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AIMS & SCOPE:

The Green Life Medical College Journal is an english language scientific papers dealing with clinical medicine, basic sciences, epidemiology, diagnostic, therapeutics, public helath and healthcare in relation to concerned specialities. It is an official journal of Green Life Medical College and is published bi-annually.

This Joural is recognized by Bangladesh Medical & Dental Council (BM&DC).

The Green Life Medical College Journal of Bangladesh intends to publish the highest quality material on all aspects of medical science. It includes articles related to original research findings, technical evaluations and reviews. In addition, it provides readers opinion regarding the articles published in the journal.

INSTRUCTION TO AUTHORS:

Papers:

The Green Life Medical College Journal (published bi-annually) accepts contributions from all branches of medical science which include original articles, review articles, case reports, and letter to the Editor.

The articles submitted are accepted on the condition that they must not have been published in whole or in part in any other journal and are subject to editorial revision. The editor preserves the right to make literary or other alterations which do not affect the substance of the contribution. It is a condition of acceptance that the copyright becomes vested in the journal and permission to republish must be obtained from the publisher. Authors must conform to the uniform requirements for manuscripts submitted to biomedical journals (JAMA 1997; 277: 927-34).

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In preparing the manuscript, use double spacing throughout, including title, abstract, text, acknowledgement, references, table and legends for illustrations and font type and size 'Times New Roman 12'. Begin each of the following sections on a separate paper. Number pages consecutively.

The standard layout of a manuscript:

- Title page
- Abstract, including Keywords
- Introduction
- Methods
- Results
- Discussion
- Acknowledgements
- Funding
- List of references
- Tables & Figures
- Illustrations

The pages should be numbered in the bottom right-hand corner and the title page being page one, etc. Start each section on a separate page.

Title page:

A separate page which includes the title of the paper. Titles should be as short and concise as possible (containing not more than 50 characters). Titles should provide a

reasonable indication of the contents of the paper. This is important as some search engines use the title for searches. Titles in the form of a question, such as 'Is drinking frequent coffee a cause of pancreatic carcinoma?" may be acceptable.

The title page should include the name(s) and address(es) of all author(s). Details of the authors' qualifications and post (e.g., professor, consultant) are also required. An author's present address, if it differs from that at which the work was carried out, or special instructions concerning the address for correspondence, should be given as a footnote on the title page and referenced at the appropriate place in the author list by superscript numbers ([1, 2, 3] etc.) If the address to which proofs should be sent is not that of the first author, clear instructions should be given in a covering note, not on the title page.

Abstract:

The 'Abstract' will be printed at the beginning of the paper. It should be on a separate sheet, in structured format (Introduction/Background; Methods; Results; and Conclusions) for all Clinical Investigations and Laboratory Investigations. For Reviews and Case Reports, the abstract should not be structured. The Abstract should give a succinct account of the study or contents within 350 words. The results section should contain data. It is important that the results and conclusion given in the 'Abstract' are the same as in the whole article. References are not included in this section.

Keywords:

Three to six keywords should be included on the summary page under the heading Keywords. They should appear in alphabetical order and must be written in United Kingdom English spelling.

Introduction:

The recommended structures for this section are:

- Background to the study/Introduction
- What is known/unknown about it
- What research question / hypothesis you are interested in
- What objective(s) you are going to address

The introduction to a paper should not require more than about 300 words and have a maximum of 1.5 pages double-spaced. The introduction should give a concise account of the background of the problem and the object of the investigation. It should state what is known of the problem to be studied at the time the study was started. Previous work should be quoted here but only if it has direct bearing on the present problem. The final paragraph should clearly state the primary and, if applicable, secondary aims of the study.

Methods:

The title of this section should be 'Methods' - neither 'Materials and methods' nor Patients and methods'. The Methods section should give a clear but concise description of the process of the study. Subjects covered in this section should include:

- Ethics approval/license
- Patient/population
- Inclusion/exclusion criteria
- Conduct of the study
- Data handling
- Statistics
- Cognitive Task Analysis (CTA)

Ethical clearance:

Regardless of the country of origin, all clinical investigators describing human research must abide by the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki, and adopted in October 2000 by the World Medical Association. This document can be found at: http://ohsr.od.nih.gov/guidelines/helsinki.html. Investigators are encouraged to read and follow the Declaration of Helsinki. Clinical studies that do not meet the Declaration of Helsinki criteria will be denied peer review. If any published research is subsequently found to be non-compliant to Declaration of Helsinki, it will be withdrawn or retracted. On the basis of the Declaration of Helsinki, the Green Life Medical Journal requires that all manuscripts reporting clinical research state in the first paragraph of the 'Methods' section that:

- The study was approved by the appropriate Ethical Authority or Committee.
- Written informed consent was obtained from all subjects, a legal surrogate, or the parents or legal guardians for minor subjects.

Human subjects should not be identifiable. Do not disclose patients' names, initials, hospital numbers, dates of birth or other protected healthcare information. If photographs of persons are to be used, either take permission from the person concerned or make the picture unidentifiable. Each figure should have a label pasted on its back indicating name of the author at the top of the figure. Keep copies of ethics approval and written informed consents. In unusual

circumstances the editors may request blinded copies of these documents to address questions about ethics approval and study conduct.

The methods must be described in sufficient detail to allow the investigation to be interpreted, and repeated if necessary, by the reader. Previously documented standard methods need not be stated in detail, but appropriate reference to the original should be cited. However, any modification of previously published methods should be described and reference given. Where the programme of research is complex such as might occur in a neurological study in animals, it may be preferable to provide a table or figure to illustrate the plan of the experiment, thus avoiding a lengthy explanation. In longitudinal studies (case-control and cohort) exposure and outcome should be defined in measurable terms. Any variables, used in the study, which do not have universal definition should be operationalised (described in such terms so that it lends itself to uniform measurement). Where measurements are made, an indication of the error of the method in the hands of the author should be given. The name of the manufacturer of instruments used for measurement should be given with an appropriate catalogue number or instrument identification (e.g. Keyence VHX-6000 digital microscope). The manufacturer's town and country must be provided, in the case of solutions for laboratory use, the methods of preparation and precise concentration should be stated.

Single case reports:
Single case reports of outstanding interest or clinical relevance, short technical notes and brief investigative studies are welcomed. However, length must not exceed 1500 words including an unstructured abstract of less than 200 words. The number of figures/tables must not be more than 4 and references more than 25.

Animal studies:
In the case of animal studies, it is the responsibility of the author to satisfy the board that no unnecessary suffering has been inflicted on the animal concerned. Therefore, studies that involve the use of animals must clearly indicate that ethical approval was obtained and state the Home Office License number or local equivalent.

Drugs:
When a drug is first mentioned, it should be given by the international non-proprietary name, followed by the chemical formula in parentheses if the structure is not-well known, and, if relevant, by the proprietary name with an initial capital letter. Dose and duration of the drug should be mentioned in sufficient details. If the drug is already in use (licensed by appropriate licensing authority), generic name of the drugs should preferably be used followed by proprietary name in brackets.

Present the result in sequence in the text, table and figures. Do not repeat all the data in the tables and/or figures in the text. Summarize the salient points. Mention the statistics used for statistical analysis as footnote under the tables or figures. Figures should be professionally drawn. Illustration can be photographed (Black and White glossy prints) and numbered.

Discussion:
Do not repeat the data in detail, already given in the results. Give implications of the findings, their strengths and limitations in comparison to other relevant studies. Avoid un-qualified statements and conclusions which are not supported by the data. Avoid claiming priority.

Conclusion:
Comments on the observation of the study and the conclusion derived from it. New hypothesis or implications of the study may be labeled as recommendations.

References:
References should be written in Vancouver style, numbered with arabic numerals in the order they appear in the text. The reference list should include all information, except for references with more than six authors, in which case give the first six names followed by et al.

Examples of correct forms of references:
Dorababu M, Prabha T, Priyambada S, Agrawal VK, Aryaa NC, Goel RK. Effect of Azadirachta indica on gastric ulceration and healing of bacopa monnierang in experimental NIDDM rats. *Indian J Exp. Biol 2004; 42: 389-397.*

Chapter in a book:
Hull CJ. Opioid infusions for the management of postoperative pain. In: Smith G, Covino BG, eds. Acute Pain. London: Butterworths. 1985,1 55-79.

All manuscripts for publication should be addressed to the executive editor.

LETTER TO THE EDITOR:
Any reader can provide feedback regarding published articles by writing letter to editor. The reader can also share any opinion in relation to medical science.

Prof. Dr. ABM Bayezid Hossain
Editor-in-chief
Green Life Medical College Journal and
Principal
Green Life Medical College

ABOUT THE COLLEGE

INTRODUCTION

In 2005, about fifty distinguished physicians of the country started a hospital to give specialized care in the private sector. They named it Green Life Hospital and it turned out to be a great success. So in 2009, they decided to establish a medical college which will be a non-government, non-profit, self-financing project and will serve the humanity.

This College came into existence in 2009. The college commences its activities with the enrollment of 51 students in the 1st batch in 2010. Since inception, the college has undergone tremendous development and became a splendid centre for learning and development. At present we are enrolling 110 students each year. Among them, numbers of seats are reserved for overseas students.

We continue to evaluate and improve our programme to ensure the best medical education for the students. Our educational strategy is to create a conducive learning environment and to steer our students to acquire adequate knowledge, skills and temperament to practice medicine and be a competent health care professional group.

Green Life Medical College (GMC) is approved by the Ministry of Health and Family Welfare (MOHFW), Government of Bangladesh and Bangladesh Medical and Dental Council (BMDC) and affiliated to the University of Dhaka.

AIMS AND OBJECTIVES OF THE COLLEGE

Aims:

To create a diverse and vibrant graduate scholars in medical discipline and to create highly competent and committed physicians for the country.

Objectives:

- To provide an appropriate learning environment where medical students can acquire a sound theoretical knowledge and practical skills with empathetic attitude to the people.
- To carry out research in medical sciences to scale up the standard of medical education in the country.

LOCATION

The campus is located at 31 and 32, Bir Uttom K. M. Shafiullah Sarak (Green Road), Dhanmondi, Dhaka. The location is at the heart of the mega city Dhaka and is facilitated with very good communication networks.

The Medical College and the Hospital complexes have been raised in a multistoried fully air-conditioned building with an arrangement of approximately 500 patients. The building is equipped with state-of-the-art infrastructure, excellent with an out-patient department and adequate in-patient facilities.

EDITORIAL

When Relief Becomes Risk: The Prolonged Use of Proton Pump Inhibitors

Proton pump inhibitors (PPIs) have revolutionized the treatment of gastroesophageal reflux disease, peptic ulcers, and other acid-related disorders. By effectively inhibiting the gastric acid secretion mechanism, these medications have provided substantial relief and improved the quality of life for millions of patients worldwide. However, the increasing prevalence of PPI prescriptions and prolonged use over the last two decades has raised significant concerns regarding their long-term safety profile. Recent studies have suggested a troubling correlation between prolonged PPI use and a variety of health issues, prompting healthcare providers to re-evaluate their prescribing practices.

Rising Prevalence and Uncertain Necessity:
PPIs are frequently prescribed without adequate review or reevaluation of the underlying condition. A study published in 2020 noted that approximately 25% to 70% of patients receiving PPIs for non-ulcer dyspepsia or GERD continue therapy long after symptoms have resolved, often without a clear indication for ongoing treatment.[1] This trend of indefinite PPI therapy is concerning, leading to the potential for serious adverse effects.

Kidney disease:
One of the most alarming associations with long-term PPI use is the risk of chronic kidney disease (CKD) and acute kidney injury (AKI). Research has shown a significant increase in the risk of developing CKD among PPI users. A meta-analysis indicating that PPI use is linked to a 20-50% increased risk of CKD compared to non-users.[2, 3] The mechanisms are still being studied, but one theory suggested that PPIs may induce acute interstitial nephritis, leading to long-term renal damage.

Increased Risk of Gastrointestinal Infections:
Prolonged use of PPIs poses an increased risk of gastrointestinal infections. Research indicates that PPI users have a two- to threefold higher risk of developing Clostridium difficile infections, which can lead to severe diarrhea and colitis.[4] The reduced gastric acidity allows for the survival of pathogens, leading to an increase in gastrointestinal complications. PPIs may promote small intestine bacterial overgrowth, leading to symptoms such as bloating, diarrhea, and malabsorption.[5]

Nutritional Deficiencies:
Another critical issue with long-term PPI use is the risk of nutritional deficiencies. PPIs can interfere with the absorption of various nutrients, most notably vitamin B12, iron, magnesium, and calcium. A systematic review highlighted that individuals on long-term PPIs are at increased risk of iron and vitamin B12 deficiency, which can lead to anemia and neurological complications.[6] The malabsorption of magnesium is particularly concerning, as it can lead to muscle spasms, cardiac arrhythmias, and other serious conditions. Additionally, impaired calcium absorption raises concerns over osteoporosis and fracture risk.[7]

Potential Cardiovascular Implications:
Emerging evidence has suggested a possible association between long-term PPI use and cardiovascular risks, including myocardial infarction. A study found that PPI users exhibited a significantly increased risk of heart attacks.[8] While research in this area is still developing, the implications of these findings are profound and warrant further research.

Cancer Risks: The Ongoing Debate
The relationship between long-term PPI use and gastric cancer risk has become a hot topic in recent studies. Some evidence suggested that chronic use of PPIs may increase the risk of developing gastric cancer, particularly in patients with long-standing conditions like Barrett's esophagus or chronic gastritis.[9] Although the data is not yet definitive, these findings emphasize the importance of monitoring and reassessing risk factors regularly.

A Clinical Imperative: Reducing Risks
Given the evidence surrounding the risks associated with prolonged PPI use, healthcare providers must adopt a more cautious and comprehensive approach. Continuous re-evaluation of treatment necessity is critical. Clinicians should be vigilant in monitoring potential complications arising from long-term PPI use. Routine assessments of kidney function, magnesium levels, iron and vitamin B12 status can facilitate early detection of adverse effects.

Conclusion:

While proton pump inhibitors have undoubtedly provided significant benefits in managing acid-related disorders, the increasing body of evidence regarding their long-term risks cannot be overlooked. Chronic kidney disease, gastrointestinal infections, nutritional deficiencies, cardiovascular risks, and potential links to cancer all warrant serious consideration. As healthcare providers, it is our responsibility to ensure the safe, judicious use of these medications, weighing the benefits against the mounting evidence of their risks.

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ORIGINAL ARTICLE

A Study on Comparison between Clinical and Laboratory Parameters in the Diagnosis of Acute Appendicitis

AKTER R[1], KARIM MA[2], KABIR F[3]

Abstract

Introduction: *Various tools and investigations such as Modified Alvarado Score (MAS) and Ultrasonography (USG) of whole abdomen are in use for the diagnosis of acute appendicitis. The aim of the study was to compare the Clinical and Laboratory Parameters in the Diagnosis of Acute Appendicitis.*

Methods: *This cross-sectional observational study was conducted at the Department of Surgery, Sir Salimullah Medical College Mitford Hospital in Dhaka. Patients were selected according to inclusion and exclusion criteria. Total 60 patients were operated upon and subsequently evaluated. All patients were subject to detailed history taking, physical examination and laboratory investigation before operative procedure and histopathological examination of resected vermiform appendix. Data were collected by checklist and analyzed statistically by the SPSS 26.0 package for windows.*

Results: *The mean age was 28.6 years with age range from 16 to 65 years. Maximum 56.7% patients belonged to 16-25 years. 51.7% patients were male and 48.3% patients were female. Patients in this study with Modified Alvarado Score (MAS) ≥7 had histopathological features of acute appendicitis in 97.6% of the cases. Sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of MAS score vs. histopathology findings were 75.93%, 83.33%, 76.67% 97.62% and 27.78% respectively. By USG, 47 patients were detected acute appendicitis. Among them 45 (95.7%) patients were acute appendicitis on histopathology. Sensitivity, specificity, accuracy, PPV and NPV of USG vs. histopathology findings were 83.33%, 66.67%, 81.67%, 95.74% and 30.77% respectively.*

Conclusion: *The diagnosis of acute appendicitis is mainly clinical which is supported by laboratory test and USG. The MAS is used in clinical diagnosis of acute appendicitis. The USG is an effective imaging technique in diagnosing acute appendicitis. The diagnosis of acute appendicitis is confirmed by histopathology. Combined use of MAS and USG increases the number of positive cases of acute appendicitis.*

Keywords: *Acute appendicitis, Modified Alvarado Score, Appendisectomy*

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Introduction:

Acute appendicitis is one of the most common abdominal surgical emergency. Appendicectomy for acute appendicitis is one of the most common emergency surgical procedures performed.[1]

The diagnosis of acute appendicitis is mainly clinical but definitive diagnosis is essential to prevent negative appendicectomy. The diagnosis of acute appendicitis by clinical evaluation may be challenging for physicians in cases when the presentation is atypical and overlaps with other conditions. In these situations, the use of laboratory test and imaging studies are helpful. Achieving the correct diagnosis reduces the risk of complications like perforation, lump formation. It also reduces negative appendicectomy. Different scoring systems for the diagnosis of acute appendicitis have been proposed. Modified Alvarado Scoring (MAS) system is widely used. Modified Alvarado Score is non-invasive diagnostic method which is simple and reproducible. In practice, the diagnosis of acute appendicitis is supported by ultrasonography. The diagnosis of acute appendicitis is confirmed by histopathology.

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2. Md. Abdul Karim, Director, Long Life Hospital Ltd., Dhaka
3. Farzana Kabir, Registrar, Department of Surgery, Dhaka National Medical College, Dhaka

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This study was designed with the objective to evaluate the diagnostic performance of MAS and USG, individually or in combination for the diagnosis of acute appendicitis.

Methods:

This Observational, cross sectional study was conducted at the department of Surgery, Sir Salimullah Medical College Mitford Hospital, Dhaka during May'2020 to April'2021. The sampling technique was purposive and total 60 participants were included according to inclusion criteria. Male and female with age equal to or more than 16 years, admitted in surgery department with suspected acute appendicitis were included in the study. The patients with missing data and those with appendicular lump formation at admission in hospital were excluded from the study. After taking written informed consent, the age, sex, and detailed clinical history with physical examination was done. Every patient was assessed by Modified Alvarado Score (MAS) and USG of whole abdomen with special attention to vermiform appendix. MAS is based on patient's symptoms, specific abdominal signs and laboratory findings.[2] Blood sample from a vein was taken for CBC measurement. The blood sample was then sent to laboratory and analyzed. All patients underwent open appendicectomy. All the excised appendix were collected into 10% buffered neutral formalin (BNF) for fixation and then sent to laboratory for histopathological examination. Data were collected by checklist. Later, the data were put into the computer and analyzed with SPSS 26.0 for windows. Unpaired student's 't' test was calculated for continuous variables. P-value of less than 0.05 was considered as significant. Diagnostic performance was evaluated by sensitivity, specificity, positive predictive value, negative predictive value and accuracy or efficacy.

Prior to the commencement of this study, the research protocol was approved by the Research Review Committee of Department of Surgery and the Ethical Committee of Sir Salimullah Medical College Mitford Hospital, Dhaka.

Results:

Table-I Shows that majority (56.7%) patients belonged to 16-25years. 51.7% patients were male and 48.3% patients were female.

Table I

Demographic variables (n=60)

Variables		No of patients	Percentage (%)
Age group (years)	16-25	34	56.7
	26-35	9	15.0
	36-45	11	18.3
	46-55	3	5.0
	56-65	3	5.0
Gender	Male	31	51.7
	Female	29	48.3

Table-II Shows 41.7% patients had pain around umbilicus, 100% patients had pain in right iliac fossa, 95% patients had anorexia, 70% patients had nausea/vomiting, 83.3% patients had fever. Tenderness in right iliac fossa and rebound tenderness were both found in 60 (100%) cases.

Table II

Clinical symptoms and examination findings according to MAS (n=60)

Symptoms	No of patients	Percentage (%)
Pain around umbilicus	25	41.7
Pain in right iliac fossa		
Mild	3	5.0
Moderate	51	85.0
Severe	6	10.0
Anorexia	57	95.0
Nausea/vomiting	42	70.0
Fever	50	83.3
Abdomen examination for MAS		
Tenderness in right iliac fossa	60	100.0
Rebound tenderness (Blumberg's sign)	60	100.0

Table-III Shows patients with MAS e"7 were found in 42 (70%) cases and MAS < 7 in 18 (30%) cases. 47 (78.33%) patients were diagnosed as acute appendicitis by USG.

Table III

Distribution of the study patients by Modified Alvarado Score (MAS), USG findings, CRP and NLR (n=60)

Modified Alvarado Score (MAS)	No of patients	Percentage (%)
MAS group		
≥7 42	70	
< 7 18	30	
Total	60	100.0
USG findings		
Suggestive of acute appendicitis	47	78.33
Normal study	13	21.67
Total	60	100.0

Table-IV Shows 54 (90.0%) patients were acute appendicitis on histopathology and 6 (10.0%) patients were normal study on histopathology.

Table IV

Distribution of the study patients by histopathological findings (n=60)

Histopathological findings	No of patients	Percentage (%)
Acute Appendicitis	54	90.0
Normal appendixTotal	660	10.0100.0

Table-V Shows 42 patients with MAS ³7 MAS had positive histopathology in 41 (68.34%) patients. 47 patients were diagnosed by USG, 45 (75.0%) patients were acute appendicitis on histopathology. 53 patients with combined MAS and USG had positive histopathology in 50 (83.34%) patients.

Table-VI Shows to detect acute appendicitis higher percentage of sensitivity of combined MAS and USG (92.59%); higher percentage of specificity of MAS (83.33%); higher percentage of accuracy of combined MAS and USG (88.34%); higher percentage of positive predictive value of MAS (97.62%); the higher percentage of negative predictive value of combine MAS and USG (42.86%).

Table V

Histopathological findings in patients diagnosed by MAS and USG (n=60)

Diagnostic parameters			Histopathology	
			Normal appendix	Acute appendicitis
	> 7	42	1 (1.66%)	41 (68.34%)
MAS	**< 7**	18	5 (8.34%)	13 (21.66%0
	Total	60	6 (10.0%)	54 (90.0%)
	Acute appendicitis	47	2 (3.33%)	45 (75.0%)
USG Findings	Normal appendix	13	4 (6.67%)	9 (15.0%)
	Total	60	6 (10.0%)	54 (90.0%)
	Acute appendicitis	53	3 (5.0%)	50 (83.34%)
MAS+USG	Normal appendix	7	3 (5.0%)	4 (6.66%)
	Total	60	6 (10.0%)	54 (90.0%)

Table VI

Diagnostic performance of MAS, USG, combined MAS and USG with histopathology to detect acute appendicitis (n=60)

	Histopathology versus				
	MAS	USG	CRP	NLR	Combined MAS and USG
Sensitivity	75.93%	83.33%	75.93%	62.96%	92.59%
Specificity	83.33%	66.67%	50.00%	83.33%	50.00%
Accuracy	76.67%	81.67%	73.33%	65.0%	88.34%
Positive predictive value	97.62%	95.74%	93.18%	97.14%	94.34%
Negative predictive value	27.78%	30.77%	18.75%	20.0%	42.86%

Discussion:

The diagnosis of acute appendicitis is mainly clinical which is supported by laboratory test and USG. The MAS compiles the clinical features and laboratory tests like WBC count. As the imaging techniques have improved, the USG appears to be an effective imaging technique in diagnosing acute appendicitis. The diagnosis of acute appendicitis is confirmed by histopathology.

In our study, USG has been found to be more effective than MAS in predicting acute appendicitis. Combined use of MAS and USG increases the number of positive cases of acute appendicitis.

Male patients were predominant gender in this study. The majority (56.7%) were in younger age group of 16 to 25 years. Similar to that of Ahmed et al. and other studies.[3,4,5]

In this study, the majority (70%) of the patient diagnosed acute appendicitis had MAS of ≥7. Mandal et al. also reported the same MAS ≥7 with positive acute appendicitis diagnosis.[6]

The patients with MAS ≥7 had histopathological features of acute appendicitis in 68.34% cases. This study showed sensitivity and specificity of MAS vs histopathology findings which were statistically significant. In concordance with this study Jaykumar et al. reported the higher sensitivity and specificity of MAS. Positive predictive value of MAS in this study was high and negative predicitive value was low. This is comparable with the study by Jaykumar et al.[8]

This study showed that 78.34% of patients were detected acute appendicitis by USG. Among them 75% patients had histopathological features of acute appendicitis. Sensitivity, accuracy, positive predictive values, negative predictive value of USG vs histopathology were higher than MAS vs histopathology. Dsouza et al. and Gujar et al. reported the sensitivity, specificity, accuracy, positive predictive value and negative predictive values of USG in acute appendicitis diagnosis were high.[9,7]

In this study, combined MAS and USG showed that 88.34% patients were diagnosed as acute appendicitis; among them 83.34% patients were proven by histopathology. Sensitivity, accuracy and negative predictive value of combined use of MAS and USG were higher than individual use of MAS or USG. The positive predictive value of combined MAS and USG was 94.34%.

Some limitations were observed in this study like variation in clinical presentations, laboratory test results variations and operator dependency of abdominal USG. The study population was selected from one hospital in Dhaka city.

Conclusion:

The diagnosis of acute appendicitis is mainly clinical which is supported by laboratory test and USG. The MAS is used in clinical diagnosis of acute appendicitis. The USG is an effective imaging technique in diagnosing acute appendicitis. The diagnosis of acute appendicitis is confirmed by histopathology. Combined use of MAS and USG increases the number of positive cases of acute appendicitis. So our recommendation is multicentered and bigger studies can be undertaken for better reflection in bigger population. Knowledge of variations in clinical presentation, increase accuracy of laboratory tests results and better USG imaging will increase the diagnostic accuracy of acute appendicitis.

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ORIGINAL ARTICLE

In Vitro Study of Root Canal Morphology of Mandibular First Premolars in Bangladeshi Population

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Abstract

Introduction: *Internal root canal morphology directly influences the outcome of Root Canal Treatment. Mandibular 1st premolar shows wide variation of root canal morphology and also roots number. Determination of root canal morphology and root number of mandibular first premolars collected from the Rajshahi (Bangladeshi) population using a canal staining and tooth clearing technique.*

Methods: *2126 extracted mandibular 1st premolars collected from Rajshahi Medical College dental Unit and Private dental practitioner chamber within Rajshahi were selected for this study and stored in normal saline. Root numbers were determined by Visual and radiographic examinations. 5%nitric acid was used to decalcify teeth after pulp tissue removal. Ascending concentrations of alcohol and methyl salicylate were used for dehydrating and clearing teeth respectively. India ink was used for staining and 5 x magnifications were used for evaluating the number of roots, root canals, and location of apical foramina.*

Results: *Of the 2126 teeth, 2031 (95.53%) had one, 88 (4.13%) had two, and seven mandibular 1st premolars (0.33%) had three roots. Of these, 83.06% (1766 teeth) had a single canal, 16.60% (353 teeth) had two canals, and 0.33% (7 teeth) had three canals. About Seventy nine percent had Type I, 12% had Type V, and 4% had Type III, root canal configuration. Lateral canals were found in 36% and apical delta in 6.06% teeth. In 79% cases apical foramens were located lateral to apex and in 16% teeth intracanal communications were present.*

Conclusion: *Bangladeshi Mandibular first premolars are mainly single rooted and predominantly have Type I Vertucci's classification of canal morphology. While performing the endodontic treatment, different variations in root morphology and canal configuration of mandibular first premolars should be kept in mind by the clinician.*

Keywords: *Root morphology, Mandibular first premolar, dental anatomy, Bangladeshi population*

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Introduction:

The internal morphology of teeth is complex and canals may branch, divide, and rejoin.[1] Proper knowledge regarding the internal root canal configuration and its possible variations of teeth undergoing endodontic therapy is a prerequisite to proper root canal preparation, obturation, and an acceptable outcome.[2] Roots number and canal configuration variation make the maxillary 1st premolar's internal anatomy complex with relatively innocent simplicity of the external surface of roots.[3] The mandibular first premolar should be evaluated properly as extra roots, extra canals, canal configuration, apical delta, accessory canal and intracanal communication may appear as a complicated and challenging work for clinician.[2] Brescia 1961 reported that the mandibular first premolar

teeth had the most variable canal pattern.[4] A study at the University of Washington 1955 assessed the failure rate of non-surgical root canal treatment in all teeth.[5] The studies on root canal morphology of mandibular premolars were mainly performed in United States of America,[1] India,[6] Sri Lanka,[7] Jordan,[8] Kuwait,[9] France,[10] Japan,[7] and Iran[11]. Asian populations present one of the widest variations in coronal shape, external root form and internal canal space morphology.[6] The studies by Serman and Hasselgren[12] as well as by Trope et al[13] reported higher incidences of multiple root canals in mandibular 1st premolar in their studies (7% and 3.1%, respectively).

A variety of techniques has been used to study the anatomy of the root canal system. These techniques have included Radiographic examination, [11,13] canal staining and clearing technique,[8] cross sectioning of teeth,[11] microcomputed tomography,[14] and more recently, cone beam computed tomography.[15] The present study was conducted using the decalcification and tooth clearing technique because most detailed information can be obtained ex vivo by demineralization and staining[3]. Unlike radiographic images, the clearing technique provides a three dimensional view of the pulp cavity in relation to the exterior of the teeth.[15] No data is available on root canal morphology of mandibular premolars in northern region of Bangladesh. Therefore, the aim of this study was to prepare detailed investigation of root canal morphology of mandibular first premolar in a Rajshahi (northern region of Bangladesh) population by using clearing technique and to compare these findings with the published reports of different population.

Methods:

Total 2126 extracted Mandibular 1st premolar extracted due to carious or periodontal problems and prosthodontics or orthodontics needs were randomly collected from Dental Unit Rajshahi Medical and also from different private oral care center within Rajshahi, Northern area of Bangladesh over a 5-year period from January 20117 to December 2021. Mature teeth with intact clinical crowns (four walls present) were included in this study and teeth having Immature or resorbed apices were excluded from the study and the samples are selected randomly. Blood, saliva or any debris were removed from the extracted teeth by thorough washing. All teeth were immersed in 5.25% sodium hypochlorite (Organo Biotech laboratories Pvt Ltd New Delhi, India.) for 30 minutes. Calculus or any remaining external tissues were cleaned by scaling. The study samples were saved in normal saline until further evaluation. Root numbers of the study samples were visually examined and note down the observation. The study samples were then gathered into four groups centered on root numbers. Internal root canal morphology was evaluated by radiograph in two planes (mesiodistal and mesiodistal + 40- degree horizontal angle).[13] After access cavities preparation the study samples were immersed in 5.25% sodium hypochlorite for 24 hours for dissolving pulp tissue. Teeth were washed under running tap water for 2 hours and dried overnight.[16] 27 gauge endodontic irrigating syringe needle (BU Kwang Medical Inc., Seoul, Korea) was used to inject India ink (Sanford Rotring GmbH, Hamburg, and Germany) into the pulp chamber.[16] By applying negative pressure by using the central suction system the ink was drained into the root canal up to the apical foramen. Gauze soaked in alcohol was used to remove the excess ink. After staining the samples were dried up in the air and 5% nitric acid (Analytical reagents 69-71%; Gainlad Chemical Co., Clwyd, UK) was used for 3 days for decalcification.[16] The solution of nitric acid was changed daily and anticipated decalcification was checked by periodic radiography. Under running tap water the teeth were washed overnight and then dried in the air. Ascending concentrations of ethyl alcohol (70%, 96%, and 99%) were used for 12 hours for dehydrated specimens. The study samples were dipping in methyl salicylate solution (Regent Chemicals, Mumbai) to make it transparent.[16] The specimens were inspected using 5X magnification with a magnifying glass and photographed using a digital camera. Internal root-canal anatomy was evaluated according to Vertucci[17] classification.

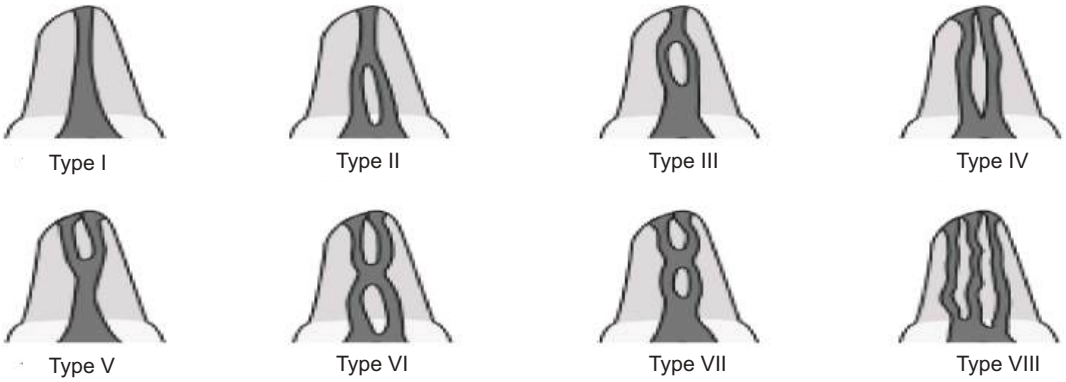

Fig.-2: *show diagrammatic representation of Vertucci's canal configurations*

Results:

Among 2126 specimens, 2031 teeth (95.53%) were recognized as single-rooted, 88 teeth (04.13%) as double rooted and seven teeth (0.33%) as a triple rooted (Table I).

Table I

Distribution of Number and Percentage of Root types in Mandibular 1st premolar (n = 2126)

Root Morphology	Frequency	Percentage
Single	2031	95.53
Double roots	88	04.13
Triple roots	07	00.33
Total	2126	100%

Of these, 83.06% (1766 teeth) had a single canal, 16.60% (353 teeth) had two canals, and 0.33% (7 teeth) had three canals (Table II).

Table II

Distribution of Number and Percentage of Root canal types in Mandibular 1st premolar (n = 2126)

Root Morphology	Frequency	Percentage
Single root canal	1766	83.06
Double root canal	353	16.60
Triple root canal	07	00.33
Total	2126	100%

About 79% cases (1678 teeth) apical foramens were located lateral to apex and in 448 teeth (21.07% cases) apical foramens were located at the apex (Table III).

Table III

Distribution of apical foramen location in Mandibular 1st premolar (n = 2126)

Location of apical foramen	Frequency	Percentage
At apex	448	21.07
At lateral to apex	1678	78.92
Total	2126	100%

About Seventy nine percent had Type I, 12% had Type V, and 4% had Type III, root canal configuration Type II, Type IV, Type VII, Type VI, and Type VIII Vertucci18 canal configuration were found in 38 teeth(1.78%), 36 teeth(1.69%), 22 teeth(1.03%), 18 teeth (0.84%), and 6 teeth(0.26%) respectively (Table IV).

Table IV

Distribution of Number and Percentage of Root Canal configuration according to Vertucci[18] in Mandibular 1st premolar (n = 2126)

Root Canal Morphology	Frequency	Percentage
Type I	1674	78.73
Type II	38	01.78
Type III	78	03.66
Type IV	36	01.69
Type V	254	11.94
Type VI	18	00.84
Type VII	22	01.03
Type VIII	06	00.28
Total	2126	100%

1674 teeth (78.73%) had a single apical foramen, 316 teeth (14.86%) had two foramens, 7 teeth (0.33%) had three apical foramens, and 129 teeth (6.06%) had multiple apical foramina (apical delta) (Table V).

Table V

Distribution of Number and Percentage apical foramen in Mandibular 1st premolar (n = 2126)

Root Morphology	Frequency	Percentage
Single apical foramen	1674	78.73
Double apical foramen	316	14.86
Triple apical foramen	07	00.33
Multiple apical foramen (apical delta)	129	06.06
Total	2126	100%

Lateral canals were found in 766 teeth (36%) and 568 teeth (74.15%) had lateral canals in apical area, 131 teeth (17.10%) in mid root area, and 67 teeth (8.74%) in cervical area of root. About 79% cases (1678 teeth) apical foramens were located lateral to apex and in 448 teeth (21.07% cases) apical foramens were located at the apex. 14% teeth had intercanal communications.

Table VI

Distribution of Number and Percentage of accessory canals in Mandibular 1st premolar (n = 2126)

Root Morphology	Frequency	Percentage
Accessory canals	766	36.00% (n=2126)
Apical root area	568	74.15 % (n=766)
Middle root area	131	17.10% (n=766)
Cervical root area	67	08.74% (n=766)

Table VII

Showed a comparative in vitro study findings regarding root number of the mandibular 1st premolar

Reference	Method of study	Population	Number of roots		
			One %	Two %	Three %
Jain and Bahuguna	Tooth clearing	India	97.11	02.89	00.00
Peiris	Tooth clearing	Sri Lanka	98.80	01.20	00.00
Awawdeh and Al-Qudah	Tooth clearing	Jordan	97.00	03.00	00.00
Iyer et al.	In vivo; digital radiography	India	95.90	03.90	00.20
Zaatar et al	In vivo; postoperative radiographs	Kuwait	85.00	15.00	00.00
Geider et al	Tooth sectioning and radiography	France	90.60	06.40	02.40
The present study	Tooth clearing	Bangladesh	95.53	04.13	00.33

Table VIII

Showed a comparative study of Canal configuration in the mandibular first premolar according to percentage of Vartucci's classification

Reference	Population	Percentage of Vartucci classification							
		I	II	III	IV	V	VI	VII	VIII
Vartucc	USA	70.00		00.00	04.00	01.50	24.00	00.00	00.00
Awawdeh and Al-Qudah	Jordan	58.20	04.80	01.40	14.40	16.80	00.80	01.00	00.00
Peiris	Japan	82.60	01.10	01.10	00.00	15.20	00.00	00.00	00.00
Khidmat et al.	Iran	88.47	01.84	03.22	00.90	04.14	00.00	00.00	00.00
Jain and Bahuguna	India	67.39	07.97	03.62	02.89	17.39	00.72	00.00	00.00
The present study	Bangladesh	78.73	01.78	03.66	01.69	11.94	00.84	01.03	00.28

Discussion:

The teeth clearing technique was used for evaluating the internal anatomy of the teeth in the present study as it delivered better visualization of the canal configuration of teeth.[16] The tooth clearing technique provides the greatest information on the original internal root canals morphology. Gupta et al.[16] stated that the combination of nitric acid and methyl salicylate for the transparent tooth model provided the best results.[18] Mandibular premolars account for 15.8%–21.5% of all endodontically treated teeth.[19] The literature review showed that there were no studies on Mandibular premolars in the Rajshahi- a northern region of Bangladeshi population. Roots number of Mandibular 1st premolars shows a varied diversity.[18] Canal configuration differs significantly amongst various inhabitants worldwide in many studies.

The most commonly observed root morphology was the single rooted mandibular first premolars (95.53%), followed by double (4.13%), and triple rooted (0.33%). The one-root percentage is close to the rate of an Indian population according to Jain and Bahuguna[6] and a Jordanian population according to Awawdeh and Al-Qudah[8]. Findings of roots number of maxillary 1st premolars of several studies are summarized in Table IV together with the findings of the present study. There was a prevalence of about 17% of Bangladeshi mandibular first premolars having more than one root canal, 19.2% of Egyptians,[19] 19.4% of Japanese,[20] and a range of 14%–30.7% of Americans[3] exhibited more than one root canal. Apically, Vertucci[17] reported (85%) of apical foramina located laterally which is the closest percentage to what observed in the present study (78.92%). Vertucci's canal classiûcation[17] was used in this study because in 1984, Vertucci[17] determined canal numbers and conûgurations by percentages for each of the human permanent teeth. In the current study, Vertucci Type I canal conûguration represented the highest percentage (78.73%) of all canal types found in this study. The highest frequency of simple one canal (Class I) was reported as 88.47% in an Iranian population[11] and the lowest was 58.2% in Jordanian.[8] The highest frequency of class V (1-2 pattern) was reported in a Sri-Lankan population (28.4%)[7] compared to the current

study (11.94%) and similar to Egyptian population (16.2%)[19]. Findings of root canals number of mandibular 1st premolars of several studies are summarized in Table VIII together with the findings of the present study. Accessory canals were detected in 36% of the studied ûrst mandibular premolar that were mainly located in the apical third. Vertucci[17] also reported a high percentage (44.3%) of accessory canals. Regarding the apical delta, there was 6.06% of mandibular ûrst premolar observed with apical delta in this study which is similar to a study of Lu et al.[21] (6%) in a Chinese population.

Conclusion:

Observations of the current study provided some information about the internal anatomy of the mandibular ûrst premolar in Bangladeshi population. Such information helps Clinicians to achieve a satisfactory prognosis for root canal treatment.

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Viral Hepatitis in Pregnancy – A study of its Effect on Maternal and Foetal Outcome

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Abstract

Introduction: *Viral hepatitis alone is responsible for about 70% to 80% of all intrapartum jaundice. But the feto maternal outcome in viral hepatitis patients is yet to be discussed broadly in Bangladesh context. The present study was conducted to assess feto-maternal outcome in patients with viral hepatitis in pregnancy.*

Methods: *This was a cross sectional descriptive study conducted in the Department of Obstetrics & Gynecology, BSMMU during the period of September 2016 to February 2017. Total 30 pregnant women were included in this study who were diagnosed as viral hepatitis. All were selected according to purposive sampling. All the data regarding patients' demographic, clinical, biochemical, and outcome profiles were recorded through a semi structured data collection sheet. Data were compiled, edited and prepared in tabular and figure form. Categorical data were analyzed by chi square test. p value was determined as significant when it was <0.05.*

Results: *Out of 30 mothers 56.67% were from 20-25 years age group followed by 26.67% from 26-30 years age group. The mean age of mothers was 24.17±2.19 (age range: 19-36 years) 19(63.33%) had parity 2-4, 10(33.33%) had parity 0-1 and lastly 1(3.33%) had the parity >4. out of 30 mothers mostly were attacked by hepatitis E virus (76.67%). Among rest of the mothers 6.67%, 10%, 3.33% were attacked by Hepatitis A, B, E+A and B+E respectively. The last two claimed 3.33% patients each. 4(13.33%) expired finally and rest 26(86.66%) were being alive. Out of 30 patients 46.67% had PPH whereas 20% had DIC. 13.33% mothers suffered from septicemia, 10% and 6.67% mothers suffered from renal dysfunction and hepatic coma respectively.Out of 32(2 mothers gave birth twin babies) neonates, 34.37% had neonatal sepsis whereas 20% had neonatal jaundice. 27.58% babies required NICU admission 10% babies were still birth, 16.67% and 10% babies suffered from hypoglycemia and birth asphyxia respectively. Some neonates have multiple complications.*

Conclusion: *Viral hepatitis is not rare in our perspective. In most of the cases, hepatitis E virus is the main culprit for the disease. PPH, DIC, septicemia, renal dysfunction are the common maternal morbidity which can lead to a significant number of maternal mortality. Neonatal sepsis, jaundice, asphyxia may be the significant perinatal complications in spite of all standard medical treatment.*

Keywords: *Viral hepatitis, Maternal Outcome, Foetal Outcome*

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Introduction:

Viral hepatitis is reported to be the most common form of liver disease in pregnancy.[1] Hepatitis and pregnancy is a deadly combination. Hepatitis requires early diagnosis and careful monitoring. Viral hepatitis is most prevalent in pregnancy among all the causes of hepatitis. Viral hepatitis alone is responsible for about 70% to 80% of all intrapartum jaundice. Incidence of hepatitis varies greatly around the world. In developed countries, the incidence is around 0.1% whereas in developing countries it can range from 3-20% or higher. There is no difference in the course of the disease in pregnant and non-pregnant women in developed countries. However, in developing countries, there is a higher incidence of maternal mortality with fulminant hepatitis.[2,3]

Clinical manifestations of all forms are almost similar. Fulminant type is more common in Hepatitis E, less common in Hepatitis C and rare in Hepatitis A. Unfortunately, ithas as high as 20% mortality in pregnant women.

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Women living in low socioeconomic groups are usually exposed to unhygienic environment and consume untreated, unpurified water. They are at a greater risk of development of the disease. Hepatitis A and E viral infection are water borne diseases and spreads by faeco-oral route. On the other hand, hepatitis B is spread through sexual contact, blood transfusion or exposure to an infected person's blood via cuts, open sores, needle sharing, razor sharing or ear piercing tools. Additionally, hepatitis B can be spread from mother to child. Formerly called non-A non-B hepatitis; hepatitis C is transmitted primarily by direct blood contact - via blood transfusion or contaminated needles. Less common ways are through sexual contact or from mother to child. Formerly called delta hepatitis, hepatitis D is found mainly in intravenous drug users who are carriers of the hepatitis B virus.

Pregnancy is generally considered to be an immuno-suppressed state; however, the impact of pregnancy on mothers with viral hepatitis and the impact of viral hepatitis on fetuses/infants are not the same for all types of hepatitis

Each type of Viral Hepatitis has its own concerns. Hepatitis A is a common cause of hepatitis transmitted by the faeco–oral route and does not influence the course of pregnancy. Hepatitis B, when acquired at or near delivery, is transmitted vertically as high as 60% of unborn children. This has grave consequences for the child as nearly 90% of these infections shall become chronic and develop Liver cirrhosis, Portal hypertension or Hepato-cellular Carcinoma in the child. Hepatitis C is well known to get transmitted vertically and the virus may lead to Hepato-cellular Carcinoma in the mother as well as the child. Hepatitis E, while remaining a self limited, usually benign, hepatic infection in men and non pregnant women, acquires a grave form in pregnant women. It shows an increased rate of infection in pregnancy. The incidence of Fulminant Hepatic Failure and mortality rate is much higher than that associated with other hepatic viral infections.[4,5,6]

The various maternal complications associated with viral hepatitis are preterm labour, obstetric haemorrhage, fulminant hepatitis, hepatic encephalopathy, renal failure, DIC and death. The various foetal complications are intrauterine death, prematurity and risk of vertically transmitting the hepatitis infection.[7,8]

HEV and HBV infections were most frequent cause of fulminant hepatic failure in pregnancy.[9,10,11] As far as developing countries like India is concerned, Hepatitis E is the most common cause of fulminant hepatic failure. Fulminant hepatitis was seen in high percentage in third trimester pregnant women with high maternal mortality ranging from 15%-45%.[12,13]

The risk of vertical transmission of hepatitis viruses is higher in pregnant women with acute versus chronic infection. In general, the risk is not increased with amniocentesis, fetal monitoring, or vaginal birth, and cesarean section should not be recommended to prevent transmission of hepatitis viruses. Breastfeeding is safe for women with chronic hepatitis B virus (HBV) or chronic hepatitis C virus (HCV) infections— unless they have cracked nipples.[14] Hepatitis A and B vaccines are safe to be administered during pregnancy.

Methods:

The study was carried out in department of obstetrics & gynaecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from September 2016 to February 2017. The research protocol was reviewed & approved by IRB of BSMMU on 25-06-2016. An approval number was collected (No. BSMMU/2016/5876). All participants (patients) included in the study were informed about the nature & purpose of the study. A written consent was obtained from each person included in the study.

Enrolment of patients were performed by following specific inclusion criteria:

Recent onset of jaundice in absence of any chronic liver disease or past history of jaundice. Patients with following characteristics were excluded from the study:

HELLP syndrome (Haemolysis, elevated liver enzymes, low platelet count), acute fatty liver of pregnancy and Intrahepatic cholestasis.

This was a cross sectional descriptive study. Total 30 pregnant women were included in this study who were diagnosed as viral hepatitis. All were selected according to purposive sampling. All the data regarding patient's demorgraphic, clinical, biochemical and outcome profiles were recorded through a semistructured data collection sheet. Data were compiled edited and prepared in tabular and figured form. Categorical data were analyzed by Chi Square test. P value was determined as significant when it was < 0.05.

Results:

Table I

Distribution of patients according to age (n=30)

Age group (in years)	No. of patients	Percentage
<20	1	3.33%
20 – 25	17	56.67%
26 – 30	8	26.67%
31 – 35	3	10%
>35	1	3.33%
Mean age ±SD	24.17±2.19	
Age in years	19 – 36	

Table-l shows that out of 30 mothers 56.67% were from 20-25 years age group followed by 26.67% from 26-30 years age group. The least number of mothers from <20 years and >35 years age each as 3.33%. Besides 31-35 years age group mothers claimed 10% of total sample size.

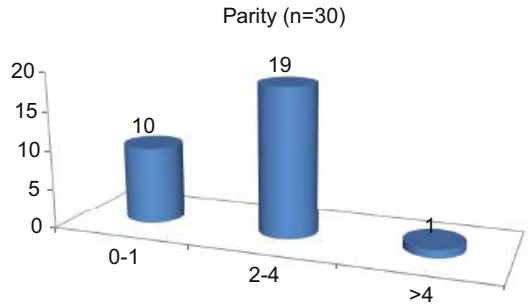

Figure-1: *Distribution of mothers according to parity (n=30)*

Figure-1 shows that out of 30 mothers maximum 19(63.33%) had parity 2-4, 10(33.33%) had parity 0-1 and lastly 1(3.33%) had the parity >4.

Table ll

Distribution of patients according to socioeconomic status (n=30)

	Number	Percentage
Low	12	40%
Middle	17	56.67%
High	1	3.33%

Table-ll shows the overall socioeconomic status of respondents where we can observe that 56.67%, 40% and 3.33% mothers economic status were middle class, poor class and upper class respectively. 36.67% mothers lived in semipacca/tin shed house whereas 33.33% mothers lived in pacca/brick built house. Rest 30% mothers lived in kantcha/mud built house.

Table lll

Distribution of patients according to gestational age (n=30)

Gestational age (in week)	No. of patients	Percentage
<28	5	16.67%
28 – 32	12	40%
33 – 37	11	36.67%
>37	2	6.67%
Mean gestational age (in week)	31.17±1.02	
Gestational age range (in week)	27 – 38	

Table-lll shows that out of 30 mothers, 40% presented at 28-32 weeks of gestational age. Among the rest 36.67%, 16.67% and 6.67% patients presented at 33-37, <28 and >37 weeks of gestational age respectively.

Table lV

Distribution of patients by specific type of hepatitis virus(n=30)

	Number	Percentage
HAV	2	6.66%
HBV	3	10%
HEV+HAV	1	3.33%
HCV	0	0%
HBV+HEV	1	3.33%
HEV	23	76.66%

Table-lV shows that out of 30 mothers mostly were attached by hepatitis E virus 23(76.67%). Among rest of the mothers 2(6.67%), 3(10%), 1(3.33%) were attacked by Hepatitis A, B, E+A and B+E respectively. The last two claimed 1(3.33%) patients each.

Table V

Distribution of patients according to maternal complications (n=30)

Maternal outcome	Number of patients	Percentage (%)
No complication	11	36.66%
Complication	19	63.33%
Acute renal failure	3	10%
Coagulation failure	14	46.67%
DIC	6	20%
Septicemia	4	13.33%
Hepatic coma	2	6.67%

*Same patient has multiple complications.

Table-V shows that 11(36.66%) had no complication and 19(63.33%) complications. 4(13.33%) mothers suffered from septicemia, 3(10%) and 2(6.67%) mothers suffered from acute renal failure and hepatic coma respectively.

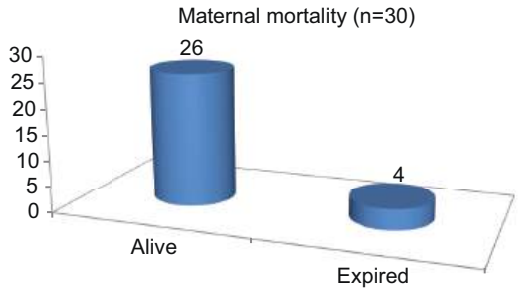

Figure-2: *Distribution of mothers according to maternal mortality (n=30)*

Figure-2 shows that out of 30 mothers 4(13.33%) expired finally and rest 26(86.66%) were being alive.

Table Vl

Distribution of mothers according to cause of maternal mortality (n=4)

Cause of Maternal Death	Number of Patients	Percentage (%)
PPH	2	50%
DIC	1	25%
Hepatic coma	1	25%

Table-Vl shows causes of maternal death- 2 (50%) were due to PPH, 1 (25%) was due to DIC and 1 (25%) was due to hepatic coma.

Table Vll

Distribution of neonates according to APGAR score (n=32)

APGAR score	Number of neonates	Percentage
In 1st minute (n=32)		
>7	19	59.37%
4 – 6	8	25%
<4	5	15.62%
At 5 minute (n=29)		
>7	21	72.41%
4 – 6	6	20.68%
<4	2	6.89%

*2 mothers gave birth twin babies.

Table-Vll shows that among 32 neonates 3(10%) were still birth which was fallen in <4 APGAR score maximum 19(59.37%) babies were found as APGAR score >7 in 1st minute which was 21(72.41%) in the same category after 5 minute. At 5 minute calculation 3(10% still birth were excluded 6(20.68%) and 2(6.89%) were categorized as 4-6 and <4 respectively. These 8(25%) babies were admitted in NICU.

Table Vlll

Distribution of babies according to admission (n=29)

Neonatal admission	Number of neonates	Percentage
No admission	13	44.82%
Admission in NICU	8	27.58%
Admission in neonatal ward	8	27.58%

*3 babies were still born; so total n=29 here.

Table-Vlll shows that out of 29 alive babies, 13(44.82%) required no admission whereas 8(27.58%) required NICU and neonatal ward admission each.

Table lX

Distribution of fetus according to outcome (n=32)

Fetal outcome	Frequency (%) (n=32)*
Neonatal sepsis	11 (34.37%)
Neonatal jaundice	6 (20%)
Birth asphyxia	3 (10%)
Hypoglycemia	5 (16.67%)
Required NICU	8 (26.67%)
Still birth	3 (10%)

*2 mothers gave birth twin babies.

Table lX shows that out of 32 babies neonatal sepsis were in 11 (34.37%), neonatal jaundice were in 6 (20%), birth asphyxia were in 3 (10%), hypoglycemia were in 5 (16.67%), NICU were required in 8 (26.67%) and still birth were in 3 (10%).

Table X

Distribution of neonates according to outcome (n=32)

Neonatal outcome	Number of neonates	Percentage
Liver birth	29	90.62%
Take home alive	28	96.55%
Early Neonatal Death	1	3.44%
Still birth	3	10.34%

Table-X shows that out of 32 babies, 28 were discharged and also some of them were discharged from neonatal ward and NICU also 1 died in NICU and 3 were still born.

Discussion:

In our study, 18(60%) mothers' age was < 25 years which was almost similar with the report of Acharya N et al from India in 2013.[15] The mean age was 24.17±2.19 years (age range was 19-36 years). It is very much nearer to the report of a previous study where the mean age was 26.03±2.73 year.[16]

33% of our mothers presented with parity 0-1 and 63.33% mothers were presented with parity 2-4. Our findings are agreed by Qumrunnahar et al.[17] Our maximum 56.57% mothers came from middle class family followed by 40% from poor class. These findings are also agreed by Qumrunnahar et al.[17]

The mean gestational age in our research was determined as 31.17±1.02 years. It was also very nearer to that of previous study.[16] The responsible causative agent in viral hepatitis was mostly HEV claimed 76.67%. Besides Hepatitis A,B,E+A, C, B+V are responsible for very negligible number. The study of Acharya N et al also revealed the similar results.[15]

As reported by Simms HF et al the vertical transmission rate with HbeAg+ve and HBeAb -ve is as high as 90%,whereas if patient is HbeAb+ve the vertical transmission reduces to 10%.The risk of vertical transmission to the fetus is directly proportional to HBV-DNA viral load.[18]

Our study did not have a single case of HCV infection. Though the reported incidence is being rare; it is rising in developed countries like USA.

Simms H F et al studied the course of viral hepatitis in pregnancy and concluded that its course is unaltered in pregnancy, except in cases of HEV infected cases, in which cases hepatitis has more fulminant course.[18]

In our study, Hepatitis E was found to be the main causative organism responsible for Hepatitis in 76.67% pregnant women. This figure was higher than that reported by other authors from India, except Khuroo et al who have reported the rate of HEV infection amongst pregnant women as 86%.[19] Studies done from North India have revealed widely varying rates of Hepatitis E infection ranging from 32% to 86%.[4]

The maternal mortality in our study was 13.33% which was not very low. Sweta Sahai et al reported 19% maternal mortality due to viral hepatitis.[20]

The high mortality rate was comparable to most of the other studies conducted in North India, ranging from 12% to 64%. This finding is different from certain other studies done in other parts of the world, e.g. a study from Egypt revealed a very high rate of Hepatitis E infection (84.3%), but there was not a single case of maternal mortality.[21] Similarly, a study carried out in South India showed a very high infection rate with Hepatitis E but the mortality rate was very low – only 3.4%. The high incidence of Hepatitis E IgG antibody was probably protective in Egypt and South India. The sero-positive of Hepatitis E IgG antibody was found to be low (33.67%) in New Delhi by Begum et al, probably leading to higher rates of clinical disease and maternal mortality.[22]

In our study, 11(36.66%) mothers had no complication and 19(63.33%) mothers had complications. Among them 4(13.33%) mothers suffered from septicemia, 3(10%) and 2(6.67%) mothers suffered from acute renal failure and hepatic coma respectively and 4(13.33%) mothers expired finally. Two maternal deaths were due to PPH and one was due to DIC and another was due to hepatic coma. Two mothers gave birth of twin babies. Perinatal outcome was observed among 32 babies. 10% neonatal mortality was found of which all were still born. Acharya N et al in their study revealed 16.6% babies died in the same ways.[15] Besides, neonatal jaundice, neonatal sepsis, birth asphyxia were the significant complications we observed. Our 27.58% babies' required ICU to save lives.

Conclusion:

Global prevalence of Viral hepatitis is high and is rising. It can profoundly affect pregnant women causing significant maternal and perinatal morbidity and mortality. Viral hepatitis is not rare in our perspective. In most of the cases, hepatitis E virus is the main culprit for the disease. PPH, DIC, septicemia, renal dysfunction are the common maternal morbidity which can lead to a significant number of maternal mortality. Neonatal sepsis, jaundice, asphyxia may be the significant perinatal complications in spite of all standard medical treatment. Multidisciplinary care including obstetrics, fetomaternal medicine, hepatology and pediatrics is crucial for optimizing outcomes for both mother and child.

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ORIGINAL ARTICLE

Sociodemographic Characteristics at Baseline in a Randomized Control Trial Among csDMARD Treated Rheumatoid Arthritis Patients at BSMMU

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Abstract

Introduction: The incidence of Rheumatoid Arthritis is rising. In females between the ages of 25 and 55, it was more prevalent. The aim of the study was to examine the sociodemographic characteristics of patients with rheumatoid arthritis who received csDMARD treatment in a randomized clinical trial.

Methods: The Rheumatology Rehabilitation Clinic of the Department of Physical Medicine and Rehabilitation at BSMMU collaborated with the Department of Pharmacology to conduct this study, which was a randomized, double-blind, placebo-controlled trial. A total of 52 RA participants who were included in the study's baseline were eligible for analysis. 23 patients with csDMARDs were in the placebo group while 29 patients with csDMARD were included in the intervention group.

Results: A total of 52 patients of which most of the patients were between 29 to 58 years of age in both the placebo and intervention groups. Among them in the placebo arm, 30.4% in the 29-38, 13.04% in the 39-48 and 39.1% in the 49-58 age group. In the intervention arm, 31.03% in the 29-38, 41.4% in the 39-48, and 13.8% in the 49-58 age group. The mean age and SD of the patients in the intervention arm were 41.93 ± 11.26 and 47.83 ± 10.70 in the placebo arm respectively. There was no statistically significant difference between the two groups (p = 0.06). In the placebo arm, 4.35% of patients were male, which were 6.90% in the intervention arm respectively. Whereas, 95.65% of patients were female in the placebo arm, and 93.10% in the intervention arm (p = 0.70).

Conclusion: This study showed that most of the participants were adult females.

Keywords: Rheumatoid arthritis, csDMARD, Inflammatory arthritis

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Introduction:

Rheumatoid Arthritis (RA) is inflammatory arthritis and the main cause of disability. It is a symmetric Polyarticular arthritis affects the small diarthrodial joints of the hands and feet.[1] Incidence and prevalence research on RA indicate that the disease's occurrence in different populations varies significantly. The worldwide prevalence of Rheumatoid arthritis is 0.5-1%.[2] Its prevalence in Bangladesh is 1.6%.[3] Rheumatoid arthritis (RA) is two- to three-fold higher in women than men.[4] The incidence of RA started to increase in the last decade following a 4-decade period in which the prevalence fell and it only affects women[5]. The incidence of RA increases between 25 and 55 years of age, thereafter it reaches a plateau until age 75, after which it starts to decline.[6] Rheumatoid arthritis can be caused by both genetic and environmental factors.[7]

The effectiveness of treatment was affected by smoking, age, comorbidity status, educational level, and duration of rheumatoid arthritis. It is also important to increase patient compliance with treatment and reduce treatment-related risks. and advise people on how to take care of their illnesses and treatments.[8]

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The quality of life of RA patients is affected by daily pain, stiffness, exhaustion, and physical impairment, regardless of treatment. The goal of the present research was to examine the sociodemographic characteristics of patients with rheumatoid arthritis who received csDMARD treatment in a randomized clinical trial.

Methods:

This research was double-blind, randomized, and placebo-controlled. Between March 2020 and January 2022, it was done at the Bangabandhu Sheikh Mujib Medical University (BSMMU) between the Department of Physical Medicine and Rehabilitation and the Department of Pharmacology**.**

According to the 2010 ACR/EULAR criteria for Rheumatoid Arthritis, the study was conducted on individuals with Rheumatoid Arthritis. The clinical trial (BSMMU/2021/3958) was approved by the ethical committee and registered on www.clinicaltrials.gov with the identifier NCT05078502. All study participants gave written consent after being fully informed. Patients who met the 2010 ACR/EULAR criteria for rheumatoid arthritis, were at least 18 years old and were of both sexes, were included in the study.[9] The Questionnaire for Socio-Demographic Data was used to evaluate the patients. All the patients diagnosed as RA according to 2010 ACR/EULAR criteria by a competent Physiatrist were recruited in this study. The inclusion and exclusion criteria were applied to the assessment of all the recruited patients. Patients were also made aware that participation was entirely voluntary. They had the freedom to withdraw or refuse at any stage without compromising their medical care. Only patients who were convinced and gave their written consent after receiving an adequate explanation participated in the trial. The Patients who were enrolled after giving informed written consent were treated with csDMARD. Microsoft Office Excel 2007 was used to conduct the statistical analysis. To determine the relationship between the intervention and the placebo arm, a chi-squared test was used for categorical variables. An unpaired t-test was used to compare the mean age of the participants in the placebo arm and that of the participants in the intervention arm. p- values below 0.05 were considered to be significant.

Results:

fifty-two (52) patients were examined and evaluated. Table I shows that most of the patients were between 29 to 58 years of age in both the placebo and intervention groups. Among them in the placebo arm, 30.4% in the 29-38 age group, 13.04% in the 39-48 and 39.1% in the 49-58 age group. In the intervention arm, 31.03% in the 29-38 age group, 41.4% in the 39-48 and 13.8% in the 49-58 age group.

Table II demonstrates that the mean age and SD of the patients in the intervention arm were 41.93 ± 11.26 and 47.83 ± 10.70 in the placebo arm respectively. The two groups had no statistically significant difference (p = 0.06).

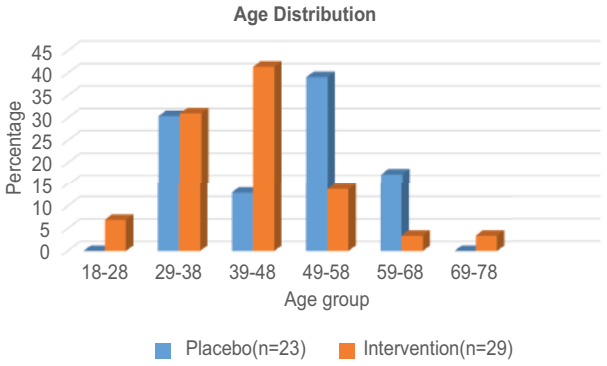

Fig.-1: *Distribution of the participants according to age group*

Table I

Demographic characteristics of the patients (n=52) at baseline

Age Group	Placebo (23)	Placebo (%)	Intervention (29)	Intervention (%)
18-28	0	0	2	6.9
29-38	7	30.4	9	31.03
39-48	3	13.04	12	41.4
49-58	9	39.1	4	13.8
59-68	4	17.4	1	3.4
69-78	0	0	1	3.4

Table II

Demographic characteristics of the patients (n=52) at baseline

Variables	Placebo[a] (n=23)	Intervention[b] (n=29)	P - value
Age (years)			
Mean ± SD	47.83 ± 10.70	41.93 ± 11.26	0.06[x]
Range, 95% CI	43.20-52.45	37.65-46.21	

x Unpaired t-test was done

Table III shows, that in the placebo arm, 4.35% of patients were male, which was 6.90% in the intervention arm. Whereas, 95.65% of patients were female in the placebo arm, which was 93.10% in the intervention arm (p = 0.70).

Table III

Demographic characteristics of the patients (n=52) at baseline

Variables	Placebo[a](n=23)	Intervention[b](n=29)	P - value
Gender			
Male	1(4.35%)	2(6.90%)	0.70[z]
Female	22(95.65%)	27(93.10%)	
Habitat			
Urban	10(43.48%)	16(55.17%)	0.40[z]
Rural	13(56.52%)	13(44.83%)	
Educational Status			
Illiterate	7(30.43%)	5(17.24%)	0.15[z]
Primary level	4(17.39%)	9(31.03%)	
Secondary level	10(43.47%)	8(27.59%)	
Higher Secondary level	0(0%)	5(17.24%)	
Graduation level	2(8.70%)	1(3.45%)	
Post-Graduation level	0(0%)	1(3.45%)	
Occupation			
Student	0(0%)	2(6.90%)	0.57[z]
Housewife	20(86.96%)	24(82.76%)	
Service Holder	1(4.35%)	0(0%)	
Retired	0(0%)	0(0%)	
Others	2(8.70%)	3(10.34%)	
Duration of Disease			
0.5-5 year	17(73.91%)	20(68.97%)	0.70[z]
>5-10 year	6(26.09%)	9(31.03%)	
BMI (kg/m^2) at baseline			
Underweight	5(21.74%)	2(6.90%)	0.13[z]
Normal	5(21.74%)	15(51.72%)	
Overweight	12(52.17%)	11(37.93%)	
Obese	1(4.35%)	1(3.44%)	
Family History			
Yes	1(4.35%)	5(17.24%)	0.15[z]
No	22(95.65%)	24(82.76%)	

z Chi-square (X^2) test was done

In the placebo arm, 43.48% of patients were from the urban area whereas, 56.52% of patients in the placebo arm were from the rural area. Regarding the educational status in the placebo arm, 30.43% of patients were illiterate, 17.39% were at the primary level, 43.47% were secondary level and 8.70% were graduation level. In the placebo arm, 86.96% of patients were housewives, 4.35% were service holders and 8.70% were in the other group. The duration of disease in the placebo arm was 73.91% in the 0.5 to 5-year group, and 26.09% was in the >5 to 10-year group. The BMI status in the placebo arm, 21.74% of patients were underweight, 21.74% were normal, 52.17% were overweight and 4.35% were obese. In the placebo arm, 4.35% of patients had a positive family history and 95.65% had no family history of Rheumatoid Arthritis.

In the intervention arm, 55.17% lived in urban areas, whereas 44.83% in rural areas. 17.24% of patients were illiterate, 31.03% were at the primary level, 27.59% were secondary level, 17.24% were at the higher secondary level, 3.45% were at the graduation level and 3.45% were at the post-graduation level. Regarding occupation, in the intervention arm, 6.90% of patients were students, 82.76% were housewives and 10.34% were in the other group. 68.97% were in the 0.5 to 5-year group and 31.03% were in the >5 to 10-year group in the intervention arm. the intervention arm, 6.90% of patients were underweight, 51.72% were normal, 37.93% were overweight and 3.44% were obese. In the intervention arm, 17.24% of patients had a positive family history and 82.76% had no family history of Rheumatoid Arthritis

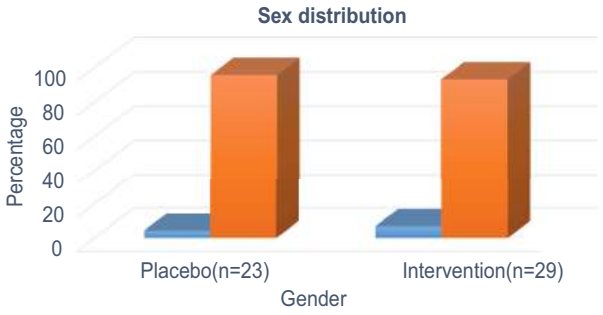

Fig.-2: *Distribution of the participants according to sex*

Discussion:

The present study showed that most of the patients were between 29 to 58 years of age in both the placebo and intervention groups. Among them in the intervention arm, 31.03% in the 29-38 age group, 41.4% in the 39-48 and 13.8% in the 49-58 age group. In the placebo arm, 30.4% in the 29-38 age group, 13.04% in the 39-48 and 39.1% in the 49-58 age group. The mean age and SD of the patients were 47.83 ± 10.70 in the placebo arm and in the intervention arm were 41.93 ± 11.26 respectively. The two groups had no statistically significant difference (p = 0.06). These findings are similar to another study.[10] In that study, the mean age of the study was 49 years.

In the placebo arm, 4.35% of patients were male, which were 6.90% in the intervention arm respectively. Whereas, 95.65% of patients were female in the placebo arm, and 93.10% in the intervention arm (p = 0.70). This result was similar to another study where the majority of patients were female (76.3%).[10] However, the study design was different.

Another study showed the mean age of the participants was 56 and 58 years in two groups and 19% of the women reached the university level compared to 12% of the men.[11] In comparison to our study, where 43.47% of participants had secondary-level education in the placebo arm, 31.03% had primary-level education in the intervention arm. The design of the study was different from my study.

The above-mentioned sociodemographic factors of the study reiterated that some similarities were found in different populations compared to the Bangladeshi population.

Study Limitation

A small size was the main limitation of our study.

Conclusion:

Rheumatoid arthritis is more common in adult women, which was reflected in this study. A larger study will be helpful to more clearly reflect other sociodemographic characteristics of Rheumatoid Arthritis patients in our country.

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REVIEW ARTICLE

Use of Methotrexate in Osteoarthritis of Knee: Review Article

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Abstract

Osteoarthritis (OA) is accepted as a major public health problem. It is one of the major causes of impaired function that reduces quality of life (QOL) worldwide. It's a very common disorder affecting the joint cartilage. The molecular basis of osteoarthritis has been generally accepted; however, the exact pathogenesis is still not known. Management of patients with osteoarthritis involves a comprehensive history, thorough physical examination and appropriate radio logical investigation. There is no cure for this disease despite the availability of a large number of therapeutic options, including non-pharmacological, pharmacological and surgical treatments. In this review, we look at a variety of theories to help us understand how methotrexate works to treat OA. Methotrexate (MTX) is widely used in the treatment of all inflammatory rheumatic diseases, where it seems to act primarily through a mechanism to reduce inflammation. Imaging studies have established that synovitis is common in OA, supporting the suggestion that inflammation may be important in both peripheral nociception and response to anti-inflammatory treatment. Accordingly, the aim of this review was to explore the efficacy of MTX in decreasing pain and inflammation in symptomatic knee OA.

Keywords: Osteoarthritis, Knee pain, MTX

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Introduction:

Osteoarthritis (OA) is a progressive complex, multifactorial disease that affects all joint structures, with patients classified as heterogeneous groups, exhibiting varying degrees of inflammation, in some cases comparable with rheumatoid arthritis. The precise aetiology remains unclear.[1] Inflammation has been implicated in the pathogenesis of OA and may be either a primary event or secondary to other aspects of the disease, such as biochemical changes within the cartilage.[1-3] Synovial inflammation and proliferation is a key component of OA and a predictor of worsening disease. Synovial inflammation due to the release of prostaglandins and cytokines is an important cause of pain.[3-5] Knee pain, the leading symptom of knee OA, is often chronic, leading to significant morbidity and disability.[1]

Thus, for clinical management, pain reduction and functional improvement are of utmost importance in the treatment of knee OA. Treatments offer limited symptomatic effect and are associated with significant side effects. There is no cure for this disease despite the availability of a large number of therapeutic options.[6] Primary treatment approaches for knee OA have centered on lifestyle modifications, analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs), and intra-articular corticosteroid or hyaluronic acid injections, there remains an ongoing need for disease-modifying interventions that can alter the disease's progression, especially in inflammatory subsets of OA.[7] Methotrexate (MTX) is widely used in the treatment of all inflammatory rheumatic diseases, where it seems to act primarily through a mechanism to reduce inflammation.[7] Imaging studies have established that synovitis is common in OA, supporting the suggestion that inflammation may be important in both peripheral nociception and response to anti-inflammatory treatment.[8] Accordingly, the aim of this study was to

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assess the efficacy of MTX in decreasing pain and inflammation in symptomatic knee OA.

Methods:
We systematically searched to identify published articles on use of Methotrexate (MTX) in Knee osteoarthritis at the national and international level using the search engine google, google scholar, PubMed, Med Facts, BanglaJol by using the different sets of keywords.

Aetiology:
OA is a complex disorder with multiple risk factors. These include both generalized constitutional factors (age, female sex, obesity, family history) and local adverse mechanical factors (trauma, occupational and recreational wear, malalignment, generalised laxity.[9-10] There is a significant genetic component to the prevalence of knee OA, but the exact gene responsible is unknown. Classic twin studies have revealed that the influence of genetic factors is between 39% and 65% in radiographic OA of the hand and knee in women.[11]

Pharmacology and Mechanism of Action of Methotrexate:
Methotrexate is a folate antagonist that inhibits dihydrofolate reductase (DHFR), an enzyme crucial for the synthesis of purines and thymidylates, which are necessary for DNA replication and cell division. Its immunosuppressive properties arises from its ability to reduce the proliferation of activated immune cells, particularly T lymphocytes and macrophages, which play a central role in the inflammatory processes of diseases like rheumatoid arthritis.[12-13]

While methotrexate's primary role in diseases like rheumatoid arthritis and psoriasis is through immune modulation, its potential in OA likely stems from its ability to reduce the inflammatory processes that exacerbate cartilage breakdown and pain. OA patients may exhibit synovial inflammation, which can contribute to pain and disease progression.[14] Methotrexate has been shown to reduce the infiltration of inflammatory cells in the synovium, specifically macrophages and T lymphocytes, which are known to contribute to the inflammatory microenvironment of OA.[14] Methotrexate may also inhibit the activity of matrix metalloproteinases (MMPs), enzymes responsible for the degradation of cartilage and extracellular matrix components.[14] This would help reduce the breakdown of articular cartilage, a hallmark of OA. Methotrexate has been shown to decrease the levels of pro-inflammatory cytokines such as TNF-á and interleukins (IL-1, IL-6), which are implicated in cartilage degradation and synovial inflammation in OA.[14]

Clinical Evidence Supporting Methotrexate in Knee Osteoarthritis:
The use of methotrexate in OA has been an area of growing interest in the last two decades, with several studies assessing its effects in knee OA, both alone and in combination with other agents. However, the clinical evidence remains mixed, with some studies suggesting benefit and others showing limited or no effect.

1. **Early Clinical Trials:** Early studies have focused on the effects of MTX on synovial inflammation in OA. A study by *Gossec et al. (2008)* indicated that MTX could reduce synovial membrane thickness and inflammation in OA patients, suggesting that its anti-inflammatory effects might help alleviate symptoms in cases where inflammation is a predominant feature.[15]
2. **Randomized Placebo Controlled Trials:** A notable RCT conducted by Abou-Raya A et al. 2014 investigated the efficacy of MTX in patients with symptomatic knee OA. The trial included 144 patients with primary knee OA, then randomised in a 1:1 ratio to receive up to 25 mg/week oral MTX (n=72) or placebo (n=72) for 28 weeks. Outcome measures included reduction in pain and inflammation and improvements in physical function scores. Pain was assessed using the visual analogue pain scale, (VAS, 0–100 mm). Functional assessment was performed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and activities of daily living (ADL) scores. Synovitis was detected clinically and by ultrasound imaging at baseline and at the end of the study significantly improved pain scores and functional outcomes compared to placebo. This study suggested that methotrexate might be beneficial in reducing pain and improving joint function in patients with inflammatory OA.[16]
3. **Open label study:** A open-label study of Claire Y. J. Wenham et.al 2013 evaluated that oral MTX for painful knee OA using modern dosing (7.5-15mg/weekly) demonstrated a high proportion of participants with important reduction in pain, comparable to that achieved with commonly used NSAIDs and also comparable to the mean pain reduction achieved with opioids. The participants in this study had inadequate analgesia or side effects from either NSAIDs or opioids; therefore, MTX has demonstrated analgesic effect for people with at least moderate OA knee pain who are refractory to traditional analgesics.[17]

4. **Combination Therapy:** Some studies have also evaluated methotrexate in combination with other therapeutic agents, such as biologics or intra-articular corticosteroids. A study by *Mediati et al. (2016)* found that MTX combined with intra-articular corticosteroid injections led to better pain relief and improved function in knee OA patients than corticosteroids alone, particularly in those with evidence of synovitis.[18]
5. **Safety and Long-Term Outcomes:** Long-term studies on the use of methotrexate in OA are still limited. However, available data do not indicate any major safety concerns when methotrexate is used in low doses. The most commonly reported side effects include gastrointestinal disturbances (nausea, vomiting), mild liver enzyme elevations, and occasional bone marrow suppression. These adverse effects are generally manageable with careful monitoring, particularly in patients with pre-existing liver or renal conditions.

Benefits of Methotrexate in Knee OA:

Studies suggest that MTX significantly reduced pain and improved synovitis. There was a significant improvement in physical function. MTX may be a therapeutic option in the treatment of pain and inflammation related to knee OA. This is particularly evident in those with moderate to severe symptoms who are not adequately managed with conventional analgesics and anti-inflammatory drugs. In patients with inflammatory features of OA, methotrexate may potentially slow disease progression by reducing inflammation and cartilage breakdown, providing a degree of disease modification, something that current therapies do not offer.[19] When used at low doses (7.5–15 mg/week), methotrexate is generally well tolerated with a low incidence of severe side effects, making it a viable option for long-term use in elderly patients who are commonly affected by OA.[19]

Safety Considerations and Side Effects:

Methotrexate is associated with several potential side effects, although they are rare at low doses.[20-21] Common side effects include gastrointestinal disturbances (nausea, diarrhea), mild liver enzyme elevations, and leukopenia. Serious adverse events such as liver toxicity, pulmonary toxicity, and bone marrow suppression are rare but require careful monitoring, especially in elderly patients with comorbidities.[20-21] In clinical practice, methotrexate therapy should be closely monitored with regular blood tests (liver function, renal function, complete blood count) and periodic assessments for gastrointestinal side effects. It is contraindicated in pregnant women and individuals with active liver disease or renal insufficiency.[22]

Conclusion and Future Directions:

Methotrexate represents a promising option for the management of knee OA, particularly in patients with an inflammatory component. While the clinical evidence is still evolving, current studies suggest that MTX may provide significant benefits in terms of pain relief, functional improvement, and potentially modifying disease progression in knee OA.

However, further large-scale, well-designed randomized controlled trials are necessary to better define the role of methotrexate in OA, to determine optimal dosing regimens, and to assess long-term outcomes. Additionally, research into biomarkers that can identify patients most likely to benefit from MTX will be crucial in personalizing treatment approaches for OA.

In summary, methotrexate holds potential as an adjunctive therapy in the management of knee osteoarthritis, especially in those with synovial inflammation or inflammatory markers. As more data emerge, MTX may become an integral part of the treatment for knee OA, particularly for those with more complex and inflammatory forms of the disease.

This review summarizes the current evidence on methotrexate as a potential treatment for knee osteoarthritis and highlights areas where future research is needed to establish its place in clinical practice.

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CASE REPORT

Adrenal insufficiency due to Bilateral Adrenal Adenocarcinoma: Case Report

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Abstract

Addison's disease due to bilateral adrenal adenocarcinoma is an exceptionally rare condition. A 65-years-old male patient presented with symptoms and signs of adrenal crisis. Primary adrenal insufficiency was confirmed based on clinical findings and diagnostic criteria. While looking for aetiology, radiological imaging revealed bilateral adrenal mass and fine needle aspiration cytology confirmed adenocarcinoma. The patient was managed initially with supportive therapies and corticosteroid replacement, which led to significant clinical improvement. After stabilisation, further investigations were carried out, and the patient has been sent to oncology for specilaised management. Long term steroid hormone replacement was prescribed to alleviate symptoms and improve quality of life.

Keywords: Primary adrenal insufficiency, Adrenal malignancy, Addison's disease, Adrenal mass

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Introduction:

Addison's disease, the primary adrenal insufficiency (PAI), was first described in 1855 by Addison, a British surgeon.[1] PAI is characterised by inadequate production of glucocorticoids and mineralocorticoids, resulting in gradual onset of symptoms, unless complicated by an acute adrenal crisis.[2] The clinical presentation varies and may include symptoms such as dizziness upon standing, fatigue, and, in severe cases, life-threatening adrenal crisis if not recognised and treated promptly.[3] Early diagnosis and treatment with corticosteroids are lifesaving, often producing a dramatic response.[4] Addison's has multiple aetiologies, with autoimmunity and tuberculosis being the most common. Malignancies had been reported as a cause, although, they were usually metastatic and unilateral.[5]

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Case Presentation:

In October 2024, a 65-years-old man presented with two-day history of nausea, vomiting and abdominal pain. He reported six episodes of bile-stained, non-bloody vomiting, with persistent nausea. The abdominal pain was diffuse, non-radiating, colicky, and gradually worsening. Both symptoms had no relation with food.

For the past four months, the patient experienced fatigue and dizziness upon standing, which escalated to mild confusion upon admission. Furthermore, he reported blackening of the skin, involving palms, soles, lips, mouth, and knuckles, which had developed for same duration without any itching, pain, or photosensitivity. During this time, he had lost 8 kg weight, associated with loss of appetite. But he did not complain of any fever, night sweats, abdominal symptoms, or white patches on skin. Bowel and bladder habits were normal.

Past medical history included an ischaemic stroke 7 months prior, resulting in left sided weakness. However, the recent generalised fatigue was different from that. He had about 20-pack -year smoking history. Aspirin and Statins were given for long term for secondary prevention of stroke, both of which were well tolerated. He denied any history of steroid use or herbal intake, recent surgery, infections, or significant stress.

Physical examination revealed a lethargic man with signs of dehydration. Blood pressure was 80/50 mmHg on admission, with a weak thready rapid pulse. Skin hyperpigmentation, digital clubbing, mild anaemia and mild muscle wasting were noted, shown in Figure 2. He had dryness, fissuring and pigmentation on dorsal surface of the tongue. Systemic examination was otherwise unremarkable.

The primary differential diagnosis was adrenal crisis with primary adrenal insufficiency (PAI), which accounted for the symptoms discussed above. Shock could be another differential favoured by hypotension and rapid thready pulse but was deemed less likely. Suspecting adrenal crisis, patient was stabilised with intravenous fluid and hydrocortisone. Then serum electrolytes, cortisol level, ACTH (Adrenocorticotropic hormone) level, complete blood count, serum creatinine, random blood sugar, and serum thyroid levels were sent. To exclude infection, blood culture-sensitivity, urine culture-sensitivity, C-reactive protein (CRP) and montaux test for tuberculosis were sent.

Results revealed very low cortisol level in the morning and evening sample and markedly elevated baseline ACTH level. Hyponatraemia was present, but potassium levels were normal at admission. ESR (Erythrocyte sedimentation rate) and CRP were high, but cultures and tuberculosis tests were negative. He had mild anaemia and normal renal function tests. All the positive findings of initial work up are shown in table 1.

Initial investigation confirmed primary adrenal insufficiency, with a negative infection panel. So, to identify the aetiology, when the patient was stabilised, imaging studies were conducted. A chest X-ray was unremarkable. Next Computed Tomography (CT) of abdomen was carried out. CT abdomen had an impression of bilateral adrenal mass, described as "both adrenal glands are enlarged showing strong enhancement, right about 33 x 28 mm & left about 26 x 18 mm in size." Having found that, fine needle aspiration cytology (FNAC) was done, which confirmed adrenal cortical adenocarcinoma.

Table I

Findings of initial workup during adrenal crisis

Initial Blood Profile	Result	Normal Range
Sodium	**118** mmol/L	136-145 mmol/L
Potassium	3.8 mmol/L	3.5-145 mmol/L
Chloride	85 mmol/L	98-107 mmol/L
Sr. Creatinine	1.0 mg/dL	0.6-1.3 mg/dL
Sr. Cholesterol	**110** mg/dL	150-220 mg/dL
Sr. Cortisol (Evening)	**2.34** ug/dL	2.5 to 12.5 ug/dL (Evening)
Sr. Cortisol (Morning)	**4.1** ug/dL	6.4 to 22.8 ug/dL (Morning)
Sr. ACTH	**867.29** pg/ml	5-60 pg/mL
Short synacthen test	**Positive**	-
Haemoglobin	**11.1** g/dL	13-17 g/dL
Erythrocyte Sedimentation Rate (ESR)	**80** mm in 1st hour	0-10 mm in 1st hour
CRP	**36.5** mg/L	< 6 mg/L
Blood culture	Negative	-
Urine culture	Negative	-
Spiral CT scan of KUB	**Bilateral adrenal mass**	
FNAC Report	**Malignant neoplasm of adrenal glands favouring adrenal cortical adenocarcinoma**	

Since admission, patient was given steroid replacement with hydrocortisone. Initially empirical antibiotics were started to address any potential infectious triggers. Aspirin was temporarily withheld. Patient had postural hypotension, recorded several times. Hypotension and hyponatraemia were corrected with intravenous normal saline and oral sodium chloride. After admission, patient had more episodes of vomiting which resulted in hypokalaemia, which were corrected with ondansetron and potassium supplements.

Management involved medicine specialists, endocrinologists, and radiologists. With ongoing steroid replacement, the patient was referred to oncologists for further evaluation and management.

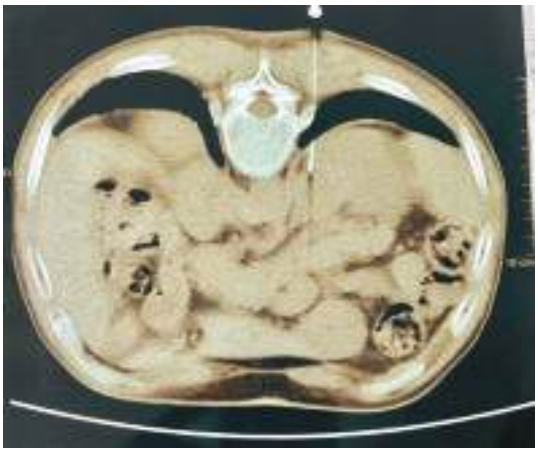

Figure 1: *Computed tomography showing bilateral adrenal mass*

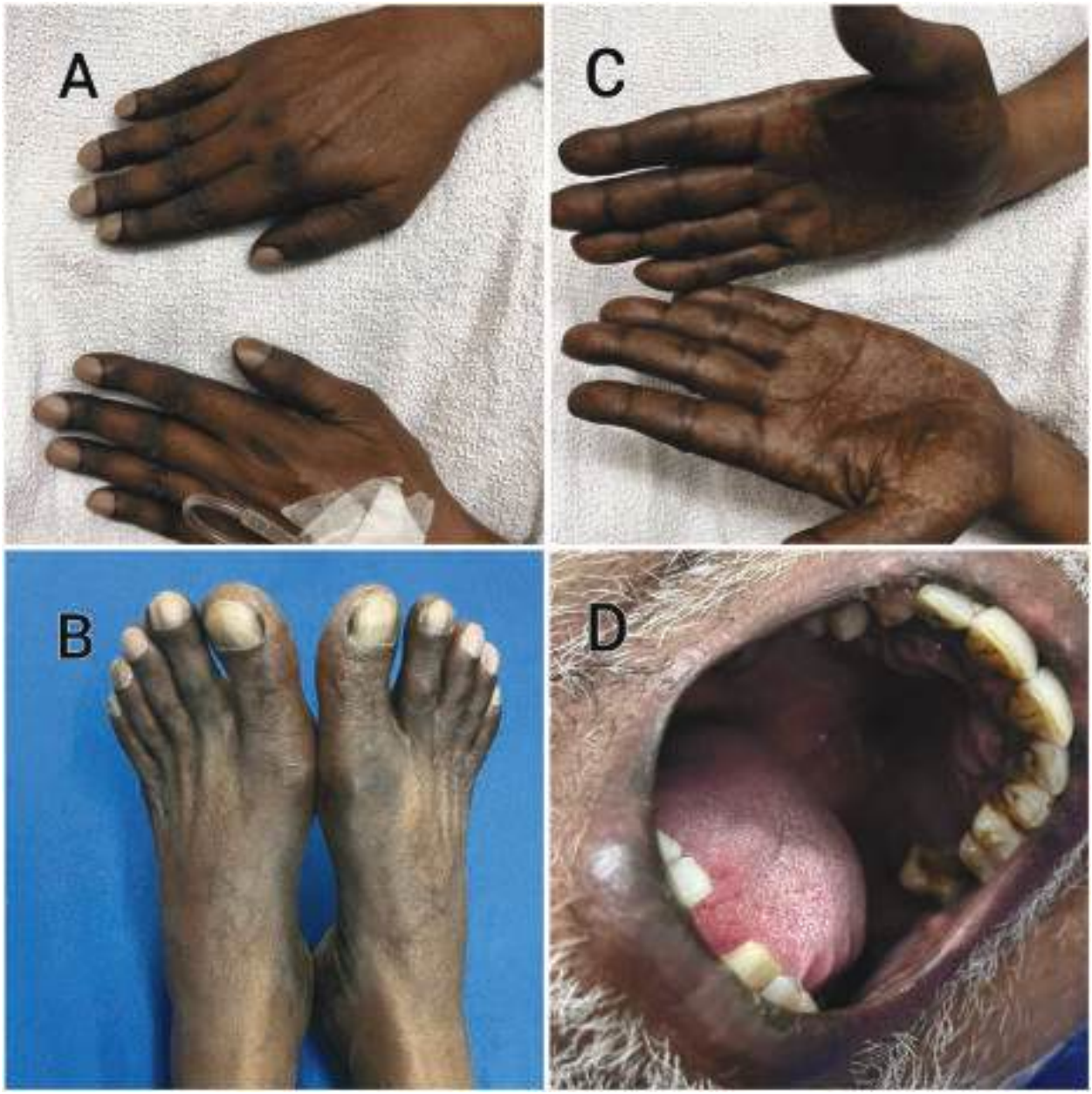

Figure 2: *Legends: Hyperpigmentation of the skin due to primary adrenal insufficiency: A. Hyperpigmentation on dorsum of the hands, over the metacarpophalangeal and interphalangeal joints, finger clubbing, nail pallor, mild muscle wasting; B. Hyperpigmentation on dorsum of the feet, over the the metatarsophalangeal and interphalangeal joints, toe clubbing, nail pallor, muscle wasting; C. Diffuse hyperpigmentation on both palms; D. Hyperpigmentation on hard palate (consent has been taken before taking pictures)*

Discussion:

Patients with Primary Adrenal insufficiency (PAI) who develop adrenal crisis usually present with sudden onset nausea, vomiting, abdominal pain, confusion, dehydration, hypotension, hypoglycaemia, hyponatraemia, and hyperkalaemia.[6] All these features were present in this case, but potassium levels were not elevated due to vomiting. In the hospital, vomiting episodes led to further hypokalaemia. Common aetiologies of adrenal crisis are steroid withdrawal, infections, and stress.[7] None of them were present in the history, and infection markers were negative.

Patient had been suffering from PAI for earlier several months, as suggested by symptoms as such fatigue, dizziness upon standing, postural hypotension,

hyperpigmentation, and weight loss. In clinical practice PAI is diagnosed based on low cortisol levels in early morning samples (< 6.4 ug/dL), high basal plasma ACTH level (> 60 pg/mL) and a positive short synacthen test.[8] The levels in this patient have met the diagnostic criteria.

The most common cause of PAI or Addison's disease is autoimmunity, due to formation of autoantibodies against 21-hydroxylase.[9] However, no signs of polyglandular syndromes or coexisting autoimmune diseases have been observed in this patient. The second most common cause is tuberculosis, especially given the South-Asian origin of the patient.[10] However, this has also tested negative. Other causes include lymphoma, amyloidosis, malignancy, metastasis, congenital causes, and drug-induced causes etc.[11]

Therefore, a CT scan has been performed which has revealed bilateral adrenal mass. Tissue sampling from the mass has suggested adenocarcinoma. Notably, adrenal masses are usually unilateral and metastatic from primary carcinomas of the lungs, stomach, oesophagus, colorectal region, melanoma and lymphoma. No cases of adrenal carcinoma in the literature were found to be primary.[12, 13] In this case, initial chest X-ray and abdominal CT have not appreciated any primary carcinoma. However, the patient has been referred to oncology for further assessment, where CT chest and PET-CT maybe taken into consideration.

The case has been symptomatic, presenting with adrenal crisis. In contrast, earlier studies suggested that adrenal adenocarcinoma, when metastasic, are generally small, asymptomatic, and identified during postmortem examinations.[14, 15]

Conclusion:

Adrenal insufficiency secondary to bilateral adrenal cortical adenocarcinoma is a unique case. Firstly, adrenal carcinomas are usually unilateral, with only few bilateral cases reported. Secondly, most adrenal carcinomas reported in the literature were asymptomatic, while this case presented with adrenal crisis. Thirdly, many cases in the literature were found postmortem, unlike this antemortem diagnosis.

Therefore, high index of clinical suspicion is necessary for early detection and prevention of fatal outcome.

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COLLEGE NEWS

Continuing Medical Education (CME)

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Date	Topics	Department
05.07.2023	Simulation in Medical Education	Department of Community Medicine
12.07.23	Updated management of Chronic Hepatitis-B infection	Department of Medicine
19.07.23	Traumatic injury of tooth in conservative dentistry& endodontics	Department of Dentistry
26.07.23	Melioidosis: Unmasking the great mimicker	Department of Microbiology
02.08.23	Medical negligence	Department of Forensic Medicine & Toxicology
09.08.23	A young lady presented with difficulty in walking	Department of Orthopaedic Surgery
16.08.23	Hypertensive disorder of pregnancy & its newer thoughts	Department of Gynaecology and Obstetrics
23.08.23	Evaluation of deaf or hearing impaired child & its management	Department of Otolaryngology & Head neck surgery
30.8.23	An 8-year-old boy with muscle weakness: An outline of muscle diseases & biopsy as a diagnostic tool	Department of Pathology
13.9.23	Art of effective medical communication through power point presentations	Department of Pharmacology
20.9.23	Cranial nerves having parasympathetic components	Department of Anatomy
4.10.23	Physiology of micturition with some abnormalities	Department of Physiology
11.10.23	Mental health is a universal human right	Department of Psychiatry
18.10.23	Let there be light	Department of Ophthalmology
1.11.23	A young boy presented with recurrent lump in left arm	Department of Orthopaedics
8.11.23	Are we ready to save a life?	Department of Anaesthesiology
15.11.23	Diabetes complications-know your risk	Department of Endocrinology
22.11.23	Celebrating World Prematurity Day 2023	Department of Paediatrics
13.12.23	LASER in Dermatology	Department of Dermatology
20.12.23	Journey from Bogura to Dhaka of a 55-year-old lady with jaundice, abdominal pain and vomiting	Department of Surgery
27.12.23	Metabolic dysfunction-Associated fatty liver disease	Department of Medicine

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