flat surface (or falling over), and others (such as strike by heavy objects or unknown cause and mechanism of the injury).[5] The site of injury in the C2 can occur at any part, but mostly in the facet joints followed by bony fracture. Anterior element injury is more than middle or posterior element injury.[10] There are two types surgery preferred for Hangman's fracture: either the anterior cervical discectomy and fusion between C2-C3 or the posterior cervical fixation and fusion can be done in these patients. However, the procedure depends on the type of injury and stability of the fracture.[8,11] If necessary combined procedure (i.e., both anterior and posterior approach) can be done.[4] Here, we describe a case of Hangman's fracture type IIA admitted under our care. It was unstable and with a bony fragment. In this patient, anterior cervical decompression and fixation was done between C2 and C3.

CASE REPORT

A 45-year old non-diabetic, non hypertensive male patient was admitted under our care following a motor vehicle accident. He was well alert and oriented without any signs of cerebral concussion. He had neck pain, weakness of the left upper limb and lower limb. His weakness was more at the grip of the right hand, and flexion of the elbow joint. He had weakness of the flexion of the hip and flexion of the knee. The muscle power was 4/5 in the rt. upper limb and 4/5 in the right lower limb. His x-ray of cervical spine showed forward displacement of the C2 over the C3. in the lateral view there was also a fracture fragment behind the body of the C 2 (Fig. 2). CT scan of cervical spine showed displacement of the C2 over the C3, fracture fragment behind the body of C2, bilateral pars

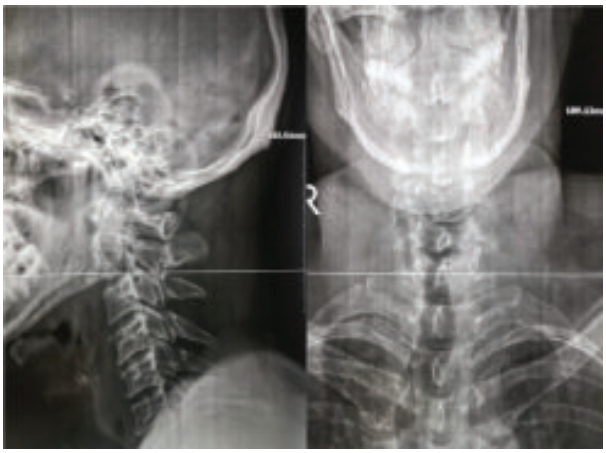

Fig. 2: Preoperative x-ray of cervical spine showing fracture of the posterior part of C2 vertebral body

inter articularis fracture of C2 (Fig. 3), while MRI of cervical spine showed displacement of C2 over the C3 and compression of the dural tube on the left side (Fig. 4).

He was prepared for operation. He was positioned supine on the operating table with head slightly extended and in the midline. A skin crease incision was given. The C2-C3 was reached in the anterior approach. Discectomy of C2/C3 was done. There was fracture fragment in the posterior aspect of the body of the C2 vertebra. This was also removed. The dural tube became free. Then a tricortical bone graft, taken from the right iliac crest was placed in the C2/C3 space. C2-C3 was fixed with titanium plate and screws (Fig. 5). Wound was closed in layers. The patient was reversed after surgery. Then he was shifted to recovery ward, from there he was shifted to general ward. On the next day the patient said that he was feeling more power on his left side. He was released on the fourth post operative day. Before discharge the patient had regained full power of both upper and lower limb muscles. His post operative x-ray showed a good alignment and good fixation (Fig. 6). The patient improved rapidly without any notable complication.

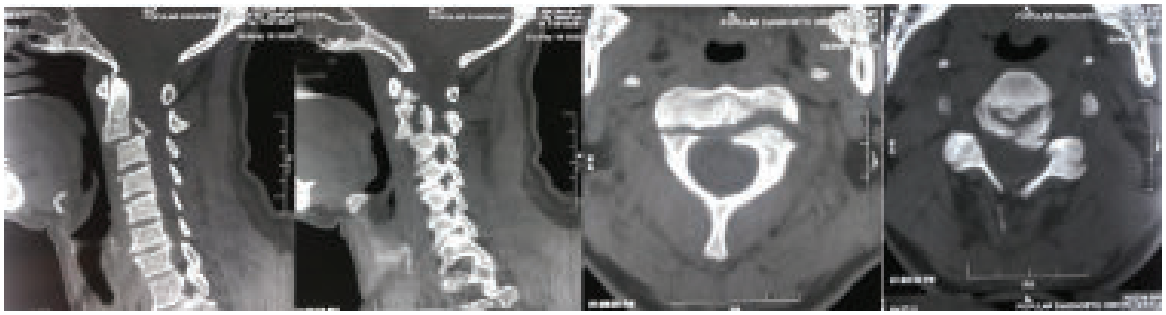

Fig. 3: *Preoperative CT scan of cervical spine*

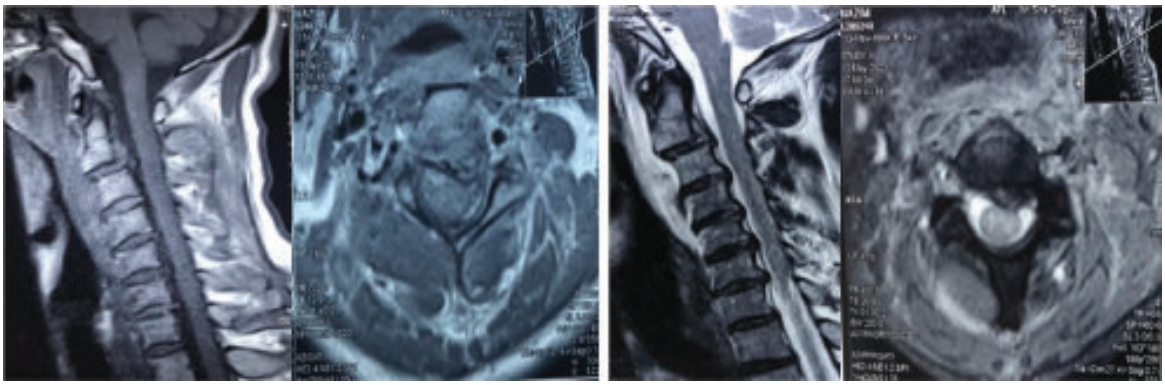

Fig. 4: *Preoperative MRI of cervical spine*

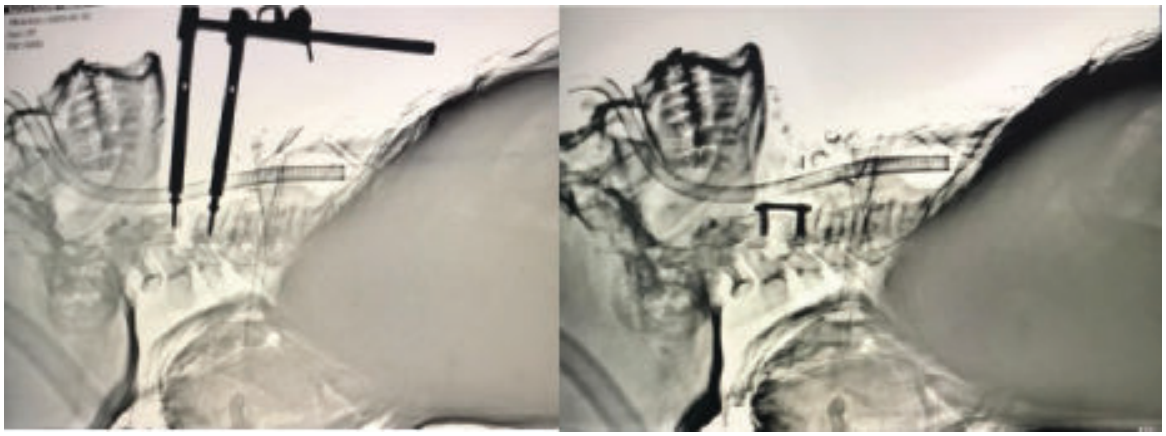

Fig. 5: *Peroperative x-ray of cervical spine*

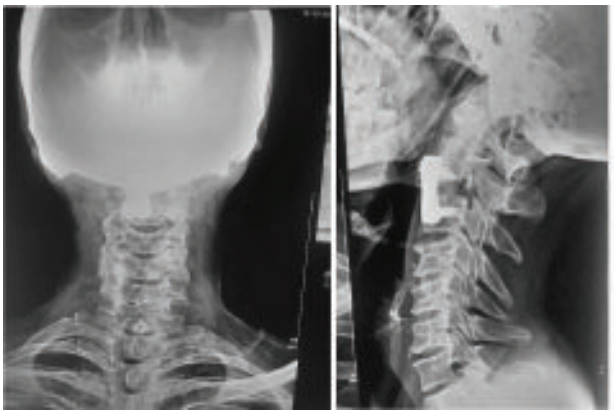

Fig. 6: *Postoperative x-ray of cervical spine*

DISCUSSION

Some of the authors follow the Roy-Camille criteria, which are similar to those developed by White and Panjabi, are reliable in the selection of patients for surgical treatment.[12] Depending on the site of fracture surgical approach can be modified. Therefore, a surgeon has to be accustomed with both anterior and posterior approaches. A high cervical extra-pharyngeal approach in all 12 patients, cervical discectomy, and autologous bone fusion of C2–C3 with a titanium plate were performed by Rajadurai et al. they also followed them up to one year and the result was good.[3] In our patient we have used tricortical autologous bone graft and anterior approach. Prost et al. reported anterior approach in four patients and posterior approach in seven patients with excellent outcome.[2] Khan et al. also reported posterior fixation of the C2 and C3 for Hangman's fracture.[13] Mahmoud et al. compiled the complications of anterior approach. These were surgical site infections, local hematoma, voice alterations, donor site pain, dysphagia and transient cerebral ataxia.[1] However, we observed none of those complications in our patient.

The most common cause of neurological deficit in hangman's fracture presents clinically as an incomplete neurological impairment.[14] It may be due to the translation or angulation of C2/3 or the bony fracture fragment compressing the dural tube. Our patient had presented with left sided hemiparesis, which had improved after the surgery. The muscle power of upper and lower limb before surgery was 3/5 and after surgery was 5/5.

Effendi type 1 fractures are usually considered stable and type 3 fractures are considered unstable, but there is no consensus regarding the stability of type 2 or type 2a fractures.[15] Our patient had a fracture of the C2 vertebral body and the fracture fragment displaced posteriorly, resulting in compression of the dural tube. Therefore, surgery was undertaken to decompress the dural layer and fusion by tricortical bone graft. Following this, it was fixed with plate and screw between C2 and C3. The result was very good and the patient rapidly improved.

CONCLUSION

The anterior approach to the Hangman's fracture is a very effective and easy procedure. Autologous tricortical bone graft gives strength as well as good fusion to the spinal column. However, careful patient selection is necessary for this. The outcome is very much rewarding to the patient.

Conflict of Interest: The authors have nothing to disclose.

Funding Statement: No funding.

Ethical Approval: Permission was taken from the patient and the hospital authority.

Authors' Contribution: Both authors were equally involved in patient selection, clinical diagnosis, management and data collection. Both of them were equally involved in literature search and review as well as manuscript preparation, editing and final submission.

REFERENCES

1. Mahmoud A, Shanmuganathan K, Montgomery A. Surgical management of Hangman's fracture: a systematic review. Int J Spine Surg. 2023;17(3): 454-67.
2. Prost S, Barrey C, Blondel B, Fuentes S, Barresi L, Nicot B, et al. Hangman's fracture: management strategy and healing rate in a prospective multi-centre observational study of 34 patients. Orthop Traumatol Surg Res. 2019;105(4):703-7.
3. Rajadurai OJW, Roberts RO, Thangapandi M, Pooja M, Sukanthi P. Hangman's fracture of the cervical spine: a prospective study. Int J Sci Stud. 2020;8(4): 58-60.
4. Murphy H, Schroeder GD, Shi WJ, Kepler CK, Kurd MF, Fleischman AN, et al. Management of Hangman's fractures: a systematic review. J Orthop Trauma. 2017;31:S90-5.
5. Li G, Wang Q. Analysis of the clinical characteristics of adult patients with Hangman's fractures: a

retrospective study based on multicenter clinical data. Front Surg. 2023;10:949987.

6. Levine AM, Edwards CC. The management of traumatic spondylolisthesis of the axis. J Bone Joint Surg Am. 1985;**67**(2):217-26.
7. Goel A, Hawaldar A, Shah A, Bhambere S, Lunawat A, Singh M, et al. Hangman's fracture: a clinical review based on surgical treatment of 15 cases. Neurosurg Rev. 2022;45(1):595-606.
8. Li X-F, Dai L-Y, Lu H, Chen X-D. A systematic review of the management of Hangman's fractures. Eur Spine J. 2006;15(3):257-69.
9. Li G, Zhong D, Wang Q. A novel classification for atypical Hangman fractures and its application: a retrospective observational study. Medicine. 2017;96(28):e7492.
10. Li G, Wang Q. Detailed observation of anatomical location and pattern in Hangman's fracture based on computed tomography three-dimensional reconstruction. J Orthop Surg Res. 2023;18(1):136.
11. Patel JYK, Kundnani VG, Kuriya S, Raut S, Meena M. Unstable Hangman's fracture: anterior or posterior surgery? J Craniovertebr Junction Spine. 2019;10(4):210-5.
12. Samaha C, Lazennec JY, Laporte C, Saillant G. Hangman's fracture: the relationship between asymmetry and instability. J Bone Joint Surg Br. 2000;82(7):1046-52.
13. Khan SIMKN, Rahman M, Khan RA, Munir SF, Sharif S. A study on management of Hangman's fracture. J Med Sci Clin Res. 2019;7(3):258-63.
14. Li G, Wang Q. Analysis of the clinical characteristics and predisposing factors for neurological deficit with Hangman fractures. J Orthop Surg Res. 2023;18(1):179.
15. Al-Mahfoudh R, Beagrie C, Woolley E, Zakaria R, Radon M, Clark S, et al. Management of typical and atypical Hangman's fractures. Glob Spine J. 2016;6(3):248-56.

Case Report

Acute Kidney Injury Due to Anti-Tuberculosis Drugs: How Much Are We Aware of It?

Kaiser AM[1], Islam RN[2], Jalil ME[3], Morshed ASM[4]

ABSTRACT

The global scenario of tuberculosis (TB) infection varies from one country to another; according to the World Health Organization (WHO), Bangladesh is one of the world's 30 high TB burden countries and near about 73,000 people die annually due to tuberculosis. Several drugs are used in Category-1 and Category-2 regimen for TB treatment. Despite several side effects of these drugs, we have to use them invariably following the WHO guideline in our country. Although isoniazid and ethambutol have been associated with acute kidney injury (AKI), recent evidence showed that rifampin is the most common anti-TB drug responsible for AKI. Rifampicin toxicity may appear at both the initial administration and readministration. A 50-year old male pulmonary TB patient developed severe renal impairment after taking Category-1 anti-TB drugs. When severe renal impairment developed, anti-TB therapy was stopped and five sessions of hemodialysis were given. When renal function came back to normal, treatment was resumed with oral ethambutol and levofloxacin in full dose (excluding rifampicin). Later, oral isoniazid was added with low dose and increased dose was given based on monitoring of renal function. Even after adding injection streptomycin no deterioration of renal function was observed. We herein report this rare case and review of literature for academic interest and creating more awareness among the physicians.

Keywords: *Acute kidney injury, anti-tuberculosis drugs, pulmonary TB*

Mugda Med Coll J. 2026; 9(1): 92-94
DOI: https://doi.org/10.3329/mumcj.v9i1.90840

INTRODUCTION

Tuberculosis (TB) is a communicable disease affecting one-third of the global population. According to the World Health Organization (WHO), most people who developed TB in 2019 were in the South-East Asia region (44%).[1] Bangladesh is one of the world's 30 high TB burden countries and near about 73,000 people die annually due to tuberculosis.[1] Prompt anti-tuberculosis treatment remains the most important and effective intervention for controlling spread, but adverse events from first-line anti-TB drugs are not uncommon.[1,2] Several drugs are used in Category-1 and Category-2 regimen for TB treatment. Despite several side effects of these drugs, we have to use them invariably following the WHO guideline in our country. Acute kidney injury (AKI) is a rare and severe complication that can interrupt treatment and cause permanent kidney damage.[3] Although isoniazid and ethambutol have been associated with AKI,[2-4] in recent years, evidence showed that rifampin is the most common anti-TB drug responsible for AKI.[5-10] Reviewing literature of rifampin-induced AKI, the mean age of reported cases was around 40–45 years and the recovery rate ranged between 40% and 96%.[5-10] However, the incidence to rifampin-induced AKI is uncertain because the definitions of AKI used in previous studies had much variations.[2] Recently, a male TB patient was admitted in a tertiary level specialized hospital in Dhaka, Bangladesh with acute kidney injury due to anti-tuberculosis drugs.

1. Dr. Amir Mohammad Kaiser, Associate Professor, Department of Nephrology and Dialysis Unit, Gonoshasthaya Samaj Vittik Medical College & Hospital, Savar, Dhaka-1344 & Gonoshasthaya Nagar Hospital, Dhaka-1205. Email: amirkaiser32@gmail.com (Corresponding author).
2. Dr. Rafi Nazrul Islam, Assistant Professor, Department of Nephrology, Dialysis and Kidney Transplant Unit, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital, Dhaka-1000.
3. Dr. Muhammad Ehsan Jalil, Associate Professor, Department of Nephrology, MH Samorita Hospital & Medical College, Tejgaon, Dhaka-1208.
4. Dr. Abu Sayed Mohammad Morshed, Assistant Professor, Department of Nephrology, National Institute of Kidney Diseases & Urology (NIKDU), Dhaka-1207.

CASE SUMMARY

A 50-year-old man hailing from a sub-urban area with a history of receiving five sessions of hemodialysis following severe renal impairment was admitted to the Gonoshasthaya Nagar Hospital, Dhaka, Bangladesh, in the beginning of 2024. He stated that he was diagnosed with pulmonary TB in 2011, and he received category-1 anti-TB therapy for 6 months and got recovery. However, he was diagnosed once again in the end of 2023 and started category-1 anti-TB therapy. After a week of treatment, he suddenly developed severe nausea and vomiting. He got admitted in a local hospital; he had severe renal impairment with serum creatinine 13.30 mg/dL at that time. Then he was referred to a private clinic where anti-TB therapy was stopped and five sessions of hemodialysis given. After that he was shifted to this hospital for better management. After admission, he was clinically improved and urine output was adequate. On investigation, his serum creatinine was 6.5 mg/dL, while blood urea was 90mg/dL and urine analysis revealed no abnormalities. Moreover, serum electrolytes and sonography of the urinary system revealed no abnormalities. To find out the cause of renal impairment, patient's history and pathological investigations done earlier were revisited (including urine analysis, sonography of urinary system, serum HBsAg, Anti-HCV, C-ANCA, P-ANCA, ANA, and chest x-ray P/A view). However, no abnormalities were detected except in the chest x-ray, which revealed a cavitary lesion in the upper zone of the right lung. It was assumed that the AKI was due to ingestion of anti-TB drugs. After few days, hemodialysis was stopped and the patient was managed conservatively with close monitoring. After a week, his condition further improved with adequate urine output and investigations revealed serum creatinine 4.19 mg/dL and blood urea 80 mg/dL. The patient was discharged from the hospital. After one and a half month, his condition further improved and serum creatinine came back to the baseline (1.27 mg/dL). He was advised for further investigations, e.g., sputum for acid-fast bacilli (AFB) and Gene Xpert; both reports were suggestive of active TB infection. Chest radiograph also revealed the same cavitary lesion in the lung. Then alternate regimen of anti-TB medication was prescribed, i.e., with oral ethambutol 400 mg 3 tablets daily, levofloxacin 500 mg once daily (for 2 months) and later added with oral isoniazid 300 mg ¼ tablet for 2 days, then ½ tablet another 2 days, followed by 1 tablet once daily. After one month of regular treatment, there was mild clinical improvement; however, chest x-ray still showed that cavitary lesion of the lung. Then intramuscular injection of streptomycin 1 gm daily was added for 2 months along with previous drugs. After 2 months, patient's chest x-ray showed significant change by healing of the cavitary lesion. Then injection streptomycin was withdrawn from the list and continued with oral ethambutol and isoniazide. After 6 months of complete anti-TB treatment, his serum creatinine was found 1.06 mg/dL and chest x-ray showed few fibrotic areas. The patient was advised to continue anti-TB therapy for another 3 months. During our treatment with alternate anti-TB regimen, patient's renal function was stable and serum creatinine level was around 1.10 mg/dL.

DISCUSSION

Acute kidney injury (AKI) is usually a rare complication in patients on anti-TB therapy.[11] However, several reports addressed this rare event and most revealed rifampicin as the most common responsible drug.[5-10] The mechanism of rifampicin-induced AKI is not well established. Evidence suggests that it is either a type II or type III hypersensitivity reaction induced by rifampicin antigens in which anti-rifampicin antibodies form immune complexes that are deposited in renal vessels, the glomerular endothelium, and the interstitial area. These reactions cause two different pathologic changes in the kidneys. The deposition of immune complexes in the vessels causes vascular constriction and tubular ischemia, leading to acute tubular necrosis, Whereas the deposition of immune complexes in the interstitial area leads to acute interstitial nephritis.[5,8,11] Renal biopsies may reveal either tubulo-interstitial or glomerular lesions. Oedema resulting from proteinuria is also relatively common.[8,10,11] In our case, the cause of AKI was not confirmed because renal biopsy was not performed. However, the results of previous studies suggest that even without histology studies, the diagnosis of rifampin-induced AKI can be made based on the typical time course and by excluding other etiologies.[5] In this case, after one week of taking anti-TB therapy, the patient developed severe renal impairment. To exclude other cause and previous renal impairment, we tried our best to be informed about patient's demographic, family and clinical history

meticulously and did all relevant investigations. Since rifampicin is commonly associated with AKI, we started alternate regimen of anti-TB therapy by excluding rifampicin. Firstly, ethambutol and levofloxacin were started in full doses, then isoniazid was added with low dose and the dose was increased based on monitoring of renal function. Even after adding injection streptomycin no deterioration of renal function was observed. Rifampicin toxicity may appear at both the initial administration and readministration. However, with treatment, the clinical course of rifampicin-induced acute kidney injury is considered favourable in most patients.[10,11] We herein report this rare case and review of literature for academic interest and creating more awareness among the physicians.

Conflict of Interest: None declared by the authors.

Funding Source: None.

Ethical Approval: Written informed consent was taken from the patient and permission was obtained from the hospital authority.

Authors' Contribution: AM Kaiser was involved in patient selection, data collection and clinical management; AM Kaiser, RN Islam, ME Jalil and ASM Morshed were equally engaged in patient's data analysis, literature search and review as well as manuscript writing, editing and final submission.

REFERENCES

1. World Health Organization (WHO). Global Tuberculosis Report 2020. Geneva: WHO; 2020.
2. Chang CH, Chang LY, Ko JC, Wen YF, Chang CJ, Keng LT, et al. Incidence of and risk factors for acute kidney injury during antituberculosis treatment: a prospective cohort study and literature review. Infect Dis Ther. 2023;12(3):919-31.
3. Kwon SH, Kim JH, Yang JO, Lee EY, Hong SY. Ethambutol-induced acute renal failure. Nephrol Dial Transplant. 2004;19(5):1335-6.
4. Chang CH, Chen YF, Wu VC, Shu CC, Lee CH, Wang JY, et al. Acute kidney injury due to anti-tuberculosis drugs: a five-year experience in an aging population. BMC Infect Dis. 2014;14:23.
5. De Vriese AS, Robbrecht DL, Vanholder RC, Vogelaers DP, Lameire NH. Rifampicin-associated acute renal failure: pathophysiologic, immunologic, and clinical features. Am J Kidney Dis. 1998;31(1): 108-15.
6. Covic A, Goldsmith DJ, Segall L, Stoicescu C, Lungu S, Volovat C, et al. Rifampicin-induced acute renal failure: a series of 60 patients. Nephrol Dial Transplant. 1998;13(4):924-9.
7. Muthukumar T, Jayakumar M, Fernando EM, Muthusethupathi MA. Acute renal failure due to rifampicin: a study of 25 patients. Am J Kidney Dis. 2002;40(4):690-6.
8. Jawandhiya P, Dhote G, Gupta A, Admane V, Atram J. Rifampicin-induced acute kidney injury due to pigment nephropathy: a lesson for the clinical nephrologist. J Nephrol. 2025;38(2):771-5.
9. Bhowmik D, Dash SC. Acute renal failure complicating intermittent rifampicin therapy. J Assoc Physicians India. 2002;50:856.
10. Chiba S, Tsuchiya K, Sakashita H, Ito E, Inase N. Rifampicin-induced acute kidney injury during the initial treatment for pulmonary tuberculosis: a case report and literature review. Intern Med. 2013;52(21):2457-60.
11. Schubert C, Bates WD, Moosa MR. Acute tubulo-interstitial nephritis related to antituberculous drug therapy. Clin Nephrol. 2010;73(6):413-9.

Case Report

Mucinous Adenocarcinoma of the Colon Presenting as a Psoas Abscess and Enterocutaneous Fistula: A Diagnostic Challenge

Masih N[1], Rahman MM[2], Noor M[3], Alam MS[4], Gaffar A[5]

ABSTRACT

Mucinous adenocarcinoma, also termed colloid carcinoma, represents a histological variant of colorectal cancer defined by extensive extracellular mucin production. It occurs slightly more often in females and tends to arise in the proximal colon. This uncommon malignancy may manifest with nonspecific or atypical clinical signs. We describe the case of a 37-year-old man, who presented with recurrent right-sided psoas abscesses and a discharging sinus, later complicated by the development of an enterocutaneous fistula. The definitive diagnosis of mucinous adenocarcinoma was established only after histopathological evaluation of the resected specimen. This case report emphasizes the diagnostic difficulty of atypical presentations of mucinous adenocarcinoma and underscores the need to consider an underlying malignancy in patients with recurrent or persistent abscesses.

Keywords: *Mucinous adenocarcinoma, psoas abscess, tuberculosis, enterocutaneous fistula, colorectal cancer*

Mugda Med Coll J. 2026; 9(1): 95-98
DOI: https://doi.org/10.3329/mumcj.v9i1.90841

INTRODUCTION

Mucinous Adenocarcinoma of colon was first described in early 1923 by Dr Duncan Parham. It has been previously described in many literatures as colloid carcinoma. This variant of Colo-rectal carcinoma is quite rare and often discovered at an advanced stage with a poor prognosis.[1] Key feature of this variety of carcinoma is aberrant and abundant mucin expression and composition, which can be seen on magnetic resonance imaging (MRI) scans. Clinically, mucinous adenocarcinoma often presents diagnostic and therapeutic challenges due to its aggressive behavior, tendency for local invasion, peritoneal dissemination, and relative resistance to standard chemotherapy regimens.[2] Due to this biological nature of the disease and its variable response to treatment, reporting individual cases are valuable in understanding the nature of the disease, the diagnostic pitfalls and management plan. This case report emphasizes the diagnostic difficulty of atypical presentations of mucinous adenocarcinoma and underscores the need to consider an underlying malignancy in patients with recurrent or persistent abscesses.

CASE PRESENTATION

A 37-year-old male admitted into the Department of Surgery, Mugda Medical College Hospital, Dhaka, Bangladesh, in August 2025, with the complaint of discharge from his previous operative wound for 1 week. He underwent three incision and drainage surgeries for a right-sided psoas abscess over the course of the last 10 months and excision of a fistulous tract from a right lumbar wound 3 months back. During his last admission In April 2025, he presented with loin and back pain accompanied by a fever that lasted for 2 weeks. On general examination, he had tachycardia with raised temperature. On abdominal examination, he had a fluctuant swelling in his right iliac fossa. A small opening was visualized in his right lumbar incision wound through which there was a small amount of discharge coming out. He had tenderness and guarding in his right iliac fossa and right lumbar region. He also had tenderness in his right costovertebral angle. The psoas sign was positive. Other systemic examinations, including DRE, were found normal. A diagnosis of psoas abscess was made, and excision of the fistulous tract

1. Dr Nadeed Masih, Postgraduate Trainee, Department of Surgery, Mugda Medical College Hospital, Dhaka-1214. Email: nadeed03@gmail.com (Corresponding author)
2. Prof. Md. Mustafizur Rahman, Professor & Head, Department of Surgery, and Principal, Mugda Medical College, Dhaka-1214.
3. Dr Motia Noor, Postgraduate Trainee, Department of Surgery, Mugda Medical College Hospital, Dhaka-1214.
4. Dr. Md. Shahinur Alam, Assistant Registrar, Department of Surgery, Mugda Medical College Hospital, Dhaka-1214.
5. Dr. Abdul Gaffar, Medical Officer, Department of Surgery, Mugda Medical College Hospital, Dhaka-1214.

with drainage of the abscess was done through a previous lateral loin incision. The culture of the specimen yielded growth of E. coli. A biopsy of tissue from the psoas region revealed a mucinous adenocarcinoma (metastatic). Subsequently, computed tomography (CT) scans of the chest, abdomen, and pelvis were performed, along with endoscopy and colonoscopy. All these procedures were normal. Tumour markers, however, indicated elevated CEA levels (229.11 ng/ml). As the primary source could not be identified, he was advised to consult with the department of oncology, and a follow-up appointment was scheduled in six months. Since then, he had two additional admissions for wound dehiscence and discharge. Wound swabs were taken, and they were managed as surgical site infections. Treatment was given based on culture sensitivity reports. On his latest admission, he started to experience a gradually increasing discharge. He denied history of constitutional symptoms or any changes in bowel habits. Upon examination, all vital signs were within normal limits. The physical examination was normal, and only a small, discharging sinus was identified through which whitish, non-feculent discharge was emanating. Initially, he was diagnosed as a case of chronic discharging sinus, possibly due to tuberculosis. All his tuberculosis tests done between November 2024 and September 2025 (i.e., MT test and sputum for AFB), along with the QuantiFERON gold test, were found negative. Despite the negative test results, he was still started on anti-tuberculosis medication during the assessment because of the disease's endemic nature. However, the latest magnetic resonance imaging (MRI) scans revealed large right iliopsoas abscess (Fig. 1). Magnetic resonance sinogram showed large right iliopsoas abscess with fistula at the right lateral lower abdominal wall (Fig. 2). Fistulogram showed irregular fistulous track is noted and communicated with the cecum and ascending colon, which was suggestive of entero-cutaneous fistula (Fig. 3). Due to his poor financial condition, further CT scan and colonoscopy were not done; he was diagnosed as a case of entero-cutaneous fistula, possibly as a complication from previous operative procedure, and prepared for exploratory laparotomy.

Peroperatively, a firm growth was found on the upper part of the caecum involving a portion of the ascending colon. The caecum and ascending colon were densely adherent with the lateral wall, and a fistulous tract was identified communicating with the upper part of the caecum. The decision for a right hemicolectomy with dismantling of the fistulous tract followed by ileo-colic anastomosis was taken. His postoperative course was uneventful. Histological specimen consists of a 25 cm long loop of right hemicolectomy specimen including terminal ileum, caecum and part of colon with mesenteric fatty tissue. On opening, the caecal mucosa shows a 4.5 cm tumorous lesion. Histopathological diagnosis was adenocarcinoma, mucin secreting. Grade II, with pathological stage (pTNM): pT3N0Mx and Astler Coller Stage: B2. For tissue labeled as fistulous tract showed wall of fistulous tract with infiltration by mucinous adenocarcinoma.

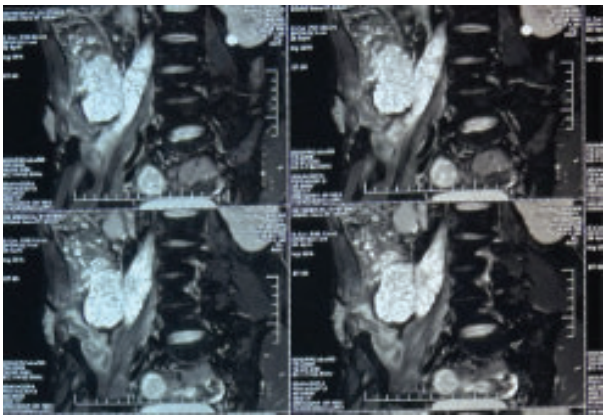

Fig. 1: *MRI scans showing large right iliopsoas abscess.*

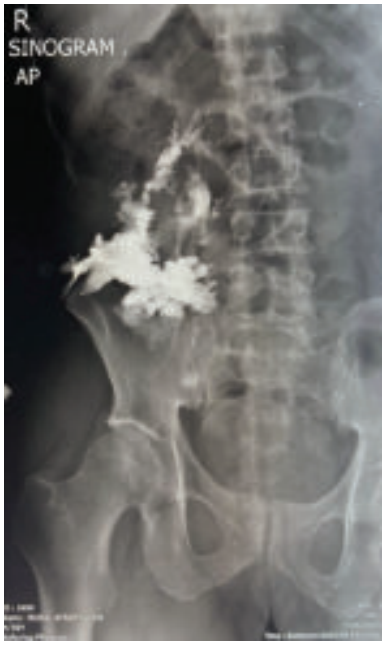

Fig. 2: *MR sinogram showing large right iliopsoas abscess with fistula at the right lateral lower abdominal wall.*

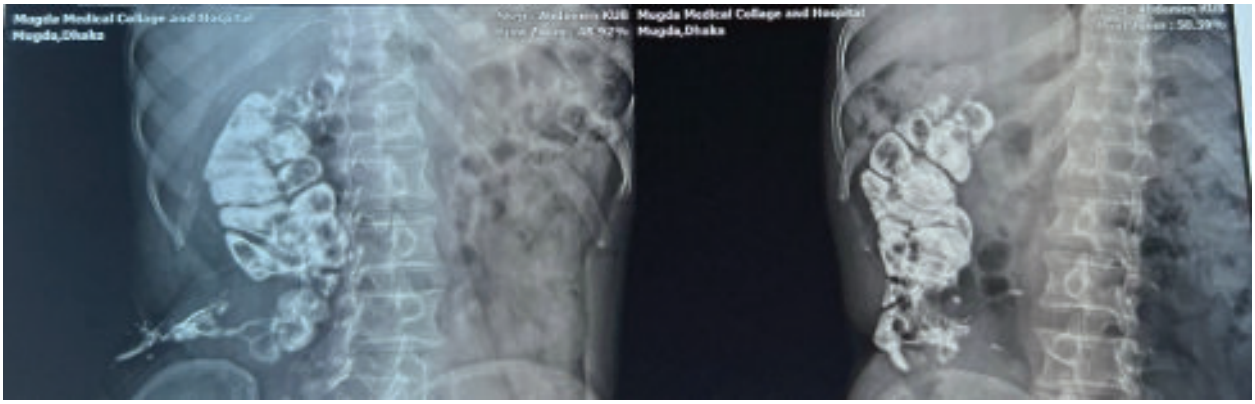

Fig. 3: *Fstulogram showing entero-cutaneous fistula.*

DISCUSSION

Psoas abscess is an abscess of the retroperitoneum. Previously they were known to be mainly caused by *Mycobacterium tuberculosis* of the spine (Potts disease).[3] Usually from an occult source, the primary type is caused by haematogenous or lymphatic spread of germs and occurs in immunocompromised persons, including diabetics, alcoholics, intravenous drug abusers, patients with HIV, cancer patients, and people with chronic illnesses. *Staphylococcus aureus* accounts for 88% of all pathogenic microorganisms, with *Streptococci* (5%) and *Escherichia coli* (3%), following closely behind. An infectious process's local extension is the cause of the secondary kind of iliopsoas abscess. The most frequent causes of secondary abscess in affluent nations are chronic inflammatory disorders of the digestive system, including Crohn's disease (60%) appendicitis (16%) ulcerative colitis, diverticulitis, and colon cancer (11%).[4,5] In Bangladesh, one of the main causes of psoas abscess is tuberculosis.

Mucinous colorectal adenocarcinoma accounts for approximately 10–20% of colorectal cancers, though its prevalence in Asian populations is lower (around 4–5%).[5] These tumors are typically located in the right colon and often detected at advanced stages. Compared with conventional adenocarcinoma, the mucinous variant tends to progress more rapidly and demonstrates poorer resection outcomes. Molecularly, it is characterized by overexpression of MUC2 and MUC5AC mucin proteins, frequent activation of the RAS/MAPK and PI3K/Akt/mTOR signaling pathways, and a higher rate of microsatellite instability. It is still unknown how psoas abscess formation occurs in colon cancer patients; it might be due to the tumour outgrowing the blood supply, followed by necrosis and abscess formation when enteric bacteria are present.[5,7] Systemic spread, direct spread, perforation of the afflicted organ, or peritoneal seedling can all cause it. It has also been observed to spread to the psoas lymph nodes, which are situated between the spine and the muscles. The classic presentation of fever, limp, and back discomfort is seen in about 30% of people.[6] Compared to other adnocarcinomas, mucinous adenocarcinoma has higher levels of arylsulphatase and lysozyme enzymatic activity. These two enzymes can break down the proteoglycan barrier, allowing the cancer to invade and spread. Abscesses develop in and around the infiltrating tissues as a result of tumour cells penetrating the intestinal wall and creating internal or exterior fistulas. Colonic cancer should be suspected in patients who come with an unexplained iliopsoas abscess that has no discernible main or secondary aetiology. At stages I and II, the prognosis for patients with colorectal mucinous adenocarcinoma is comparable to that of patients with non-mucinous carcinoma; however, at stages III and IV, the prognosis is noticeably worse.[6-8]

CONCLUSION

Diagnosing psoas abscess can be particularly challenging in regions, where tuberculosis is common, e.g., in Bangladesh. Nevertheless, when an abscess persists or recurs despite adequate antimicrobial or surgical management, clinicians should consider the possibility of an underlying sinister pathology such as malignancy.

Conflict of interest: None declared by the authors.

Funding statement: No external funding received.

Ethical approval: Permission was taken from the patient and the hospital authority.

Authors' contribution: All authors were equally involved in patient selection, clinical diagnosis, management and data collection. All of them were equally involved in literature search and review as well as manuscript preparation, editing and final submission.

REFERENCES

1. Nambiar K R, Haridas L. Malignancy presenting as a psoas abscess. Indian J Surg Oncol. 2018;9(2): 282-3.
2. Prabhu RM, Koshire SR, Khandelwal RCS. A rare case of psoas abscess secondary to mucinous adenocarcinoma of the appendix: a case report. J Orthop Case Rep. 2021;11(8):1-5.
3. Avery GR. Metastatic adenocarcinoma masquerading as a psoas abscess. Clin Radiol. 1988;39(3):319-20.
4. Fadaee N, De Clercq S, Fadaee S. A rare presentation of colonic malignancy: enterocutaneous fistula secondary to locally advanced cancer. J Case Rep Images Surg. 2019;5:100059Z12NF2019.
5. Luo C, Cen S, Ding G, Wu W. Mucinous colorectal adenocarcinoma: clinical pathology and treatment options. Cancer Commun (Lond). 2019;39(1):13.
6. Menon A, Agashe VM, Jakkan MS. Rare case of iliopsoas abscess secondary to mucinous adenocarcinoma of the colon: a case report. J Orthop Case Rep. 2018;8(1):32-5.
7. Wang J, Li H, Xiong B, Wu L, Hu J. A case report of ileocecal mucinous adenocarcinoma with abscesses in the low-right abdomen and formation of sinus tract in the abdominal wall. Int J Clin Exp Med. 2017;10(9):14001-8.
8. Koseki Y, Kamimura K, Tanaka Y, Ohkoshi-Yamada M, Zhou Q, Matsumoto Y, et al. Rapid progression of colonic mucinous adenocarcinoma with immunosuppressive condition: a case report and review of literature. World J Clin Cases. 2021; 9(30):9182-91.

INSTRUCTION TO THE AUTHORS

Points to consider before submission
Submissions are accepted on the understanding that they have not been published in their current form or a substantially similar form (in print or electronically, including on a web site), that they have not been accepted for publication elsewhere, and they are not under consideration by another publication.

Conflicts of interest
Authors must state all possible conflicts of interest, including financial, consultant, institutional and other relationships that might lead to bias or a conflict of interest

Permissions to reproduce previously published material
Authors should include with their submission copies of written permission to reproduce material published elsewhere (such as illustrations) from the copyright holder.

Ethics committee approval
All authors must declare that the research was conducted within the guidelines below and under the terms of all relevant local legislation.

Authorship
All authors must confirm that they have met the criteria for authorship as established by the International Committee of Medical Journal Editors, that they believe that the paper represents honest work, and that they are able to verify the validity of the results reported.

PRESENTATION OF PAPERS:

Title page
The title page should carry the full title of the paper (up to 100 characters including spaces) and a short title to be used as a 'running head' (45 characters including spaces). The first name, middle initial and last name of each author should appear. If the work is to be attributed to a department or institution, its full name should be included. The name and address of the author responsible for correspondence should appear on the title page.

Abstracts and key words
The second page should carry an abstract. The length is limited to not more than 250 words. The abstract should be followed by a list of 3-10 keywords or short phrases. When possible, the terms used should be from the Medical Subject Headings list of the Index Medicus (http://www.nlm.nih.gov/mesh/meshhome.html).

Text
Full papers of an experimental or observational nature may be divided into sections headed Introduction, Methods (including ethical and statistical information), Results, Discussion and a short Conclusion,

Acknowledgements
Acknowledge only those who have made a substantial contribution to the study. You must obtain written permission from people acknowledged by name.

References
Try to keep the number of references to the minimum. Not more than 30 references are recommended.

Tables
Each table should be typed on a separate page in double spacing. Do not submit tables as photographs. Assign each table an Arabic numeral, e.g. (Table 3), in accordance with order of citation, and a brief title. Do not use vertical rules. Place explanatory matter in footnotes, not in the heading. Explain in footnotes all non-standard abbreviations that are used in each table.

Illustrations
References to figures and tables should be made in order of appearance in the text and should be in Arabic numerals in parentheses, e.g. (Fig. 2). The format of figure file must be compatible with tif or jpeg.

If you need to submit hard copies, label them clearly with the figure number, the title of the paper, the first author's name and a mark indicating the top of the figure. If photographs of people are used, their identities must be obscured or the picture must be accompanied by written consent to use the photograph. If a figure has been published before, the original source must be acknowledged and written permission obtained from the copyright holder.

Original research papers
A maximum of 3000 words with five tables or figures and 30 references using the Vancouver style, http://guides.lib. monash.edu/citing-referencing/vancouver. All articles must include a structured abstract.

- **Review articles**
  A maximum of 3000 words with 30 references using the Vancouver style. All articles must include an abstract.
- **Short Communications**
  Up to 1000 words plus abstract with one table or figure (optional); 5 references
- **Letters**
  A maximum of 400 words in length, including title, text, name and address of author(s), and maximum two references included. Tables and figures are not permitted.
- **Country papers**
  Reports on matters of regional interest, current scope of medical education, innovations and curricular reforms and quality assurance limited to 2000 words with 3 tables or figures and up to 10 references.

Manuscript Submission Form

Copyright assignment

Title:

_____

_____

A signature below certifies compliance with the following statements.

Copyright Transfer. In consideration of the acceptance of the above work for publication, I do hereby assign and transfer to the Mugda Medical Journal all rights, title, and interest in and to the copyright in the above-titled work. The corresponding author's signature is sufficient provided that the corresponding author understands that he or she signs on behalf of all of the authors who have not signed the form. It should also be understood by all authors that the corresponding author has signed the manuscript submission form as their proxy.

Authors

Signature (1) _____ Printed Name _____ Date _____

Signature (2) _____ Printed Name _____ Date _____

Signature (3) _____ Printed Name _____ Date _____

Corresponding author address: _____

_____

_____

E-mail address	Phone	Fax