ISSN : 3080-1257

MARINE CITY
MEDICAL COLLEGE

# Marine City Medical College Journal

Volume 04 Issue 01 April 2025 Citation MCMCJ 2025 ; 4(1) : 1-29

## Editorial



## Review Article



## Original Articles



## Case Report



An Official Publication of Marine City Medical College
Chattogram, Bangladesh

www.mcmchedu.com

# Marine City Medical College Journal (MCMCJ)




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**Published by**
Department of Publication & Research
Marine City Medical College
Chattogram, Bangladesh.

**Printed by**
New Computer Suporna
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Editorial

Marine City Medical College Journal

# Application of Artificial Intelligence (AI) in Evidence-Based Medicine (EBM)

**Pradip Kumar Dutta**[1*]

Artificial Intelligence (AI) is rapidly transforming healthcare, with profound implications for Evidence-Based Medicine (EBM). It focuses on data synthesis, predictive analytics, clinical decision support and personalized care. AI offers opportunities to enhance the efficiency and accuracy of evidence generation and application. However still challenges such as algorithmic bias, transparency, and ethical considerations remain. Henceforth it demands that AI should be integrated into EBM frameworks maintaining rigorous scientific standards.

Evidence-Based Medicine (EBM) emphasizes the integration of the best available research evidence with clinical expertise and patient values.[1] Artificial Intelligence (AI) particularly Machine Learning (ML) and Natural Language Processing (NLP) offers new tools to collect, analyze and apply evidence in clinical decision-making.[2,3] The convergence of AI and EBM is poised to revolutionize healthcare by accelerating literature synthesis, enhancing predictive models and enabling precision medicine.[4]

## Application of AI in ABM

*i) AI in Automated Literature Search and Evidence Synthesis*

The exponential growth of biomedical literature has created significant challenges for clinicians and researchers. AI-driven algorithms can automate systematic reviews, screen thousands of abstracts within minutes and identify relevant clinical trials with higher precision and reduces time and labour in systemic review.[5] Natural language processing allows extraction of structured data from unstructured text, thereby accelerating meta-analyses and evidence summaries.[6]

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Date of Submitted : 28.02.2025
Date of Accepted : 15.03.2025

*ii) AI in Clinical Decision Support Systems (CDSS)*

AI systems trained on large clinical datasets can provide decision support by predicting disease risk, suggesting diagnostic pathways, and recommending treatment strategies. For instance, machine learning models can integrate clinical parameters, imaging data, and genomics to provide individualized patient care.[2,6] When combined with EBM, these tools can ensure that decisions are not only data-driven but also aligned with the best available evidence.[7] AI is being used to analyze medical images, such as X-rays, MRIs, and CT scans, to detect diseases like cancer or diabetic retinopathy with high accuracy, often even before human experts can.[8]

*iii) Predictive Analysis*

ML algorithms use large datasets to predict patient outcomes, aiding in personalized treatment planning.[9]

iv) *Precision Medicine*

AI enables stratification of patients based on genetic, phenotypic and behavioral data for targeted interventions.[6]

*v) Real-Time Monitoring and Feedback*

AI-based wearables and monitoring devices facilitate continuous patient assessment, improving adherence to evidence-based protocols.[10]

## Challenges and Ethical Considerations

Despite its promise, AI in EBM is not without challenges. Issues such as algorithmic bias, lack of transparency in 'Black-box' models, data privacy, and the potential over-reliance on automated systems remain critical concerns.[11] Furthermore, AI-generated insights must undergo rigorous validation before being applied in clinical practice.[5] Ethical integration requires balancing technological innovation with patient autonomy, safety and equity.[7]

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**Future Directions**

The integration of AI into EBM should be viewed as a collaborative process. Rather than replacing clinicians, AI should augment their decision-making capacity. The future lies in developing hybrid frameworks where AI tools work alongside clinicians to analyze evidence, generate real-time recommendations and facilitate shared decision-making with patients.[2,6] Continuous education of healthcare providers in AI literacy and collaboration with data scientists in will be essential.[7,11] Artificial intelligence has the potential to revolutionize evidence-based medicine by enhancing the synthesis of research, improving clinical decision-making, and promoting personalized care. However, its application must be accompanied by robust safeguards, ethical oversight, and clinician engagement.[2,6,7] The challenge ahead is not whether AI will shape EBM, but how responsibly and effectively it will be integrated into the fabric of healthcare to ensure optimal patient out come.[5,11]

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Review Article

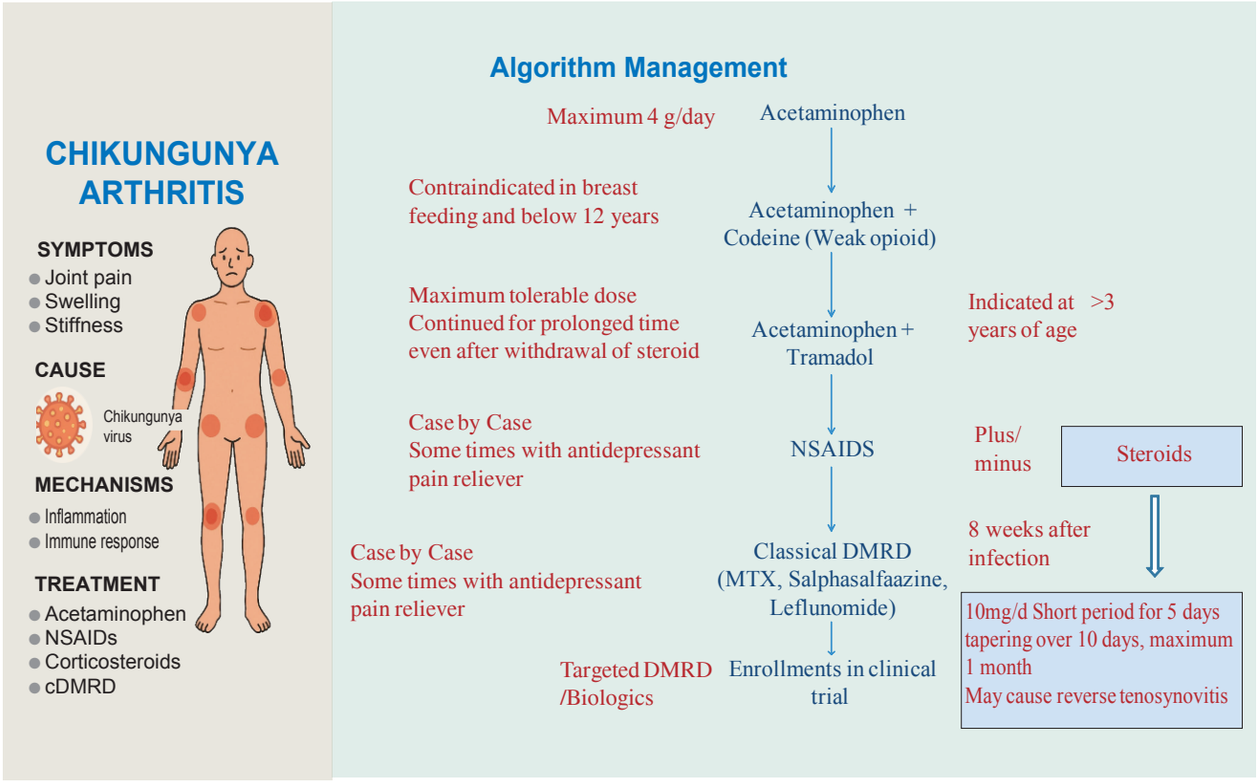
Marine City Medical College Journal

# Chikungunya Arthritis : A Contemporary Review

Pradip Kumar Dutta[1*] Sudipa Dutta[2]

## GRAPHICAL ABSTRACT

*Chikungunya Arthritis : A Contemporary Review*




**Conclusion:** Timely diagnosis and algorithm-based management using acetaminophen, NSAIDs, DMARDs and judicious corticosteroid therapy are essential to alleviate symptoms and prevent chronic arthropathy in Chikungunya arthritis.

*Dutta P K et al.* | *Graphical Abstract : Dutta P K* | *MCMC Journal. 2025;4(1) : 3-8*

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## ABSTRACT

**Background:** Chikungunya Virus (CHIKV) an alpha virus transmitted by Aedes mosquitoes, causes acute febrile illness with rash and severe polyarthralgia. A substantial subset develop persistent, sometimes erosive, inflammatory arthritis that mimics autoimmune rheumatic diseases. To summarize current evidence on epidemiology, pathogenesis, clinical patterns, diagnostic

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challenges and management of Chikungunya Arthritis (CHIKA) with updates on vaccination.

**Findings:** Chronic rheumatic manifestations follow 25–60% of infections, with risk influenced by host and viral factors. Pathogenesis involves persistent viral antigen/RNA and dysregulated host immunity (Th1/Th17, autoantibodies). Diagnosis relies on compatible exposure plus RT-PCR (Early) or IgM/IgG serology (Later) alongside exclusion of dengue and endemic rheumatic mimics. Acute management is supportive, NSAIDs are used once dengue is excluded. For persistent inflammatory disease, low-dose corticosteroids for shorter period and conventional DMARDs-especially methotrexate-have the best supportive evidence, Hydroxychloroquine (HCQ) shows little benefit. Two vaccines (live-attenuated IXCHIQ and virus-like particle VIMKUNYA) are licensed for selected travelers/lab workers, caution is advised with the live vaccine in adults ≥65years.

**Conclusion:** CHIKA is a clinically and immunologically heterogeneous post-viral arthritis. Structured assessment and step-up therapy with methotrexate-based regimens, plus rehabilitation, improve outcomes. Recently WHO has published a long cherished guideline for Arbovirus (Degue, Chikungunya, Zika and yellow. fever). Evolving vaccine guidance and safety updates should alsobe checked before travel counseling.

**Key words:** Alphavirus; Chikungunya; DMARDs; Methotrexate; Post-viral arthritis; Vaccine.

## INTRODUCTION

This arthridogenic virus is first isolated in Tanzania in 1952.[1] Recurrent outbreaks have been reported in more than 60 countries of Africa, Asia, and the Americas, with millions infected since 2004. The term "Chikungunya" itself, derived from a Kimakonde word, means "To become contorted," referring to the patient's stooped posture due to extreme joint pain.[2] While the acute febrile–arthralgic syndrome typically resolves, chronic arthralgia/arthritis (Collectively "Post-chikungunya chronic inflammatory rheumatism," pCHIK-CIR) contributes considerable disability and economic burden. 40-60% of patients may develop persistent arthritis lasting months to years resembling. Rheumatoid Arthritis (RA) or seronegative spondyloarthritis-like phenotypes.[3,4,5] This review article provides an overview of the clinical manifestations, pathophysiology, diagnosis and treatment of Chikungunya arthritis, referencing key studies and guidelines.

## SEARCH STRATEGY

We conducted a literature search using PubMed and Google scholar to identify articles related to CHIKA. The period covered January 2000 to June 2025. Included keywords were 'Chikungunya; Arthritis; Chronic joint pain; Viral arthritis and Post-viral rheumatism'. They were combined using Boolean operators (AND/OR). We included peer-reviewed original articles, case-reports, review articles and guidelines published in English. Screening andselection was based on title and abstract followed by full text review.

## DISCUSSION

### Epidemiology

Across cohorts and meta-analyses, 25–60% of patients report joint symptoms beyond 3 months; some series document persistent disease up to 6–7 years.[4] Risk factors for progression to chronic arthritis include older age (>45 years) high viral load (> $10^9$ /ml) during acute phase, high acute-phase joint burden, comorbid conditions (Obesity, DM, HTN, CKD) and pre-existing musculoskeletal disease.[1,4,6]

### Pathogenesis

Proposed mechanisms include:

i) Persistence of viral RNA/antigen in synovial macrophages

ii) Innate/adaptive immune activation with Th1/Th17 polarization, secretion of T helper type 1 (Th1) cytokines, interleukin 2 (IL-2) interferon (IFN-γ) and IL-12, which are required for maintenance of classical T cell mediated immunity, is decreased while production of Th2 cytokines, in particular IL-4, IL-5, IL-6 and IL-10, promoting B cell function, is increased similar to postulated mechanisms of autoimmunity in systemic lupus erythematous.[7]

iii) This autoantibody generation in a subset, potentially drives chronicity and erosion.

This strong immune response leads to the clearing of the virus by macrophages, Cluster of Differentiation (CD)8+ T and Natural Killer (NK) cells within 7–10 days of acute infection and virus levels become undetectable.[1] For this reason, after first week of infection, diagnosis using CHIKV Polymerase Chain Reaction (PCR) is discouraged. Immunological studies have shown decreased viral clearance due to immune deregulations in the elderly and in patients with co-morbidities such as type 2 diabetes, chronic kidney

disease and chronic heart diseases, explaining the occurrence of more intense infection in these patients. Chronic infection is associated with high levels of Monocyte Chemoattractant Protein (MCP-1) Macrophage Inflammatory Protein (MIP-1) IL-6 and IL-12 with CD4+ T cells playing a major role in ongoing inflammatory arthritis. Persistence of CHIKV ribonucleic acid in perivascular synovial macrophages has been linked to high immunoglobulin M (IgM) response and chronic arthritis symptoms.[1] However, the exact immunological basis for ongoing persistent inflammation causing musculoskeletal symptoms is still not clear. Convergence with RA pathways is supported by cohorts where 30–40% eventually fulfill ACR/EULAR RA criteria and by reports of bone erosions on imaging.[8-10]

**Clinical Spectrum**

***Acute Phase (0–10 days)***

Abrupt fever 2-12 days after mosquito bite, severe, often symmetric polyarthralgia (Distal > proximal) morning stiffness, myalgia, maculopapular rash (Diffuse/focal sometimes with pruritus) Tenosynovitis is common. Sometimes co-circulation withDengue may occur.[2,3]

***Post-Acute (10–90 days)***

Relapsing arthralgia, edema, morning stiffness, synovitis, enthesitis and dactylitis occur.

***Chronic Phase (>3 months)***

Phenotypes include:

i) Undifferentiated persistent polyarthritis

ii) RA-like disease (Symmetrical small-joint polyarthritis, seronegative or occasionally seropositive)

iii) Spondyloarthritis-like patterns. Erosive changes and functional impairment may develop without timely control.[9,11-13]

**Differential Diagnosis**

- Dengue (Early phase): Thrombocytopenia/hemorrhagic risk (CHIK is lymphopenic).
- Zika: Milder arthralgia, conjunctivitis; neuro complications.
- RA (Rheumatoid nodules)/psoriatic arthritis/spondyloarthritis, reactive arthritis, viral arthritides (Parvovirus B19, hepatitis B/C).
- Post-COVID inflammatory arthritis in endemic settings.[2]
- Ross River virus (In Australia, swollen lymph nodes).

**Diagnosis**

***Virologic Testing***

- **RT-PCR** on serum/whole blood in the first 7 days of illness (Highest yield).
- **Serology:** CHIKV-specific **IgM** appears by day 4–7, maximum after 3 weeks and can persist weeks–months (2-3 months) **IgG** develops later and persists for years. Paired sera can document Seroconversion.[1,14]

***Arthritis Work-up***

- In persistent synovitis, assess inflammatory markers, RF/anti-CCP to phenotype RA-like disease. HLAB27 tospodyloarthritis; ultrasound/MRI can detect synovitis and early erosions.[1,10]

**Management**

***Acute/Early Post-Acute Disease***

Supportive care: rest, hydration, antipyretics/analgesics. Paracetamol/acetaminophen (Upto 4gm /day in divided doses) is preferred initially; NSAIDs are avoided until dengue is ruled out, then NSAIDs (Ibuprofen, Diclofenac, Aceclofenac Naproxen) are acceptable.[1] Aspirin is avoided. Short courses (For 5 days and tapering over next 10 days,maximum 4 weeks) of low-doseoral corticosteroids (0.5 mg/kg) may help severe synovitis/tenosynovitis.[1,2,14-16]

**Chronic Inflammatory Chikungunya Arthritis (>3 months)**

**Goals:** To control synovitis, prevent damage and restore function.

**Step-up Pharmacologic Strategy (Typical)**

i) NSAIDs (If no contraindication) ± short prednisone taper for flares.

ii) Conventional synthetic DMARDs (csDMARDs):

- Methotrexate (MTX) is the anchor drug, observational cohorts and systematic review show pain and disease-activity improvement, alone or with leflunomide or sulfasalazine (1-2 g /day). Typical starting dose of MTX is10–15 mg/week with folate, titrating to response/ tolerance; labs monitoring as per RA.[1,9,15,17]
- Hydroxychloroquine (HCQ) has not demonstrated consistent benefit versus NSAID ± steroid regimens in RCTs/analyses.[15,18] However Brazilian guidelines and WHO guidelines advocate it (200mg/day ) for resistant cases of musculoskeletal symptoms for < 4 weeks.[1]

iii) Biologic (Like Abatacept) or Targeted DMARDs (Like ZAK Inhibitors) : Evidence is limited to small series; considering only for refractory, well-phenotyped RA-like disease per RA standards, ideally in consultation with rheumatology.[1,18]

Drugs in animal studies /Trials :

- Psychosocial support for chronic pain and fatigue. (Consensus-based.)

iv) **Pregnancy:** Acetaminophen is favored; NSAIDs avoided in third trimester; live vaccines and most DMARDs per obstetric–rheumatology guidance are deferred, HCQ may be used for other indications but is not effective for CHIKA.[14]

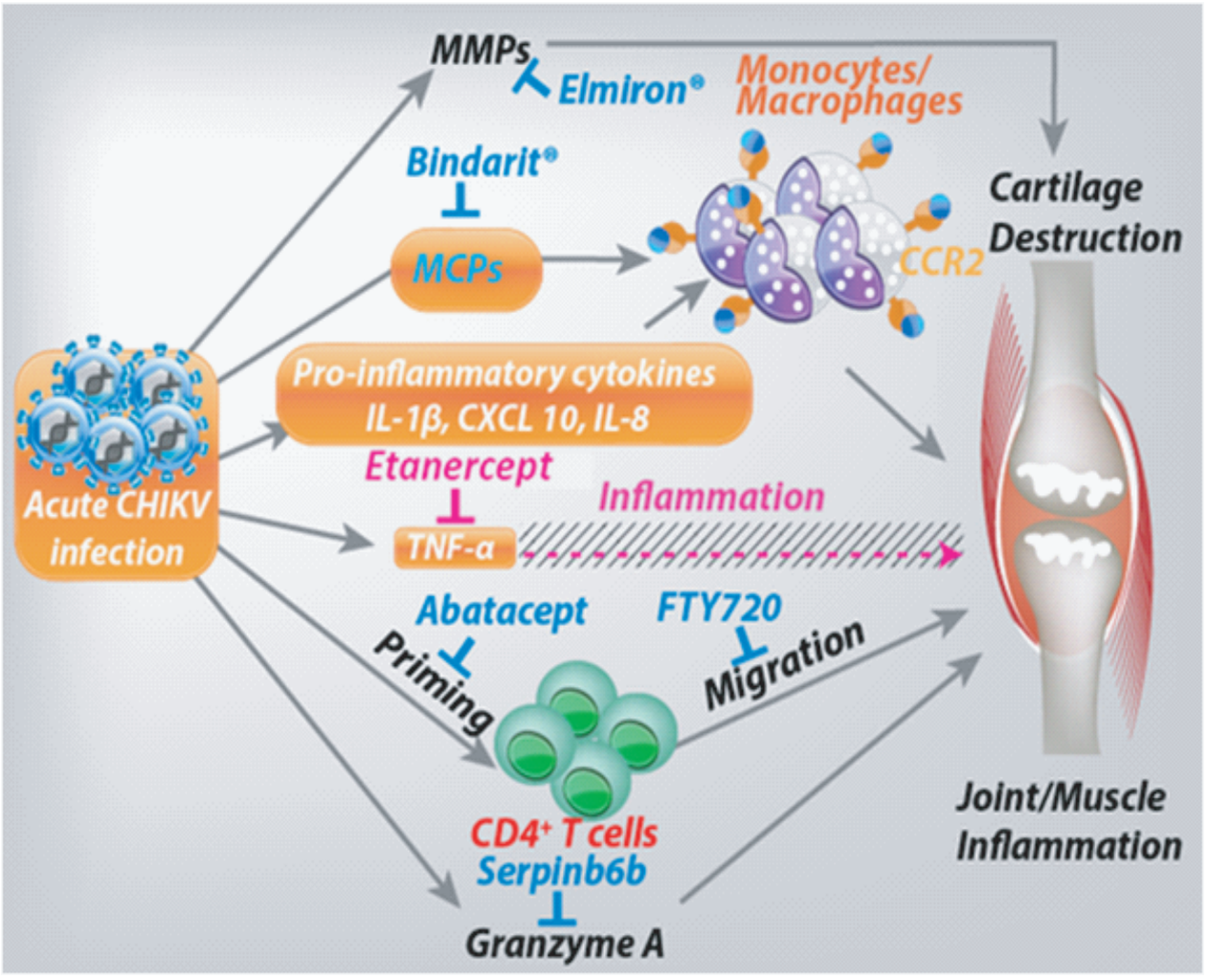



**Figure 1** Elmiron (Pentosanpolysulfate, a glycosaminoglycan) blocks metalloproteinase (MMP which destroys cartilage) in phase II trial. Badarit is against Monocyte Chemotactic Protein (MCP) decreases bone loss in mouse model. Fingolimod (FTY720) prevents migration of CD4+t cell (Mouse model). SErpinb6b inhibits Granzyme A (A serine protease which cause inflammation) and reduces foot edema in mouse.[19]

**Non-pharmacologic**

- Early physiotherapy (Range-of-motion, strengthening) hand therapy for tenosynovitis, ergonomic advice and graded return to activity.

**Vaccination and Prevention (2025 update)**

Two vaccines are licensed in the U.S. for selected travelers and laboratory workers:

- IXCHIQ (Valneva, live-attenuated, ≥18 y): ACIP recommends for travelers to outbreak areas, may be

considered for prolonged stays in higher-risk areas. Age ≥65 y is a precaution due to observed serious adverse events (Cardiac/neurologic) in general, avoid in ≥65 unless benefit outweighs risk. Single 0.5 mL IM dose.[20,21]

- VIMKUNYA (Bavarian Nordic, virus-like particle; 12 y): Recommended for travelers to outbreak areas, may be considered for prolonged stays in elevated-risk areas. Single 0.8 mL IM dose.[20,21]

General prevention remains mosquito bite avoidance (Repellents, clothing, screens) and vector control.[15]

**Prognosis**

Most patients improve over months, but a meaningful minority haveyears-long disease with functional impairment and in some cases, erosive damage. Early identification of inflammatory phenotype and timely DMARD therapy are associated with better outcomes.[6]

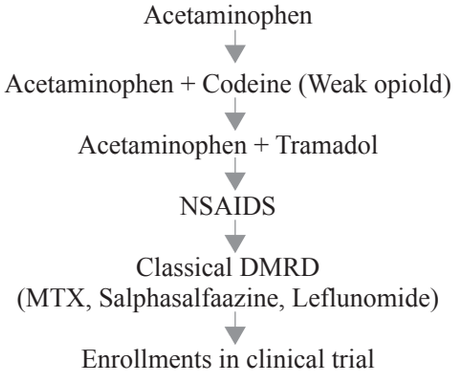
**Practical Algorithm (Textual)**

i) CHIKV is suspected in acute febrile polyarthralgia with exposure orderingRT-PCR ( 7 days) or IgM/IgG (>5–7 days).

ii) Excluding dengue before NSAIDs.

iii) If symptoms persist >6–12 weeks with synovitis:

- Baseline labs (CBC, Comprehensive metabolic panel or CMP, ESR/CRP), RF/anti-CCP, ultrasound as available.
- StartingNSAID ± prednisone 10–15 mg/day (Short tapering).
- InitiatingMTX 10–15 mg/wk + folate, titrate, considering leflunomide/sulfasalazine add-on if incomplete response.
- Reassessing at 8–12 weeks; escalating per RA principles if RA-like disease persists, considering rheumatology referral and imaging for erosions.[9]




WHO Guidelines (2025):

WHO suggests following dose schedules regarding arthritis.[22]

**Dosing of Acetaminophen**

| Age/ Clinical condition | Body weight | dose |
|---|---|---|
| Adults | >50 kg | 500mg – 1 g every 4-6 hours (Maximum daily dose, 4g) |
| Paediatrics | 10-15 mg/kg | Every 4-6 hours (Maximum daily dose 60mg/kg) |
| Renal failure (GFR (10-50ml/min) | | 500 mg every 6 hours |
| Renal failure (GFR (<10ml/min) | | 500mg every 8 hours |
| Hepatic Impairment | | Not exceeding 2 g/day |

## LIMITATIONS OF EVIDENCE

- Small sample sizes in most studies (10-75 participants).[23]
- High heterogeneity of interventions and outcomes.[3]
- Short -time follow up, limited long time safety/efficacy data.[23]
- High risk of bias (Lack of blinding, weak- outcome measures).[24]
- Diagnostic uncertainty (Clinical vs. lab-confirmed CHIK).[25]
- Unclear pathogenesis (Viral persistence vs. autoimmunity).[12]
- Few well designed randomized controlled trial.[26]
- Publication bias and outbreak –driven data.[5.]

## CONCLUSION

CHIKA is asignificant public health concern, particularly in endemic regions.It poses diagnostic challenges due to its similarity to autoimmune rheumatic diseases. Early recognition and tailored therapy are essential to prevent long- term disability. While the treatment of chronic Chikungunya arthritis is largely based on managing symptoms with drugs used for other inflammatory arthritides, the ongoing research into its pathogenesis holds the promise of more targeted therapies in the future.

## AUTHORS CONTRIBUTIONS

Contribution to Concept, Design and Data - PKD
Accountability - PKD, SD
Drafting and Critical revision - PKD
Final approval - PKD, SD.

## DISCLOSURE

All the authors declared no conflicts of interest.

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Original Article

Marine City Medical College Journal

# Assessment of Relationship between Learning Environment and Academic Performance Based on the Perceptions of Bangladeshi Undergraduate Medical Students

**Sharmista Bhattacharjee[1*] Rivu Raj Chakraborty[2] Pragwa Permita Chakraborty[3] Jehan Hashem Anny[4]**

***GRAPHICAL ABSTRACT*** ***Assessment of Relationship between Learning Environment and Academic Performance***

**Cohort**

**Study Design :** Cross Sectional

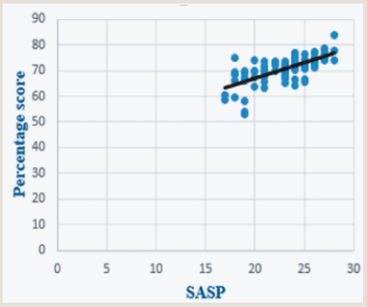
Sample size 100

Male 31%

Female 69%

**Results**

| Variables | Correlation Coefficient (r) |
|---|---|
| Percentage score | 1 |
| Dundee Ready Education Environment Measure (DREEM) | 0.49*** |
| Students' Perception of Teaching (SPL) | 0.58*** |
| Students' Perception of Teaching (SPL) | 0.28* |
| Students' Academic Self-Perception (SASP) | 0.69*** |
| Students' Perception of Atmosphere (SPA) | 0.05 |
| Students' Social Self-Perception | 0.04 |




SASP $r^2 = 0.47$ β=1.21

SPL $r^2 = 0.33$ β=0.6

DREEM $r^2 = 0.24$ β=0.2

**Conclusion:** Out of the five domains of learning environment Students' Academic Self-Perception (SASP) is the strongest predictor of academic achievement.

*Bhattacharjee S* | *Graphical Abstract : Bhattacharjee S* | *MCMC Journal. 2025;4(1) : 9-15*

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## ABSTRACT

**Background:** The learning environment encompasses educational, physical, psychological, and social dimensions of learning experience. It has significant impact on the professional growth and academic achievements of the students. This study examined how different aspects of the learning environment relate to academic performance among Bangladeshi undergraduate medical students with an aim to pinpoint areas needing targeted intervention.

Date of Submitted : 20.03.2025
Date of Accepted : 19.04.2025

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**Materials and methods:** This cross-sectional analytical research spanned over 12 months (January to December 2023). Total 100 students with 25 from each phase of MBBS course, who met the inclusion criteria, were selected randomly. The assessment of the learning environment was conducted using DREEM questionnaire. Academic performance was evaluated by percentage of score obtained in the recent university or internal examination. Data were analyzed in SPSS. The mean values and standard deviations for subscales of learning environment were calculated and linear regression models were used to conduct univariate analysis.

**Results:** The students had a more positive than negative perception about learning environment and its subscales. SASP was found to be the strongest predictor of academic performance ($\beta=1.21$, $p<0.001$).

**Conclusion:** The educators may concern themselves with remediation and intervention to improve the Students' Academic Self-Perceptions (SASP) for better academic outcome.

**Key word:** Academic performance; Learning environment; SASP.

## INTRODUCTION

The medical education is aimed to make the students competent in critical thinking and self learning as well as in clinical skills. Modern curricula also put emphasis on the environment in which the students learn. Assessment of learning environment has been identified as one of the major future trends of a curriculum.[1] Learning environment encompasses all educational, physical, psychological and social aspects which is experienced by a student in an educational institution. It plays an important role in students' professional development.[2] The culture and environment of an institution including students' interaction with their peers, their interaction with teachers, teachers' attititude toward students and organization of learning sessions influences students' behaviour and success.[3] The learning environment serves as the cornerstone of curriculum, reflecting its quality. Therefore, a comprehensive grasp of the concepts and measurements of the learning environment can offer insights into the effectiveness of medical curriculum.[4] The quality of learning environment influences students' learning style, learning efficacy, level of motivation and learning ooutcome. The assessment of learning environment is considered as an important measure in providing highquality education.[5] The way students perceive their academic environment significantly impacts their behavior, degree of satisfaction, realization of goal as well as their academic performance.[6]

It has been crucial to develop a valid and reliable instrument to measure students perception of their leatrning environment. As a result, Roff et al. has developed Dundee Ready Education Environment Measure (DREEM) to evaluate learning environment in undergraduate medical institutions.[7] The DREEM is a 50 items measure designed to evaluate students' perception of their learnong environment. It measures perception on five subscales including, Students' perception of learning (12 items) Students' perceptions of teachers (11 items) Students' academic self-perceptions (8 items) Students' perceptions of atmosphere (12 items) and Students' social self-perceptions (7 items). The DREEM has a maximum score of 200, where higher scores indicate a more positive environment.[8] A large number of students enrol each year in undergraduate medical programs in our country. Weak performance and failure in different phases of examinations in MBBS course often places strain on the students and their parents. Poor academic performance and poor attendanceoften signal challenges in adapting to the learning environment.[9] While there is evidence indicating that the learning environment plays a significant role in academic achievement, it remains a rarely explored field in our country.[10] This study aims to find out the relationship between subscales of learning environment and academic performance in undergraduate medical students.The insights into the relationship between elements of learning environment and academic performance can be helpful for the educators to implement targeted interventions in the required field to improve environment and thereby, promoting better academic success.

## MATERIALS AND METHODS

This cross sectional analyticalstudy was conducted over a period of 1 year (January to December 2023) after ethical permission for the study was obtained from Institutional Review Board. The researchers explained the procedure and purpose of the study and assured the participants about maintaining the confidentiality of data. Then a total of 100 students were selected randomly from phase 1, 2, 3 and 4 of MBBS course of

Marine City Medical College who were willing to participate. The students who were disinclined to participate or absent in the class were excluded. The 50-item DREEM questionnaire was distributed in a pre-scheduled class. These 50 items were grouped under five subscales and gave a maximum score of 200. The response for each item was quantified using a five point Likert scale where 0=strongly disagree, 1=disagree, 2=uncertain, 3=agree and 4=strongly agree. The negative statements were scored in reverse. The overall DREEM scores, subscale scores and item scores were interpreted according to the DREEM interpretation scale.[11] The academic achievement was evaluated by calculating percentage of total scores obtained by the students in the last University examination or last major internal examination.

The data were analyzed using SPSSversion 23. The descriptive statistics such as means and standard deviations were calculated for each subscale and overall environment. The Pearson correlations between academic performance and learning environment were calculated. Linear regression analyses were conducted to find out the association between academic achievement and learning environment. A 'p' value of <0.05 were considered as significant.

## RESULTS

Out of 100 participants 31 were male and 69 were female. The participants from each phases of MBBS course contributed to 25% of all participants (Table I). Table II showed that the students had a positive perception of learning (36.54±4.75), academic self-perception (32.34±4.59) and atmosphere (23.2±2.8). They perceived that teaching was in right track (33.55±4.75) and they were not too bad socially (16.93±3.08). The overall environment was perceived to be as more positive than negative (142.56±12.89). Table III presentedthe correlation between scores obtained by the students in examinations and subscales of academic environment. The percentage scores of the students showed moderately positive, statistically significant relationships with SPL (r=0.58, p<0.001), SASP (r=0.69, p<0.001) and DREEM (r=0.49, p<0.001). There was weak but statistically significant relationship with SPT (r=0.28, p<0.01). However, the correlation with SPA (r=0.05, p=0.64) and SSSP (r=0.04, p=0.68) were very weak and statistically insignificant. Figure 1 showed the positive correlation between SASP and scores obtained by the students in examination (r=0.69, p<0.001). Table IV revealed that 1 unit increase in SPL, SPT, SASP and DREEM scores would show 0.6 (p<0.001), 0.3 (p=0.01), 1.21 (p<0.001) and 0.2 (p<0.001) unit increase in examination scores, respectively. The SPL, SPT, SASP and DREEM accounted for 33%, 8%, 47% and 24% variability of examination scores respectively. SASP emerges as the strongest predictor of academic performance.

**Table I** Distribution of participants according to gender and phase of study (n=100)

| Variables | | Frequency (n=100) | Percentage (%) |
|---|---|---|---|
| Gender | Male | 31 | 31% |
| | Female | 69 | 69% |
| Phase of study | Phase1 | 25 | 25% |
| | Phase 2 | 25 | 25% |
| | Phase 3 | 25 | 25% |
| | Phase 4 | 25 | 25% |

**Table II** Students' perception of learning environment (n=100)

| Subscales | Mean | SD | Interpretation |
|---|---|---|---|
| Students' Perception of Learning (SPL) | 36.54 | ±4.75 | More positive perception |
| Students' Perception of Teaching (SPT) | 32.34 | ±4.59 | Moving in right direction |
| Students' Academic Self-Perception (SASP) | 23.2 | ±2.8 | More on the positive side |
| Students' Perception of Atmosphere (SPA) | 33.55 | ±4.74 | More positive attitude |
| Students' Social Self-Perception (SSSP) | 16.93 | ±3.08 | Not too bad |
| Total DREEM | 142.56 | ±12.89 | More positive than negative |

**Table III** Correlation between students' perception of learning environment and academic performance

| Variables | Correlation coefficient (r) |
|---|---|
| Percentage score | 1 |
| DREEM | 0.49*** |
| SPL | 0.58*** |
| SPT | 0.28* |
| SASP | 0.69*** |
| SPA | 0.05 |
| SSSP | 0.04 |

SPL: Students' Perceptions of Learning, SPT: Students' Perceptions of Teaching, SASP: Students' Academic Self-Perceptions, SPA: Students' Perceptions of Atmosphere, SSSP: Students' Social Self-perceptions, DREEM: Dundee Ready Education Environment Measure, p<0.05, significant*, p<0.005, very significant**, p<0.001, highly significant***.

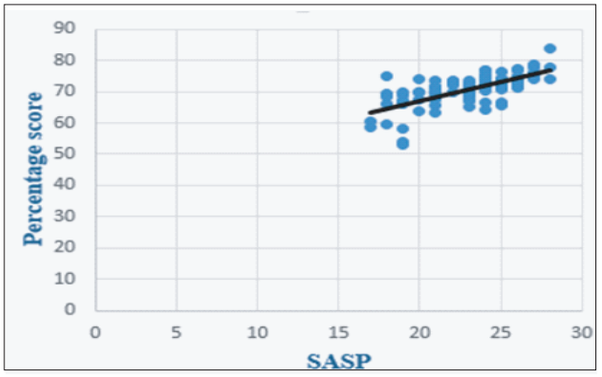


**Figure 1** Scatter diagram showing strong positive correlation between SASP and academic scores of the students

**Table IV** Linear regression analysis predictingthe relationship between learning environment and academic achievement

| Variables | $r^2$ | Regression coefficient (β) | Standard Error (SE) | 95% Confidence Interval | | p |
|---|---|---|---|---|---|---|
| | | | | Upper | Lower | |
| SPL | 0.33 | 0.6 | 0.1 | 0.77 | 0.43 | <0.001 |
| SPT | 0.08 | 0.3 | 0.1 | 0.51 | 0.09 | 0.01 |
| SASP | 0.47 | 1.21 | 0.13 | 1.47 | 0.96 | <0.001 |
| DREEM | 0.24 | 0.2 | 0.03 | 0.26 | 0.12 | <0.001 |

SPL: Students' Perceptions of Learning; SPT: Students' Perceptions of Teaching, SASP: Students' Academic Self-Perceptions, DREEM: Dundee Ready Education Environment Measure.

## DISCUSSION

The present study revealed that learning environment was found to be more positive than negative in regard to total DREEM score and subscale scores. This finding aligns with the studies conducted in Nepal, UAE, Australia, USA and Sweden.[12-16] In contrast to the current study, a study conducted inEgypt among medical students showed poor perception toward their learning environment.[17] Similarly, opposing results to the current findings were also seen in Pakistan.[18] These discrepencies in findings among different countries can be attributed to the socioeconomic status and cultural background of the students participating in the research. The socioeconomic status of students' affect their perception of learning environment as well as their academic performance. The students from high socioeconomic status tend to strive for better academic performance than the students from low socioeconomic status.[19] Many students of non-government medical colleges hail from financially stable families. Moreover, the learning environment in these medical colleges are carefully curated to take care of any difficulties they may perceive. This could be the reason for a higher DREEM score (142.56±12.89) and a more positive perception in the present study.

The perception of students may also vary when a new curriculum is introduced. Though Ogun, Nottidge & Roffet al. did notfind any significant differences between perceptions in students of teacher-centered and student-centered medical schools in Nigeria, Al-Hazimi et al. found that students in problem-based, student-centered UK medical school had better impressions of their learning environment than students in traditional medical schools of Yemen and Saudi Arab.[20,21] Therefore, when comparing Western health sciences institutions to those in Asia, Africa and the Middle East, it can be assumed that retraining of teachers and counselling of students is required when a new curriculum is introduced.[20] Medical education in Bangladesh is traditionally teacher-centered.[22] The students from teacher-centered environments tend to accept teachers' knowledge and authority without any question, both culturally and historically.[23] Therefore, teacher-centered teaching may not be perceived as a concern and which may account for higher DREEM scores in present study.

Based on the results of the present study, percentage scores of the students showed positive, statistically significant relationships with SPL (r=0.58, p<0.001), SPT (r=0.28, p<0.01), SASP (r=0.69, p<0.001) and DREEM (r=0.49, p<0.001). The correlation with SPA (r=0.05, p=0.64) and SSSP (r=0.04, p=0.68) were very weak and statistically insignificant. The findings of our study is in line with the results of other studies in regard to positive correlation between learning environment and academic achievement.[2,10,24-25] Desai et al. also identified a favorable and statistically significant relationship between academic achievement and the overall DREEM score, SPL, SPT and SASP, which lends support to the findings of the current study.[10] Al-Ansari & El Tantawi postulated that poor performance in examinations was related with poor perceptions of SPA and SSSP.[26] In contrast, Ugusman et al. found no significant relationship between learning environment and academic performance.[27]

SASP emerged as the strongest predictor of academic environment in the present study followed by SPL, DREEM and SPT. The majority of the items in the SASP domain evaluate students' self-efficacy. Self-efficacy denotes students' confidence in their capacity to complete a task independently. Therefore, self-efficacy is found to be a strong predictor for academic success irrespective of students' intelligence and prior academic ability.[28] Desai el al. also found SASP to be the strongest predictor which aligns with the findings of present study.[10] Al- Ansari & El Tantawi found SPL as the strongest predictor of good performance which is dissimilar to the present study.[26] A study on United States Medical Licensing Examination (USMLE) Step 1 examinees found that students' academic performance is associated with meaningful learning environment rather than academic ability of the students. They evaluated learning environment, emotional climate and student–student interaction as the factors influencing academic success.[29]

The quality of learning environment is crucial for better learning outcome of the students.[13] The learning environment influences the learning style and academic performance of the students.[30] Those with a positive outlook on their academic environment tended to adopt a thorough, sequential and detailed approach to studying. They employ various methods, demonstrate strong motivation to excel and attain high grades compared to their peers. Additionally, their level of academic achievement is predicted to be high.[5] Though a good academic environment can not guarantee success, it can foster effective teaching strategy, good learning practices and better social interaction. Stress and anxiety affects academic performance. The institutions can offer mentorship progams, stress managementprograms and counselling services for stressed students to keep the stressors at a marginal level.[31]

The students' choice oflearning approachesis also driven by perceived expectationsin examinations and academic success. When examinations prioritize information recall, they typically adopt a surface approach of learning to succeed in the examination.[5] An increase in assessment weight age enhances the motivation to adopt deep approach to learning. Extensive assessment and course work emerged as significant contributor to test-related anxiety.[32] The students who can manage workload better tend to do well in the examinations and have better academic self-perception.[33] While most of the students in the present study perceive learning environment in a positive light, it may not be shared by all students. The learning environment can be enriched by improving teaching, learning and assessment strategies which may potentially boost academic success.

While considering the ways to improve academic performance of the students, the educators should also consider other factors such as change of curriculum and motivation of the students which may influence students' perception of learning environment.[16,28] This study was an effort to find out the specific domains of learning environment that were better predictors of learning environment. The study's findings indicated that Students' Academic Self-Perception (SASP) is the domain requiring intervention to improve the learning environment satisfactorily, with the goal of ensuring students' academic success.

## LIMITATION

The study was based on the subjective perceptions of the medical students which may change over time.

## CONCLUSION

The results of the study indicated that the students had more positive perceptions about overall environment and all subscales of learning environment. The academic self-perception subscale (SASP) emerged as the strong predictor of academic achievement. It is essential to reevaluate and intervene in academic self-perception aspect of the learning environment in order to improve the academic performances of the students. Other factors in need of remediation are perception of learning (SPL) perception of teaching (SPT) and overall environment (DREEM) as these are also significant predictors of learning environment.

## RECOMMENDATION

Future studies may include a larger sample size from multiple medical colleges for generalization of results.

## AUTHORS CONTRIBUTIONS

Contribution to Concept, Design and Data - SB, JHA
Accountability - SB, RRC, PPC, JHA
Drafting and Critical revision - SB, RRC
Final approval - SB, RRC, PPC, JHA.

## DISCLOSURE

The authors declared no competing interest.

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Original Article

Marine City Medical College Journal

# Association of Serum Vitamin D Level with Non-Alcoholic Fatty Liver Disease in Non Diabetic Patients at Tertiary Care Hospital in Bangladesh

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## ABSTRACT

**Background:** Non-Alcoholic Fatty Liver Disease (NAFLD) has been recognized as the leading cause of liver disease, along with the rising epidemics of obesity, diabetes mellitus and metabolic syndrome.Similarly, hypovitaminosis D has been recently recognized as a worldwide epidemic. The aim of the study is to assess the association between vitamin D measured as serum 25-hydroxy vitamin D [25(OH)D] level and NAFLD in nondiabetic patients at a tertiary care hospital in Chattogram, Bangladesh.

**Materials and methods:** This cross-sectional analytical study was carried out in the Department of Biochemistry, Medicine and Hepatology of Chittagong Medical College Hospital. The study included 55 nondiabetic patients who have a diagnosis of NAFLD excluding other causes and have bright hepatic echotexture proven with an abdominal ultrasound from Chittagong Medical College Hospital. An equal number of nondiabetic individuals free from NAFLD were taken as a comparison group. NAFLD was diagnosed by upper abdomen ultrasonography. Serum vitamin D [25(OH)D] Fasting Blood Glucose (FBG) Glycated Hemoglobin (HbA1c) and lipid profile status were assessed by standard laboratory methods. Serum vitamin D levels were estimated by chemiluminescent immunoassay method. Vitamin D deficiency, insufficiency and sufficiency were defined as serum 25(OH)D levels < 20, 21-29 and ≥ 30 ng/ml respectively.

**Results:** The mean serum 25(OH)D was significantly lower in non diabetic NAFLD group than the healthy control group (25.3±9.0 versus 31.4±5.4 ng/mL, p < 0.001).Vitamin D deficiency and insufficiency were observed in 22% and 56% of the NAFLD group, respectively, whereas in the control group, these were found in 6% and 29%, respectively. Nondiabetic individuals with vitamin D deficiency weremore likely to have NAFLD than the individuals with vitamin D sufficiency. Grade of NAFLD was I, II, and III in 37 (62.7%), 15 (27.3%) and 3 (5.45%) participants, respectively. Mean serum 25 (OH)D level was 27.4±5.1, 25.7±5.2 and 20.1±2.1 ng/mL in Grade I, II, and III NAFLD (p<0.001) respectively.

**Conclusion:** Low vitamin D level is strongly associated with NAFLD among nondiabetics and vitamin D levels are inversely associated with the severity of NAFLD among them. Future research should clarify vitamin D's crucial therapeutic role in NAFLD prevention and treatment.

**Key words:** 25-hydroxyvitamin D; IR; NAFLD; VDD.

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Date of Submitted : 20.08.2023
Date of Accepted : 15.09.2023

## INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is a clinical-histopathological entity with histological characteristics that resemble alcohol-induced liver injury. By definition, this disease occurs in patients with little or no history of alcohol consumption.[1] It is a spectrum comprised of isolated steatosis, non-alcoholic steatohepatitis, advanced fibrosis and cirrhosis. NAFLD has become the most common Chronic Liver Disorder (CLD) over the last four decades. A recently conducted meta-analysis discovered that the worldwide

prevalence rate of NAFLD is 30.1% and trend analysis showed that the prevalence of NAFLD has increased from 25.3% (1990–2006) to 38.2% (2016–2019) which is about 50.4% rise in the prevalence of NAFLD over about last three decades. About 45 million (33.86%) people in Bangladesh are affected by NAFLD. Therefore NAFLD is placing a heavy financial burden on Bangladesh's healthcare system.[2] Globally, the NAFLD-related deaths and Disability-Adjusted Life Years (DALYs) in 2019 were 0.17 million and 4.42 million, increased by 80.2% and 62.9% compared with 1990, respectively. NAFLD-related deaths due to CLD and liver cancer increased by 76.7% and 95.1% between 1990 and 2019 respectively.[3] There are numerous studies on NAFLD treatment. But there is no specific pharmacological intervention for the treatment of this disease.Nowadays NAFLD is suggested to be the hepatic manifestation of insulin resistance and metabolic syndrome. Several factors such as obesity, insulin resistance, inflammation, oxidative stress and dyslipidemia through various mechanism responsible for the progression of NAFLD.[4] Both genetic predisposition and environmental variables, such as excessive intake of high-calorie meals, promote the expansion of obesity, adipose tissue malfunction, insulin resistance and alteration in the intestinal flora.[5] Vitamin D is important to regulate bone and calcium homeostasis.Numerous publications proposed that there is a potential association between NAFLD and its progressive inflammatory form- NASH and Vitamin D Deficiency (VDD).[6] It is commonly known that Vitamin D Deficiency (VDD) results in osteoporosis, osteomalacia, and an elevated risk of fractures.Vitamin D transmits its signals through its receptor VDR, which is present in numerous organs, including the pancreas, liver and skeletal muscle. VDR mediates vitamin D action in insulin sensitivity as it affects the activities of insulin genes and receptors. So vitamin D acts against IR by regulation of insulin secretion. Vitamin D inhibits activation of Tumor Necrosis Factor alpha (TNF-á) and IL-1 which are inflammatory markers of NAFLD-related liver injury. Vitamin D also exerts anti-proliferative and anti-fibrotic properties in the liver by decreasing hepatic stellate cell activation which play a major role in inducing fibrosis.[7] The potential involvement of the VD/VDR axis in the pathogenesis of NAFLD has been proposed by experimental studies linking VD-mediated pathways to key processes leading to liver inflammation, steatosis and fibrosis.[6] It is established that NAFLD is related to insulin resistance and T2DM and is not rare in nondiabetic individuals. Although NAFLD is well characterized in the patients of diabetic, the potential risk of severe NAFLD cannot be overlooked in nondiabetic patients since both NASH and advanced fibrosis occur in a considerable proportion of these patients.[8] In the light of these data, the present study evaluates the association of vitamin D level with NAFLD in nondiabetic patients at a tertiary care hospital in Bangladesh.

## MATERIALS AND METHODS

This cross-sectional analytical study of 110 subjects aged 18-60 years wascarried out in the Department of Biochemistry, Chittagong Medical College in collaboration with the Department of Medicine and Department of Hepatology of Chittagong Medical College Hospital, Chattogram during January 2023 to December 2023. 55 Nondiabetic patients diagnosed with NAFLD and 55 nondiabetic individuals without NAFLD aged 18 to 60 years, attending the Inpatient and Outpatient Department of Medicine and Department of Hepatology of Chittagong Medical College hospital during the study period were included in the study population by non probability sampling method. Individuals with viral hepatitis,liver cirrhosis, malignancies, chronic kidney diseases, diabetes mellitus, pregnancy and lactating mother and patients on vitamin D/calcium supplementation for last 3 months and with a history of alcohol consumption were excluded from the study. Based on the existence of bright hepatic echotexture by abdominal ultrasound the participants in the study were divided into two groups as Nondiabetic with NAFLD and Non diabetic without NAFLD group. Data were obtained by interview, reviewing the medical records, physical and laboratory investigations using a pre-tested structured questionnaire with all the variables of interest after taking informed and written consent. Demographic and anthropometric data including age, gender, height,weight, waist circumference, BMI were collected from the participants. With all aseptic precautions, 10 ml of morning fasting venous blood was drawn from the ante cubital vein in a disposable syringe in sitting position. After collecting 6ml fasting blood sample was allowed to clot for 15 min and then centrifuged at 4000rpm for 10 min.Then serum was taken into Eppendorf for estimation of serum 25(OH)D level, FBG, lipid profile. Another 4ml of blood was

taken in EDTA tube. Then HbA1c was measured in plasma. Data were analyzed by using SPSS version 23. Qualitative variables were expressed as frequency (Percentage) and compared between groups by Chi-square test. Continuous variables were expressed as mean ± SD and range. Independent sample 't' test and 'F' test (ANOVA) was done to test the difference between two and more than two means, respectively. p value less than 0.05 was considered as statistically significant. All the data were represented in tables and figures. Before commence the study institutional consent was taken.

## RESULTS

Out of 55 nondiabetic with NAFLD patients 47.3% were male, 52.7% were female and ranged between 18-60 years while out of 55 nondiabetic without NAFLD patients 63.6% were male and 36.4% were female. The mean age of the nondiabetic with NAFLD patients was 47.0±12.2 years which is significantly higher than the mean age of the nondiabetic without NAFLD patients while this is about was 39.8±13.1 years but both groups were similar regarding their gender distribution [Table I]. Out of 55 nondiabetic with NAFLD patients, 11 (20%) were obese by BMI criteria. The study shows that, there was no significant difference between two groups in terms of their BMI and WC [Table II]. The study reveals that the mean serum vitamin D levels in the nondiabetic with NAFLD group were 25.3±9.0 ng/mL as compared to nondiabetic without NAFLD group with 31.4±5.4 ng/mL, indicating a mean difference of 6.1 (95% CI: 4.0-8.1) ng/ml between the two groups.The difference was highly significant statistically (p<0.001).More than half (31, 56.4%) of the nondiabetic with NAFLD individuals had insufficient serum vitamin D levels, followed by (12, 21.8%), each with deficient and sufficient vitamin D levels. In contrast, nearly two-thirds (36, 65.5%) of the nondiabetic without NAFLD had sufficient levels of vitamin D, 16 (29%) had insufficient, and 3 (5.5%) had deficient levels of vitamn D [Table III]. The study depicts that the mean FBG and HbA1c levels were significantly higher in nondiabetic with NAFLD group than in nondiabetic without NAFLD group. The study also revealed that the mean serum level of TC and TG were significantly higher innondiabetic with NAFLD group than nondiabetic without NAFLD group. The mean serum level of LDL-C levels was higher in nondiabetic with NAFLD group than nondiabetic without NAFLD group without any statistical significance. And the mean serum level of HDL-C was lower in nondiabetic with NAFLD group than nondiabetic without NAFLD group without any statistical significance [Table IV]. On ultrasonography of 55 nondiabetic with NAFLD patients, NAFLD was grade I in 37(67.2%), grade II in 15 (27.3%) and grade III in 3 (5.45%) participants (Figure 1). Mean serum 25 (OH)D was 27.4 ± 5.1, 25.7 ±5.2 and 20.1±2.1 ng/mL, respectively in Grade I, II and III NAFLD. 'F' test (ANOVA) shows that the differences were highly statistically significant (F=10.26, p<0.001, Figure 2).

**Table I** Demographic characteristics of the study participants (n-110)

| Variables | Nondiabetic with NAFLD (n=55) | Nondiabetic without NAFLD (n=55) | p value |
|---|---|---|---|
| Age in years | | | |
| Mean ±SD | 47.0±12.2 | 39.8±13.1 | 0.003<0.05 (t- test) |
| Sex (In percentage) | | | |
| Male | 47.3% | 63.6% | 0.084>0.05 |
| Female | 52.7% | 36.4% | $\chi^2$(df:108;2.98) |

**Table II** Body mass index and waist circumference of the study participants (n-110)

| Variables | Nondiabetic with NAFLD (n=55) | Nondiabetic without NAFLD (n=55) | p value |
|---|---|---|---|
| BMI (Kg/m$^2$) | | | |
| Mean ±SD | 25.5±2.9 | 24.9±1.6 | 0.207>0.05 (t-test) |
| BMI category (%) | | | |
| Normal | 14.5% | 12.7% | 0.060>0.05 |
| Overweight | 65.5% | 81.8% | $\chi^2$(df:108;6.34) |
| Obese | 20.0% | 5.5% | |
| WC category (cm) | | | |
| Mean ±SD | 96.2±6.6 | 97.6±5.2 | 0.207>0.05 (t-test) |

**Table III** Comparison of the serum vitamin D status between study participants (n-110)

| Serum vitamin D level, ng/ml | Nondiabetic with NAFLD (n=55) | Nondiabetic without NAFLD (n=55) | p value |
|---|---|---|---|
| Mean ±SD | 25.3±9.0 | 31.4±5.4 | <0.001 |
| **Vitamin D status** | | | |
| Deficient | 21.8% | 5.5% | <0.001 |
| Insufficient | 56.4% | 29% | $\chi^2$(df:108;21.19) |
| Sufficient | 21.8% | 65.5% | |

**Table IV** Comparison of fasting blood glucose, glycated hemoglobin levels and lipid parameters between two groups (n-110)

| Variables | Nondiabetic with NAFLD (n=55) Mean±SD) | Nondiabetic without NAFLD (n=55) (Mean±SD) | p value |
|---|---|---|---|
| FBG, mg/dl | 112.1±9.4 | 100.1±11.1 | <0.001 (t-test) |
| HbA1c, % | 5.8±0.5 | 5.3±0.5 | <0.001 (t-test) |
| **Lipid parameters** | | | |
| Serum TC, mg/dl | 185.3±28.3 | 175.7±17.2 | 0.034<0.05 (t-test) |
| Serum TG, mg/dl | 204.0±37.7 | 177.3±30.7 | <0.001 (t-test) |
| Serum HDL-C, mg/dl | 39.7±3.3 | 40.8±2.7 | 0.060>0.05 (t-test) |
| Serum LDL-C, mg/dl | 116.3±15.2 | 111.0±13.7 | 0.062>0.05 (t-test) |

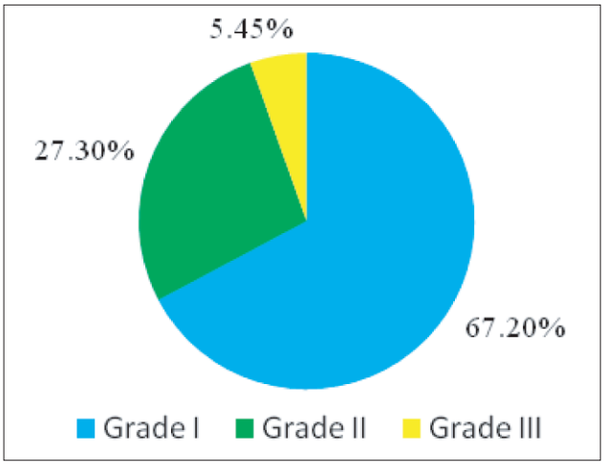


**Figure 1** Distribution of the nondiabetic NAFLD individuals according to their NAFLD grading on ultrasonography

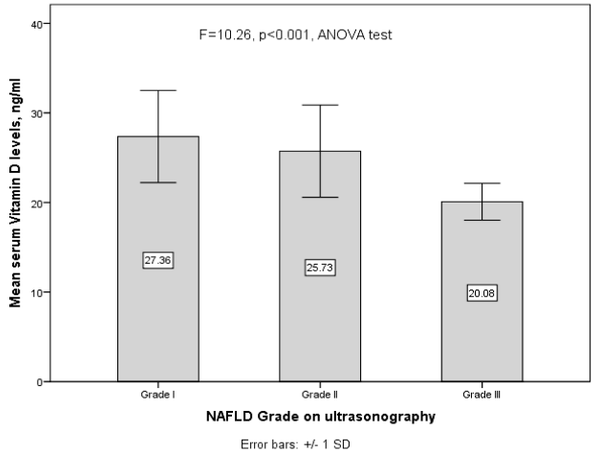


**Figure 2** Comparison of serum vitamin D levels among different grades of NAFLD in nondiabetic with NAFLD group (n=55)

## DISCUSSION

The present study was conducted to assess the association between serum vitamin D level and NAFLD in nondiabetic individuals at a tertiary care hospital in Bangladesh. In the present study, mean serum 25 (OH)D levels were 25.3±9.0 ng/mL in the nondiabetic with NAFLD group as compared with the nondiabetic without NAFLD group where vitamin D were 31.4±5.4 ng/mL, indicating a mean difference of 6.1 ng/ml between the two groups. In another study of Hosny, total vitamin D levels were 22.86 ± 9.58 and 55.8 ± 11.98 ng/ml, respectively, in the nondiabetic NAFLD group and the healthy control group.[7] The present study demonstrated that, among 55 nondiabetic NAFLD patients serum vitamin D levels were either deficient (12/55, 21.8%) or insufficient (31/55, 56.4%) in most of the cases. Only 12 (21.8%) participants had sufficient level of serum vitamin D. In contrast, nearly two-thirds (36, 65.5%) of the nondiabetic without NAFLD had sufficient vitamin D level and 3 (5.5%) and 16 (29%) participants respectively had deficient and insufficient serum vitamin D level. The results of present study agreed with the study of Gad et al. where out of 40 NAFLD patients (Majority nondiabetic) about 70% of the patients had VDD and 10% had VDI. In contrast, the control group showed lower prevalence, with only 35% participants had VDD and 10% had VDI.[9] The current study also evaluated the distribution of nondiabetic with NAFLD patients according to the fatty liver grade and its relationship with serum VD levels. Mean serum 25 (OH)D level was the highest in NAFLD grade I (27.4 ± 5.1 ng/ml) and the lowest in NAFLD grade III (20.1±2.1 ng/mL) indicating an inverse relationship between the grading of NAFLD and serum VD levels. The study results agreed with the results presented by Kumar, which demonstrated a notable correlation between fatty liver grade, evaluated through ultrasonography and the extent of VDD.[10] In another study done by Targher recruited 60 patients with histologyven NAFLD and 60 healthy controls of comparable age, sex and BMI. The study showed that decreased 25(OH)D concentrations among NAFLD patients were closely correlated with the histological severity of liver fibrosis.[11] NAFLD is a rising public health problem in Bangladesh and vitamin D deficiency is more prevalent in NAFLD among non diabetic individuals. The present study's findings would open the window for future interventional studies to confirm the association between serum vitamin D levels and

NAFLD in the nondiabetic Bangladeshi population.

## LIMITATIONS

Cross-sectional study did not allow assessment of causal relationships between the low vitamin D level and NAFLD. Information on some potential confounding variables, such as physical activity, dietary habits of the participants were not included in the study. Sun exposure index, seasonal variations of vitamin D levels was not considered in the study. It was not possible to use the gold standard method for diagnosis of NAFLD (Liver biopsy).

## CONCLUSION

NAFLD is the hepatic manifestation of insulin resistance and it is well characterized in diabetic patients. It is established that vitamin D deficiency is more prevalent in diabetic NAFLD patients. However the present study demonstrates that serum vitamin D level is significantly lower in nondiabetic with non-alcoholic fatty liver disease patients. Low vitamin D level is linked to an increased incidence of NAFLD as well as the severity of NAFLD grading. Therefore it is plausible to hypothesize that low vitamin D status might be recognized as a risk factor for NAFLD in nondiabetic patients.

## RECOMMENDATION

Given the high prevalence and mortality of CLD, individuals with low vitamin D level might be implicated in extra requirement of surveillance and prevention against NAFLD.Further prospective studies are needed to confirm the causal relationship between serum vitamin D status and NAFLD, and well-designed randomized clinical trials could show whether dietary or supplementary vitamin D might reduce the development and progression of NAFLD.

## ACKNOWLEDGEMENT

The authors acknowledges the contribution of the Department of Biochemistry, Department of Hepatology and the Department of Medicine of Chittagong Medical College Hospital.

## AUTHORS CONTRIBUTIONS

Contribution to Concept, Design and Data - JRK, SRAS
Accountability - JRK, SRAS, FH, MB, LB
Drafting and Critical revision - JRK, SRAS, FH
Final approval - JRK, SRAS, FH, MB, LB

## DISCLOSURE

All the authors declared no competing interest.

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Original Article

Marine City Medical College Journal

# Prevalence of AmpC-Producing *Klebsiella spp.* and *Escherichia coli* and Their Antibiotic Susceptibility Profiles in Urinary Samples in the Southwest Region of Bangladesh

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## ABSTRACT

**Background:** The increasing prevalence of antibiotic-resistant pathogens, particularly AmpC-producing *Klebsiella spp.* and *Escherichia coli,* poses a significant challenge in Managing Urinary Tract Infections (UTIs) in the southwest region of Bangladesh. This study aimed to investigate the prevalence of AmpC-producing *Klebsiella spp.* and *E. coli* in clinical urine samples and to assess their antibiotic susceptibility profiles.

**Materials and methods:** 51 urine samples were collected from patients at Ibn Sina Hospital and Nurul Islam Diabetic Hospital, Jashore, Bangladesh, between January and March 2025 with suspected UTIs at a tertiary healthcare facility in the southwest region of Bangladesh. Bacterial identification was performed using standard microbiological techniques and the production of AmpC β-lactamase was confirmed through phenotypic testing. The antibiotic susceptibility of the isolates was determined using the Kirby-Bauer disk diffusion method and resistance patterns were analyzed for common antibiotics.

**Results:** Of the 51 urine samples, 34 (66.7%) yielded bacterial growth. *E. coli* was the most predominant pathogen, accounting for 54.9%, followed by *Klebsiella spp.* at 31.4%. A total of 57.1% of *E. coli* and 75% of *Klebsiella spp.* isolates were found to produce AmpC β-lactamase. Both pathogens exhibited high resistance to commonly used antibiotics, including ampicillin (85.7% in *E. coli* and 87.5% in *Klebsiella spp.*) ceftriaxone (71.4% in *E. coli* and 75% in *Klebsiella spp.*) and ciprofloxacin (64.3% in *E. coli* and 62.5% in *Klebsiella spp.*). Nitrofurantoin demonstrated relatively low resistance rates, with 14.3% for *E. coli* and 12.5% for *Klebsiella spp.*

**Conclusion:** This study highlights a concerning prevalence of AmpC-producing *E. coli* and *Klebsiella spp.* In the southwest region of Bangladesh, significant antibiotic resistance was observed. The high levels of multidrug resistance emphasize the urgent need for effective antimicrobial stewardship and alternative treatment options, such as nitrofurantoin, to manage UTIs caused by resistant pathogens. These findings underscore the importance of continued surveillance of antibiotic resistance and the development of targeted treatment strategies in the region.

**Key words:** AmpC-producing Klebsiella spp., Antibiotic resistance; Escherichia coli; Urinary tract infections.

## INTRODUCTION

*Escherichia coli* and *Klebsiella pneumoniae* are among the primary causative agents of both nosocomial and community-acquired infections, notably contributing to conditions such as primary bacteremia, urinary tract infections and intra-abdominal infections.[1,2] In recent years, the global rise in antimicrobial resistance has been alarming, particularly due to the emergence of antibiotic-resistant strains producing AmpC beta-lactamases (AmpCs) and Extended-Spectrum Beta-Lactamases (ESBLs) among Enterobacteriaceae, with *E. coli* and *K.* pneumoniae being the predominant species involved. These enzymes, especially ESBLs and AmpCs are of critical clinical concern.[3-6]

AmpCs are cephalosporinases commonly encoded on the chromosomes of several Enterobacteriaceae

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Date of Submitted : 30.03.2025
Date of Accepted : 20.04.2025

Volume 04 | Issue 01 | April 2025 | 21-26

species, conferring resistance to a broad range of beta-lactam antibiotics. In contrast, ESBLs are mutant derivatives of common beta-lactamases, having undergone amino acid substitutions near the enzyme's active site. These structural changes enhance their ability to hydrolyze third-generation cephalosporins and monobactams, rendering them less effective.[3,4] The widespread use of newer cephalosporins has significantly contributed to the selection pressure favoring the emergence of these resistant enzymes. Moreover, as many of these beta-lactamase genes are located on conjugative plasmids, their horizontal transfer is facilitated, often co-transmitting resistance to other antibiotics such as aminoglycosides.[7] Initially, CTX-M-producing strains were reported only in specific regions during the 1990s, but over the last decade, their prevalence has surged worldwide. Recent epidemiological studies have confirmed a significant global rise in CTX-M enzymes among ESBL-producing organisms.[8] Additionally, in species that do not naturally express AmpC, the presence of plasmid-mediated AmpC (pAmpC) has been increasingly observed.[9] These pAmpCs are categorized into seven major families: ACC (Ambler class C-1) CMY, DHA, FOX, MIR, ACT and MOX with CMY-2 being the most prevalent variant globally.[10,11] Similarly, most ESBLs fall into three key families: CTX-M, SHV and TEM.[12,13] Regional studies, such as those conducted in northwestern Iran in 2015 and 2016, have explored both genotypic and phenotypic characteristics of ESBL and AmpC producing isolates.[14,15] *Klebsiella spp.* and *Escherichia coli* are major pathogens implicated in both hospital- and community-acquired infections. The emergence of AmpC beta-lactamase-producing strains among these organisms poses a significant threat to effective antimicrobial therapy. AmpC enzymes confer resistance to broad-spectrum cephalosporins and are often associated with multidrug resistance due to plasmid-mediated gene transfer. In recent years, their prevalence has increased globally, including in South Asia. However, data from the southwest region of Bangladesh remain limited. This study aims to determine the prevalence of AmpC-producing *Klebsiella spp.* and *E. coli* and assess their antibiotic susceptibility profiles in this region.

## MATERIALS AND METHODS

This cross sectional study was conducted in the southwest region of Bangladesh, focusing on the prevalence of AmpC-producing Klebsiella spp. and Escherichia coli and their antibiotic susceptibility profiles. A total of 51 midstream urine samples were collected from patients presenting with symptoms of Urinary Tract Infections (UTIs) at Ibn Sina Hospital and Nurul Islam Diabetic Hospital,Jashore, Bangladesh, between January and March 2025. Each sample was collected using the clean-catch method to reduce contamination risk. The samples were immediately transported to the microbiology laboratory under proper aseptic conditions and processed within two hours of collection to ensure sample integrity. In the laboratory, urine samples were cultured on selective media, including Cystine-Lactose-Electrolyte-Deficient (CLED) agar and MacConkey agar, to isolate Gram-negative bacteria, particularly uropathogens such as Klebsiella spp. and E. coli. After incubation at 37°C for 18-24 hours, bacterial colonies were identified based on their colony morphology, Gram staining, and a series of biochemical tests, including catalase, oxidase, indole, citrate utilization, urease activity and Triple Sugar Iron (TSI) reaction. For further confirmation of the bacterial species, commercial identification systems (e.g. API 20E for Gram-negative organisms) were used. AmpC production was determined using a phenotypic confirmatory test, where isolates showing resistance to beta-lactam antibiotics, such as cefoxitin, were further tested for the presence of AmpC β-lactamase production. The antibiotic susceptibility of the isolates was assessed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, in accordance with the guidelines set by the Clinical and Laboratory Standards Institute (CLSI). A range of antibiotics, including ampicillin, amoxicillin-clavulanic acid, ceftriaxone, cefoxitin, ciprofloxacin and gentamicin, was tested to evaluate resistance patterns. Isolates were categorized as resistant, intermediate or susceptible based on the zone diameter breakpoints provided by CLSI. Multidrug Resistance (MDR) was defined as resistance to at least one agent in three or more different antibiotic classes. Quality control was maintained by simultaneously processing reference strains of Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 to ensure the accuracy and reliability of the test results. Data were recorded and analyzed using descriptive statistics to identify the prevalence of AmpC-producing Klebsiella spp. and E. coli and their respective antibiotic resistance profiles.

## RESULTS

A total of 51 urine samples were analyzed in this study to assess the prevalence of AmpC-producing *Klebsiella spp.* and *Escherichia coli,* along with their antibiotic susceptibility profiles. The following tables present the distribution of bacterial isolates, AmpC production rates and antibiotic resistance profiles.

**Table I** Distribution of Bacterial Isolates from Urine Samples (n=51)

| Pathogen | Number of Isolates (n=51) | Percentage (%) |
|---|---|---|
| *Escherichia coli* | 28 | 54.9% |
| *Klebsiella spp.* | 16 | 31.4% |
| *Proteus mirabilis* | 4 | 7.8% |
| *Enterococcus faecalis* | 3 | 5.9% |

Table I presents the distribution of bacterial isolates recovered from the 51 urine samples. *Escherichia coli* was the most prevalent pathogen, accounting for 54.9% (28/51) of the isolates. *Klebsiella spp.* followed with 31.4% (16/51), while *Proteus mirabilis* and *Enterococcus faecalis* were less frequently isolated, contributing 7.8% (4/51) and 5.9% (3/51) respectively. These findings align with previous studies, where *E. coli* and *Klebsiella spp.* are commonly identified as the leading pathogen in urinary tract infections.

**Table II** Prevalence of AmpC β-lactamase Production in *Klebsiella spp.* and *Escherichia coli* (n=44)

| Pathogen | AmpC Producers | Total Isolates | Percentage of AmpC Producers (%) |
|---|---|---|---|
| *Escherichia coli* | 16 | 28 | 57.1% |
| *Klebsiella spp.* | 12 | 16 | 75.0% |

Table II shows the prevalence of AmpC β-lactamase production in *Klebsiella spp.* and *E. coli.* Of the 44 isolates that were tested for AmpC production, 57.1% (16/28) of *E. coli* strains and 75.0% (12/16) of *Klebsiella spp.* strains produced AmpC β-lactamase. These results indicate that AmpC production is highly prevalent in both *Klebsiella spp.* and *E. coli,* suggesting a significant level of resistance to β-lactam antibiotics in these pathogens. The higher AmpC production rate in *Klebsiella spp.* (75%) compared to *E. coli* (57.1%) highlights the emerging threat of AmpC β-lactamase-producing pathogens in urinary tract infections.

**Table III** Antibiotic Resistance profiles of *Escherichia coli* (n=28)

| Antibiotic | Resistant (n=28) | Percentage (%) |
|---|---|---|
| Ampicillin | 24 | 85.7% |
| Ceftriaxone | 20 | 71.4% |
| Ciprofloxacin | 18 | 64.3% |
| Gentamicin | 12 | 42.9% |
| Amoxicillin-Clavulanic Acid | 10 | 35.7% |
| Nitrofurantoin | 4 | 14.3% |

Table III displays the antibiotic resistance profiles of *E. coli* isolates. High resistance rates were observed against commonly used antibiotics. Resistance to ampicillin was observed in 85.7% of isolates, followed by ceftriaxone (71.4%) ciprofloxacin (64.3%) and gentamicin (42.9%). Resistance to amoxicillin-clavulanic acid was lower, with 35.7% of isolates showing resistance. Interestingly, resistance to nitrofurantoin, a commonly used antibiotic for urinary tract infections, was relatively low at 14.3%. This suggests that nitrofurantoin may remain an effective option for treating *E. coli*-related UTIs in this region.

**Table IV** Antibiotic Resistance Profiles of *Klebsiella spp.* (n=16)

| Antibiotic | Resistant (n=16) | Percentage (%) |
|---|---|---|
| Ampicillin | 14 | 87.5% |
| Ceftriaxone | 12 | 75.0% |
| Ciprofloxacin | 10 | 62.5% |
| Gentamicin | 8 | 50.0% |
| Amoxicillin-Clavulanic Acid | 6 | 37.5% |
| Nitrofurantoin | 2 | 12.5% |

Table IV shows the antibiotic resistance profiles of *Klebsiella spp.* isolates. Similar to *E. coli, Klebsiella spp.* exhibited high resistance to ampicillin (87.5%) and ceftriaxone (75.0%) with notable resistance to ciprofloxacin (62.5%) and gentamicin (50.0%). The resistance rates for amoxicillin-clavulanic acid and nitrofurantoin were lower, at 37.5% and 12.5%, respectively. This further corroborates the concern over the emergence of multidrug-resistant *Klebsiella spp.* strains, which complicate treatment options for UTIs in this region.

**Table V** Comparison of AmpCProduction and Antibiotic Resistance in *Klebsiella spp.* and *Escherichia coli* (n=44)

| Pathogen | AmpC Positive | AmpC Negative | Resistant to ≥3 Antibiotics | Percentage (%) |
|---|---|---|---|---|
| *Escherichia coli* | 16 | 12 | 20 | 71.4% |
| *Klebsiella spp.* | 12 | 4 | 10 | 83.3% |

Table V compares the AmpC production and antibiotic resistance profiles of *Klebsiella spp.* and *E. coli.* Of the total 44 isolates, 71.4% (20/28) of *E. coli* and 83.3% (10/16) of *Klebsiella spp.* were resistant to at least three different classes of antibiotics. The data indicated that both *E. coli* and *Klebsiella spp.* are highly resistant to multiple antibiotics, with *Klebsiella spp.* showing a slightly higher prevalence of multidrug resistance.

## DISCUSSION

These findings highlighted the growing concern over the spread of AmpC-producing strains in both pathogens, which poses significant challenges for treatment, particularly in UTIs.[9] The results of this study highlight the increasing prevalence of AmpC-producing Klebsiella spp. and Escherichia coli as significant uropathogens in the southwest region of Bangladesh. Our findings indicate that these pathogens are not only highly prevalent but also exhibit substantial resistance to commonly used antibiotics, underscoring the growing threat of Antimicrobial Resistance (AMR) in Urinary Tract Infections (UTIs).[13] In this study, *E. coli* was the most predominant pathogen, isolated from 54.9% of the urine samples, followed by *Klebsiella spp.,* which accounted for 31.4%. These findings align with several previous studies conducted globally and regionally, which consistently report *E. coli* as the leading cause of UTIs, especially in community settings.[3,14] The high isolation rate of *E. coli* in this study is consistent with its ability to colonize the urinary tract and its virulence factors, including the production of adhesins, which allow the pathogen to bind to the urinary tract epithelium and evade host defenses.[13] *Klebsiella spp.,* though less prevalent than *E. coli,* is another important uropathogen associated with both community-acquired and healthcare-associated infections, particularly in patients with underlying comorbidities.[1,4] One of the key findings of this study is the high prevalence of AmpC β-lactamase production in both *Klebsiella spp.* and *E. coli.* AmpC β-lactamase-producing strains are of particular concern because they confer resistance to a broad range of β-lactam antibiotics, including cephalosporins and penicillins, which are commonly used to treat UTIs.[5,9,10] In this study, 75.0% of *Klebsiella spp.* and 57.1% of *E. coli* isolates were found to be AmpC producers. These findings are in line with previous studies from both developing and developed countries, where AmpC production is emerging as a major mechanism of resistance in *Klebsiella* and *E.coli*.[6,11,14,15] The higher prevalence of AmpC production in *Klebsiella spp.* (75%) compared to *E. coli* (57.1%) may reflect the greater capacity of Klebsiella to acquire and express AmpC genes, which are often carried on plasmids, allowing for rapid spread in bacterial populations.[12] The emergence of AmpC-producing strains is particularly concerning as it limits the effectiveness of several first and second-line antibiotics commonly used to treat UTIs.[7,9] Furthermore, the presence of AmpC β-lactamases complicates treatment options, as it may necessitate the use of more expensive or less readily available antibiotics, such as carbapenems, which should ideally be reserved for more severe or hospital-acquired infections to prevent the development of resistance.[7,9,13] The resistance profiles of *E. coli* and *Klebsiella spp.* isolates in this study revealed a high level of multi-drug resistance, consistent with the global rise of AMR.[13,17] *E. coli* exhibited resistance rates of 85.7% to ampicillin, 71.4% to ceftriaxone and 64.3% to ciprofloxacin, while *Klebsiella spp.* showed similarly high resistance to ampicillin (87.5%) and ceftriaxone (75.0%).[14,17] These resistance patterns reflect the widespread use of these antibiotics in clinical settings and their selective pressure on bacterial populations.[8,16] The high resistance to ciprofloxacin in both pathogens suggests the development of fluoroquinolone resistance, which is particularly concerning given that fluoroquinolones have traditionally been used as first-line agents for complicated UTIs.[13] Interestingly, resistance to nitrofurantoin was relatively low in both pathogens (14.3% in *E. coli* and 12.5% in *Klebsiella spp.*) suggesting that nitrofurantoin may still be an effective option for the treatment of UTIs in this region.[17,18] Nitrofurantoin is often considered a reliable option for treating uncomplicated UTIs, especially in women, and its relatively low resistance rates in this study highlight its potential utility in the context of rising resistance to other antibiotics.[13] The overall antibiotic resistance patterns observed in this study are concerning, as they

underscore the urgent need for effective antimicrobial stewardship programs to limit the overuse and misuse of antibiotics in both community and healthcare settings.[9,13] Additionally, the emergence of multidrug-resistant strains highlights the importance of ongoing surveillance of AMR to inform treatment guidelines and to prevent the spread of resistant pathogens.[14,15] One of the most significant findings of this study is the high level of multidrug resistance among both *E. coli* and *Klebsiella spp.* isolates. Of the total 44 AmpC-producing isolates, 71.4% of *E. coli* and 83.3% of *Klebsiella spp.* were resistant to at least three classes of antibiotics.[5,13,15] This level of multidrug resistance poses a major challenge for the treatment of UTIs, as it limits the available therapeutic options. The findings also highlight the need for rapid diagnostic methods to detect resistant strains early, allowing for more targeted and effective treatment strategies.[11,12,16]

## LIMITATIONS

While this study provides valuable insights into the prevalence of AmpC-producing *Klebsiella spp.* and *E. coli* in the southwest region of Bangladesh, there are some limitations to consider. First, the study focused on urine samples and the results may not fully represent the broader spectrum of AmpC-producing pathogens in other infection sites. Second, the sample size of 51 urine samples may limit the generalizability of the findings.

## CONCLUSIONS

In conclusion, this cross sectional study provides important data on the prevalence of AmpC-producing *Klebsiella spp.* and *E. coli* in urine samples from the southwest region of Bangladesh. The high prevalence of AmpC production and multidrug resistance underscores the need for vigilant antimicrobial surveillance and the implementation of effective antimicrobial stewardship programs. The results also highlight the importance of alternative treatment options, such as nitrofurantoin, in the management of UTIs caused by resistant pathogens. Ongoing efforts to combat antibiotic resistance in *Klebsiella spp.* and *E. coli* are critical to improving patient outcomes and reducing the burden of antimicrobial-resistant infections in this region.

## RECOMMENDATION

Further studies with larger sample sizes and more diverse sample types (e.g. blood, wound and respiratory samples) are needed to better understand the regional burden of AmpC-producing pathogens and their antibiotic resistance profiles. Additionally, the study did not explore the genetic mechanisms behind AmpC production, such as the identification of specific genes (e.g., blaAmpC or plasmid-mediated AmpC genes). Future studies should aim to characterize the molecular basis of AmpC resistance and the potential for horizontal gene transfer, which can contribute to the spread of resistance in clinical settings.

## ACKNOWLEDGEMENTS

We thank all the patients, administrative officials, laboratory higher officials, lab in charge, scientific officers, medical technologists and technicians of Ibn Sina Hospital and Nurul Islam Diabetic Hospital Jashore for giving us the opportunity to study.

## AUTHORS CONTRIBUTIONS

Contribution to Concept, Design and Data - TM, KNA
Accountability - TM, KNA, FNJ, NN, ID, PP
Drafting and Critical revision - TM, KNA
Final approval - TM, KNA, FNJ, NN, ID, PP

## DISCLOSURE

The authors declared no conflict of interest.

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Case Report

Marine City Medical College Journal

# A Middle-Aged Male Presenting with Unilateral Leg Swelling and Impaired Renal Function: A Case Report and Literature Review

Pradip Kumar Dutta[1*] Rana Kumar Saha[2] Sudipa Dutta[3] Iffat Nashin[4]

## ABSTRACT

**Background:** Deep Vein Thrombosis (DVT) may serve as a paraneoplastic sign, sometimes revealing an occult malignancy. Non-Hodgkin's Lymphoma (NHL) rarely presents solely as venous thromboembolism with renal dysfunction.

**Case Presentation:** A 51-year-old man presented with painful swelling of the left leg for 1.5 months. He had controlled hypertension, diabetes mellitus and dyslipidemia. Examination revealed tense pitting edema of the left leg, generalized non-tender lymphadenopathy and left pleural effusion. Laboratory investigations showed elevated ESR (78 mm/hr), serum creatinine (1.7⇨3.44 mg/dL) hypercalcemia (14.5 mg/dL) LDH (1167 U/L) CRP (150 mg/dL) and D-dimer (5.48 mg/dL). Doppler ultrasonography confirmed extensive DVT from the external iliac to the popliteal vein. Pleural fluid analysis revealed exudate with atypical cells and FNAC of an axillary lymph node suggested NHL. Acute kidney injury was attributed to tumor lysis syndrome or obstructive uropathy. The patient was referred to oncology but was lost to follow-up.

**Discussion:** Malignancy increases DVT risk by 2.2–5.3 times compared with the general population. Approximately 7.6% of apparently idiopathic DVT cases are diagnosed with cancer within 6–12 months. NHL can rarely manifest initially as DVT without B-symptoms or bulky lymphadenopathy. Hypercalcemia and elevated LDH indicate aggressive disease biology and poor prognosis.

**Conclusion:** Thorough malignancy screening, including lymph node evaluation, pleural fluid cytology and cross-sectional imaging-should be performed in patients with unexplained DVT, particularly when systemic features such as hypercalcemia or lymphadenopathy are present.

**Key words:** Acute kidney injury; Deep vein thrombosis; Malignancy screening; Non-Hodgkin's lymphoma.

## INTRODUCTION

Venous Thromboembolism (VTE) is a well-recognized complication of cancer and may be its first clinical manifestation. Patients with malignancy have a 2.2–5.3-fold increased risk of DVT or pulmonary embolism compared to the general population.[1,2] Among those initially diagnosed with idiopathic DVT, about 7.6% are found to have cancer within 6–12 months.[3]

Non-Hodgkin's Lymphoma (NHL) one of the most common hematologic malignancies, can trigger thrombosis through tumor-derived tissue factor, cytokine release and mechanical compression of veins by lymphadenopathy.[4,7] While NHL commonly presents with lymphadenopathy or B-symptoms, rare cases manifest primarily as venous thromboembolism. Hypercalcemia and elevated Lactate Dehydrogenase (LDH) are markers of aggressive lymphoma biology and adverse prognosis.[5-7]

We report a middle-aged male whose initial presentation of NHL was extensive DVT and Acute Kidney Injury (AKI). This case reinforces the need for comprehensive evaluation of unexplained DVT and expands on current literature.

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Date of Submitted : 10.02.2025
Date of Accepted : 15.03.2025

Volume 04 | Issue 01 | April 2025 | 27-29

## CASE PRESENTATION

A 51-year-old man presented on 30th March, 2023 in the Department of Nephrology, Marine City Medical College Hospital, Chattogram with painful swelling of the left leg for 1.5 months (Fig 1). He had hypertension, type 2 diabetes mellitus and dyslipidemia controlled on insulin, linagliptin, bisoprolol and atorvastatin. He denied smoking, recent travel, surgery, trauma or prolonged immobilization.

On examination, the left leg was tense and exhibited pitting edema up to the mid-thigh, distal pulses were intact. His BMI exceeded 30 kg/m². Generalized, discrete, non-tender lymphadenopathy (1–5 cm) was palpated in cervical, axillary and inguinal areas. Chest examination showed decreased breath sounds and dullness at the left lung base, suggesting pleural effusion (Fig 2).

**Laboratory and Imaging Findings**

| Parameter | Result | Reference range |
|---|---|---|
| Hemoglobin | 12.2g/dl | 13-17g/dl |
| ESR | 78mm/hr | <20mm/hr |
| Serum creatinine | 1.7 3.44 mg/dL (Increased after 5 days) | 0.6–1.3 mg/dL |
| Serum calcium | 14.5 mg/dl | 8.5–10.5 mg/dL |
| LDH (Lactate dehydrogenase) | 1167 U/L | 140–280 U/L |
| CRP | 150mg/dl | <10 mg/dL |
| D-dimer | 5.48 mg/dL | <0.5 mg/dL |

- Doppler ultrasonography (Fig 3 ): Extensive DVT from external iliac to popliteal vein.
- Chest radiograph/ultrasound: Moderate left pleural effusion.
- Pleural fluid analysis: Exudate with atypical/suspicious cells.
- FNAC of axillary lymph node: Suggestive of non-Hodgkin's lymphoma (Subtyping pending).

**Figure 1** Unilateral leg swelling

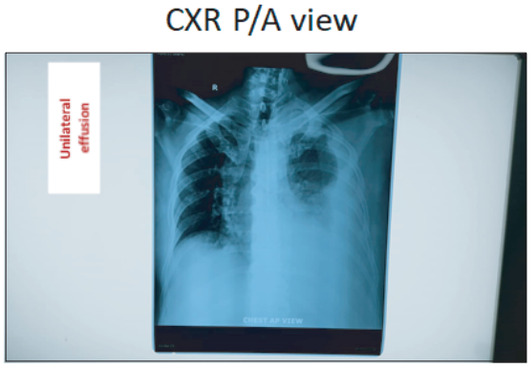


**Figure 2** Left sided pleural effusion

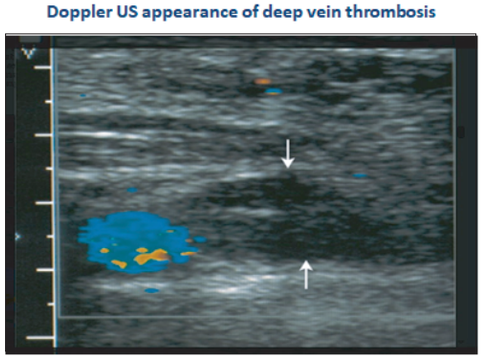


**Figure 3** Doppler USG

The AKI was attributed to tumor lysis syndrome or ureteric obstruction secondary to lymphadenopathy and hypercalcemia. The patient received anticoagulation and supportive therapy, was referred for oncology evaluation, but was lost to follow-up after discharge.

## DISCUSSION

### *DVT as a Paraneoplastic Marker*

Malignancy-associated VTE is a well-described entity, with cancer increasing thrombosis risk by 2.2–5.3 times.[1,2] Prandoni et al. reported that 7.6% of apparently idiopathic DVT cases reveal cancer within a year.[3] The pathogenesis involves tumor cell–derived tissue factor, pro-inflammatory cytokines and direct venous compression.[4,7]

### *NHL Presenting as Isolated DVT*

NHL can rarely present without constitutional symptoms (Without classic "B-symptoms") or bulky lymphadenopathy. Lee and Peterson described a follicular lymphoma case with iliac vein thrombosis

and pleural effusion.[4] Ferri documented Burkitt lymphoma with axillary vein thrombosis complicated by tumor lysis.[5] Our patient similarly had extensive iliac–popliteal thrombosis without prior hematologic signs, highlighting the importance of considering lymphoma in atypical DVT. In our case, extensive evaluation-including lymph node FNAC and pleural fluid cytology-was required to reveal the malignancy, echoing previous findings.[6]

**NHL-Associated DVT Cases in Literature**

| Author and year | Age/Sex | Site of thrombosis | Lymphoma subtype | Other features | Outcome |
|---|---|---|---|---|---|
| Prandoni et al. 2005[3] | 56/M | Femoral vein | Diffuse large B-cell | Weight loss, night sweats | Complete remission after chemo |
| Lee & Peterson, 2013[4] | 62/F | Iliac vein | Follicular | Pleural effusion | Partial remission |
| Ferri's Clinical Advisor, 2024[5] | 47/M | Axillary vein | Burkitt | Tumor lysis syndrome | Died of sepsis |
| Case presentation data[6] | 51/M | External iliac to popliteal vein | Non-Hodgkin's (Unspecified) | Hypercalcemia, AKI | Lost to follow-up |

***Renal Involvement and Hypercalcemia***

Renal impairment in NHL may result from tumor lysis, ureteric obstruction, hypercalcemia-induced vasoconstriction or parenchymal infiltration.[5,7] Hypercalcemia and markedly raised LDH, present here, though uncommon in NHL, signals aggressive subtypes and portends poor prognosis.[7,8] Our patient's AKI and elevated uric acid likely reflected tumor lysis and possible ureteric compression.

***Screening and Diagnostic Approach***

Systematic evaluation, including cross-sectional imaging, lymph node biopsy or FNAC and pleural fluid cytology-is recommended in unprovoked DVT with systemic features such as weight loss, hypercalcemia or lymphadenopathy are present.[1-3,7] Prandoni et al. emphasize follow-up imaging and laboratory evaluation for at least 12 months after the DVT episode.[3] Advanced modalities like PET-CT aid staging and treatment planning.[8]

## CONCLUSION

Non-Hodgkin's lymphoma can present as isolated DVT with renal dysfunction, mimicking idiopathic thromboembolism. This case underlines the need for comprehensive malignancy screening in patients with unexplained DVT, especially when accompanied by hypercalcemia, lymphadenopathy or elevated LDH. Early identification may improve outcomes by expediting diagnosis and therapy.

## ACKNOWLEDGEMENT

The authors acknowledge the support of diseased family. They also express their heartfelt thanks to the all associate of Marine City Medical College & Hospital for active co-operations.

## AUTHORS CONTRIBUTIONS

Contribution to Concept, Design and Data - PKD, RKS
Accountability - IN, SD, RKS, PKD
Drafting and Critical revision - PKD, RKS
Final approval - IN, SD, RKS, PKD

## DISCLOSURE

All the authors declared no conflicts of interest.

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## Editorial Review

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- **Professor Dr. Prabir Kumar Das**
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*(List is not according to seneority)*

MARINE CITY MEDICAL COLLEGE

Marine City Medical College Journal (MCMCJ)

# Information to Authors

Marine City Medical College (MCMC) started its historical and memorable journey in the year 2013. MCMC is one of the famous and reputed Medical College among the Private Medical Colleges in Bangladesh. It is situated in port city, Chattogram. The aim of the MCMC is to attain a standard level in Health & Medical education at home and abroad.

Marine City Medical College is affiliated under Chittagong Medical University & approved by the Ministry of Health & Family Welfare, Government of People's Republic of Bangladesh. A very good number of academicians, researchers and skill professionals are performing in this institute.

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Marine City Medical College inaugurated to publish a double blinded, peer reviewed scientific journal from April 2022.

The "Marine City Medical College Journal (MCMCJ)" is a half yearly published eg. April & October accorded with a view to translation of current research into clinical practice. It is the official publication of the Marine City Medical College - having ISSN : 3080-1257.

MCMCJ publishes article of authors from any part of the globe, but has a special interest in publishing research articles of authors from Bangladesh and of relevance to developing countries. It publishes Editorial, Original (Research) article, Special article, Review article, Short communication, Case report and Letters on new findings of Medical Science.

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Manuscript (Papers) are submitted to the Managing Editor or authorised persons or by Email at any time. Papers accepted for publication are subjected to peer review and editorial revision. Manuscript should be typed in English (Font size and style: 10, Times New Roman) on one side of white bond paper of A4 size with margins of at least 2.5 cm, using double space throughout. With full title (Title should be concise and informative) accompanied by a cover letter signed by Principal and Co-authors including name, academic degrees, designation, the departmental and institutional affiliation. Complete address, Cell number including Email address of Corresponding author should be mentioned. Not more than 6 (Six) authors will be accepted for all manuscripts.

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A structured abstract should not be of more than 250 words. It should be a factual description of the study (Includes aim or Objectives) Methods (Includes patient population, procedures and data analysis) Results and Conclusion. The abstract should contain the data to support the key findings or conclusions of the study and this should be self explanatory without references to the text. the first time an abbreviated term is used it should be spelled out in full form and follow with the abbreviation in parentheses for example:- CHD (Coronary Heart Disease). Please do not cite any references in the abstract.

3 (Three) to 10 (Ten) key words may be provided below the abstract.

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**Editorial :** It is a invited article. Based on current affairs of Medical Science with any disciplines. Maxium length of the editorial may be with in 1000-1200 words and number of references maxium in 10 (Ten).

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- Introduction (Length should not be more than 500 words)
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- Limitation
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- Recommendation
- Acknowledgements
- Disclosure

Single digit numbers used in the text should be in words except datas and reference numbers. Maximum length of text may be with in 2000-2500 words (Excluding references). The total number of reference should not be less than 15 (Fifteen) for the original article.

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It is a prestigious article, which is divided into the following sections with headings :

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- Figures / Legends
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- Disclosure

Maximum length of the text may be with in 1000-1500 words (Excluding references). The total number of reference should not be less than 10 (Ten).

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Letter should be brief and to the point with in 500-600 words only.

It is noted that standard abbreviations should be used whenever. The full form for which the abbreviations stands followed by the abbreviation in parenthesis should precede the use of the abbreviation in the text except for standard ones like $45^{O}$c, 35mg/L etc in all types of text.

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Regarding references please follow the Vancouver style (Uniform requirements for manuscripts submitted to biomedical journals prepared by the International Committee of Medical Journal Editors (ICMJE guideline http://www.icmje.org).

Reference citations in the text should be numbered in arabic numerals at the end of the sentence eg [1,2] consecutively in order in which they are mentioned in the text.

Book references should have the name of the authors, chapter title, editors, *Book name,* the edition, place of publication, the publisher, the year and the relevant pages.

Journal references should have the name of the authors, title of the article, editors, *name of the journal,* volume and issue number, place of publication, the publisher, the year and relevant pages.

The first six authors of a work should be named.

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**Journal reference :** Riddel V, Watkinson J, Gazet M. Thyroidectomy : Preventation of bilateral recurrent nerve palsy. *British Journal of Surgery.* 2021;57(2):8-12.

**Citation from a website :** Ardehali MM, Irani S, Firouzifar M. A unique intraluminal growth of juvenile nasopharyngeal angiofibroma : A Case report. *BioMedicine.* 2020;10(3):41-44.

DOI : 10.37796/211-8039.1019.

**Table**

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