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Original Article

Clinical Spectrum and Microbiological Profile of Acute Pyelonephritis in Patients with Diabetes Mellitus in Relation to Glycaemic Control

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ABSTRACT

Background: Diabetes mellitus is one of the most prevalent lifestyle diseases in developing countries such as India, with a steadily rising burden attributed to urbanization, obesity, and sedentary lifestyles. Individuals with diabetes are predisposed to infections due to impaired immune function, among which urinary tract infections are particularly common. Acute pyelonephritis (APN) represents a severe form of urinary tract infection and may be associated with increased morbidity in diabetic patients. Diabetes mellitus has been identified as a major risk factor for complicated pyelonephritis, including emphysematous pyelonephritis. However, limited data are available from Kerala regarding the clinical and microbiological profile of acute pyelonephritis in patients with diabetes and its association with the duration and control of diabetes.

Aims and Objectives - To study the clinical and microbiological profile of acute pyelonephritis in diabetes mellitus.

Methods: This prospective observational study was conducted in the Department of General Medicine at KMCT Medical College Hospital over a period of six months after obtaining Institutional Ethics Committee approval. Adult patients (≥18 years) with diabetes mellitus diagnosed with acute pyelonephritis based on clinical features and radiological evidence were included. Data were collected using a structured proforma. Statistical analysis was performed using SPSS version 27.

Results: Patients with moderate to poor glycaemic control (HbA1c >7%) more frequently presented with fever, dysuria, flank pain, and vomiting compared to those with well-controlled diabetes. Fever was the most common presenting symptom across all HbA1c categories. Although symptom distribution varied among glycaemic groups, no statistically significant association was observed between HbA1c levels and individual clinical symptoms. Escherichia coli was the most commonly isolated uropathogen, accounting for 48.57% of positive urine cultures, followed by Klebsiella species and mixed bacterial growth; multidrug-resistant organisms were also identified. A proportion of urine samples showed no microbial growth, likely due to prior antibiotic exposure.

Conclusion: Acute pyelonephritis in patients with diabetes mellitus showed variations in clinical presentation and microbiological profile across different levels of glycaemic control; however, these differences were not statistically significant. Larger studies with longer follow-up are required to better elucidate the relationship between glycaemic control and the clinical course of acute pyelonephritis in diabetic patients.

Keywords: *Diabetes Mellitus, Dysuria, Ecoli, Fever, Pyelonephritis, Urinary Tract Infection.*

INTRODUCTION

Diabetes Mellitus is one of the most common lifestyle diseases prevalent among developing countries like India. The disease shows an increasing trend over the years, with obesity and unhealthy lifestyle being the main contributing factors.

Estimates points towards the increased burden of Diabetes mellitus on Indian population which is around 77 million (2019) and is expected to rise exponentially in the coming years (Pradeepa R et al., 2021).[1]

Diabetes Mellitus being an immunocompromised state, it stands out as a main hub for harboring infections in which urinary tract infection appears to be one of the most common one. Acute pyelonephritis is a bacterial infection causing inflammation of the kidneys. It is a part of evolving renal infection in which bacteria ascend through the bladder in majority of cases, but may also reach the kidney through the bloodstream.

Emphysematous pyelonephritis is a type of severe acute pyelonephritis characterized by necrotizing infection and presence of gas in the renal parenchyma, perinephric tissue and collecting duct. The classical presentation of acute pyelonephritis revolves around fever, flank pain and nausea/vomiting.

Diabetes mellitus was identified as the leading risk factor for complicated pyelonephritis, accounting for 54.4% of cases. This was followed by renal stones (14.4%), benign prostatic hyperplasia (6.7%), immunocompromised status (3.3%), urethral stricture or meatal stenosis (3.3%), and neurogenic bladder (2%). Urine culture results showed that 51.7% of patients had no microbial growth, while 48.3% demonstrated positive culture findings (Umesha L et al., 2018).[2]

Pyelonephritis most commonly develops as a result of an ascending urinary tract infection that travels upward from the bladder to the kidneys. In some cases, the infection can also reach the kidneys through the bloodstream (Belyayeva M et al., 2025).[3]

These studies help in understanding the clinical pattern, microbiological profile of APN in DM. It also throws a light on the relationship of duration and control of diabetes to the incidence of pyelonephritis.

Rationale- The rationale for this research comes from the compelling need to tackle the knowledge gap revolving around acute pyelonephritis in diabetes mellitus as there haven't been much studies conducted in Kerala in the said area of focus. The increased prevalence of diabetes and its relation to acute pyelonephritis warrants a focused study into this comorbidity. By elucidating the clinical pattern, microbiological profile linked with acute pyelonephritis in diabetes, this study comprehensively aims to improve clinical outcomes and guide evidence-based practice.

REVIEW OF LITERATURE

In individuals with diabetes mellitus, pyelonephritis tends to involve both kidneys more often and is associated with increased complication rates. Nearly 90% of emphysematous pyelonephritis and emphysematous cystitis cases occur in patients with diabetes (Anandasekar P et al., 2024).[4]

Individuals with diabetes mellitus often experience weakened immune defenses, which predisposes them to more severe infections. Among the common complications seen in diabetic patients, urinary tract infections are particularly frequent (Kamei J et al., 2021).[5]

Acute pyelonephritis in individuals with and without diabetes presents with largely comparable clinical features. However, the association between diabetes and outcomes such as increased mortality and longer hospital stays remains unclear. Larger, well-designed randomized prospective studies are needed to better understand this relationship (Trivedi SC et al., 2016).[6]

Emphysematous pyelonephritis (EPN) is a life-threatening, destructive infection of the kidney in which gas forms within the renal tissue. It occurs most frequently in women with diabetes and in individuals with compromised immune systems (Kolla PK et al., 2012).[7]

Individuals with diabetes mellitus (DM) experience infections more frequently compared to non-diabetic individuals, and these infections often progress with greater severity and complications. This increased susceptibility is thought to be partly due to impaired immune function. Although certain cellular immune responses are reduced in laboratory studies, significant abnormalities in adaptive immunity have not been clearly demonstrated in diabetic patients (Geerlings SE et al., 1999).[8]

Excessive and prolonged nutrient intake, as seen in obesity, can create a chronic pro-inflammatory environment accompanied by oxidative stress. Elevated levels of cytokines such as TNF-α (Tumor Necrosis Factor - alpha) and IL-6 (Interleukin-6), commonly found in obesity and type 2 diabetes, may disrupt insulin signaling pathways and impair insulin activity. As a result, the normal anti-inflammatory role of insulin is diminished, further contributing to ongoing inflammation (Dandona P et al., 2004).[9]

Microvascular disease in diabetes also compromises renal tissue perfusion, impairing antibiotic penetration and immune cell delivery to infected tissue. In addition, high glucose concentrations in tissues may enhance bacterial virulence and biofilm formation, worsening infection outcomes.

Recent studies examining the relationship between diabetes and urinary tract infections have offered useful perspectives, especially regarding infection risk and clinical outcomes. However, significant progress in understanding the topic remains limited. Important issues such as true incidence rates, best therapeutic strategies, and the impact of metabolic control still require further investigation to improve knowledge and optimize patient care for this frequent clinical concern (Nicolle LE et al., 2005).[10]

EAU Guidelines Panel on Urological Infections states that diagnostic confirmation relies on urine analysis, urine culture, and imaging. While ultrasonography serves as an initial modality, CT scanning is superior in detecting complications like abscesses or gas formation in renal parenchyma (EAU Guidelines Panel on Urological Infections).[11]

Flores-Mireles AL et al., 2015, review highlights recent basic science research that is uncovering the molecular mechanisms involved in host–pathogen interactions during urinary tract infections (UTIs) and explains how these interactions contribute to disease development. It also examines ongoing work aimed at applying these scientific insights to develop improved therapeutic approaches for UTIs.[12]

Abu-Humaidan AH et al., 2025, study results indicate a potential link between diabetes mellitus and an increased likelihood of isolating organisms resistant to nitrofurantoin. Identifying patients based on risk factors such as diabetes may help optimize empirical treatment decisions and support efforts to limit antimicrobial resistance (AMR).[13]

Mama M et al., 2018, found that urinary tract infections were observed more frequently among individuals with diabetes mellitus. The majority of infections were caused by Gram-negative bacilli belonging to the Enterobacteriaceae family, with Escherichia coli being the most commonly isolated organism. The presence of significant bacteriuria showed a meaningful association with alcohol intake, patient gender, and poor glycaemic control.[14]

Bhat SK et al., 2021, studied that emphysematous pyelonephritis (EPN) is an uncommon yet severe, pus-forming infection of the kidney that occurs predominantly in patients with diabetes. Effective patient management requires strong clinical vigilance, early and accurate diagnosis, and a collaborative multidisciplinary approach that includes appropriate antimicrobial therapy and, when necessary, surgical intervention to achieve improved clinical outcomes.[15]

Multiple components of the immune system are impaired in individuals with diabetes. The function of polymorphonuclear leukocytes is reduced, especially in the presence of acidosis, and key processes such as leukocyte adhesion, chemotaxis, and phagocytosis can be compromised (Joshi N et al., 1999).[16]

Asymptomatic bacteriuria (ASB) occurs more frequently in women with diabetes and may be considered among the complications associated with the condition in this population (Geerlings SE et al., 2000).[17]

Bonadio M et al., 2006, studied group of patients with asymptomatic urinary tract infections, most of which were acquired in the hospital, diabetes mellitus did not appear to affect the frequency of isolating specific uropathogens or alter their antimicrobial susceptibility profiles.[18]

Most of the isolated pathogens demonstrated resistance to commonly used antibiotics such as amoxicillin, ciprofloxacin, cephalosporins, and nitrofurantoin. However, they generally remained sensitive to agents like gentamicin, amikacin, and meropenem (Shill MC et la., 2010).[19]

METHODOLOGY

A. Study design: A Prospective observational study
B. Study setting: Department of General Medicine, KMCT Hospital
C. Study duration: 6 months after IEC approval.
D. Study participants

Inclusion criteria:

- Adult diabetic patients (18 years or older) diagnosed with acute pyelonephritis admitted in KMCT hospital from May 2024 to October 2024
- Confirmation of acute pyelonephritis by combination of clinical symptoms of urinary tract infection and radiological evidence suggestive of acute pyelonephritis.

Exclusion criteria:

- Severe anemia (Hb < 8 gm%)

- Gestational diabetes
- Recent genito-urinary procedure
- Patient on other immunocompromised state/malignancy

E. Sampling

- Sampling population: Adult (18 years or older) diabetes mellitus patients diagnosed with acute pyelonephritis admitted under Department of General medicine in KMCT hospital from May 2024 to October 2024, who fulfill the inclusion criteria and consented to the study.
- Sampling size: 70 patients
- Participants are stratified into three groups based on their HbA1c levels to evaluate the impact of glycemic control on acute pyelonephritis outcomes. Group 1 includes patients with HbA1c between 5-7%, representing well-controlled diabetes. Group 2 comprises those with HbA1c between 7.1-10%, indicating moderately controlled diabetes. Group 3 consists of patients with HbA1c between 10.1-13%, signifying poorly controlled diabetes. All 3 groups were evaluated for common clinical symptoms of acute pyelonephritis.
- And the common microorganisms responsible for acute pyelonephritis are identified through urine cultures in all patient groups.

F. Study procedure: Consecutive sampling

G. Methods of data collection: This study is conducted after obtaining clearance from ethical committee of the institution. Written informed consent was taken from all the patients included in the study.

H. Prospective study conducted for all diabetic patients hospitalized at KMCT hospital with a diagnosis of acute pyelonephritis. A detailed history of the clinical pattern pertaining to acute pyelonephritis was taken with emphasis on duration, treatment and control of diabetes mellitus. Relevant investigations including HbA1C, microbiological profile of acute pyelonephritis was collected prospectively.

I. Data analysis:

Using SPSS Statistical software
Continuous variables presented by mean, standard deviation and confidence interval
Categorical variables presented using frequency and percentage
Fisher's Exact test used to study the association between sociodemographic factors and clinical pattern
$P<0.05$ considered statistically significant.

RESULTS

Table -1 **Socio-demographic Details of Participants**

Age (mean ± SD)	Gender (n=70)		Socio-economic status
61.9 ± 9.75	Female	Male	Lower middle
	44	26	

Total 70 participant data collected. The study population had a mean age of 61.9 ± 9.75 years, indicating that most participants were older adults. The study included 44 females and 26 males. Regarding socio-economic status, the majority of participants belonged to the lower-middle socio-economic class, suggesting that the study cohort largely represented individuals from a modest economic background.

Table 2 - **Relationship Between Duration of Diabetes and HbA1c Categories**

HbA1c category (%)	**Duration ≤10 years**	**Duration >10 years**
A (5 –7.0)	2	1
B (7.1–10.0)	35	23
C (10.1–13.0)	4	5

Table 2 shows the distribution of HbA1c levels among patients according to the duration of diabetes. Among patients with diabetes for ≤10 years, the majority (35/41) had HbA1c levels in the 7.1–10% range, indicating moderately uncontrolled glycemia, while only a few patients had well-controlled (5–7%) or poorly controlled (10.1–13%) HbA1c. In patients with diabetes for >10 years, a similar pattern was observed, with most patients (23/29) in the 7.1–10% range, but a slightly higher proportion had HbA1c >10% (5 patients) compared to the ≤10-year group.

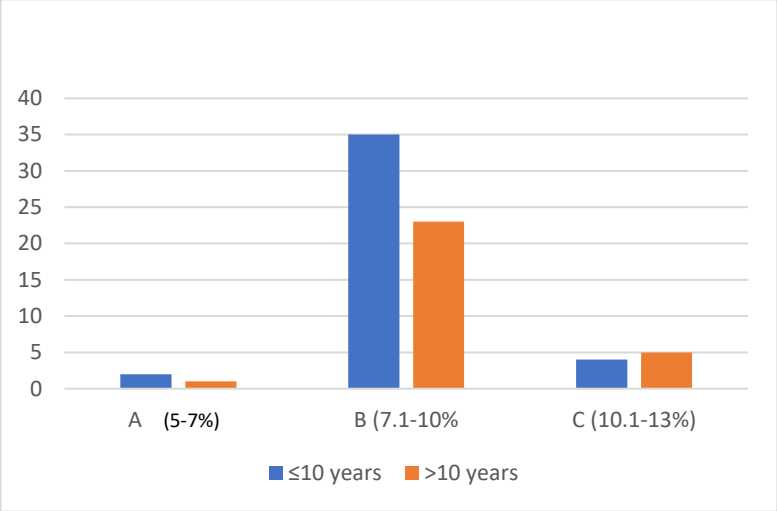

Image 1- **Relationship Between Duration of Diabetes and HbA1c Categories**

Table 3 **- Frequency of Symptoms Across Different HbA1c Categories**

Symptom	**HbA1c 5-7% n (%)**	**HbA1c 7.1–10% n (%)**	**HbA1c 10.1–13% n (%)**	**p-value**
Fever	3 (100.0%)	56 (96.6%)	9 (100.0%)	1
Dysuria	1 (33.3%)	32 (55.2%)	3 (33.3%)	0.406
Flank pain	2 (66.7%)	40 (69.0%)	6 (66.7%)	1
Vomiting	2 (66.7%)	27 (46.6%)	5 (55.6%)	0.694

Table 3 presents the frequency of various symptoms among patients stratified by HbA1c levels. Fisher's Exact test was applied to assess the association between glycemic control and the presence of symptoms due to small cell counts.

As shown in table, the distribution of clinical symptoms across different HbA1c categories is presented. Fever was the most commonly reported symptom and showed a uniformly high prevalence across all HbA1c groups, occurring in 100% of patients with HbA1c 5–7% and HbA1C 10.1–13%, and in 96.6% of those with HbA1c 7.1–10%. However, this difference was not statistically significant (p = 1.0).

Dysuria was observed more frequently in patients with moderately uncontrolled glycaemia (HbA1c 7.1–10%; 55.2%) compared with those having HbA1c 5–7% and 10.1–13% (both 33.3%), though this variation did not reach statistical significance (p = 0.406).

Similarly, flank pain was commonly reported across all HbA1c categories, with comparable proportions in the HbA1C 5–7% (66.7%), HbA1C 7.1–10% (69.0%), and HbA1C 10.1–13% (66.7%) groups, showing no significant association with glycaemic control (p = 1.0). Vomiting was most frequent in the HbA1c 5–7% group (66.7%), followed by the HbA1C 10.1–13% (55.6%) and 7.1–10% (46.6%) groups, but the differences were not statistically significant (p = 0.694).

Overall, although certain symptoms—particularly dysuria—were relatively more frequent in patients with HbA1c 7.1–10%, no statistically significant association was observed between symptom prevalence and HbA1c levels in the present study.

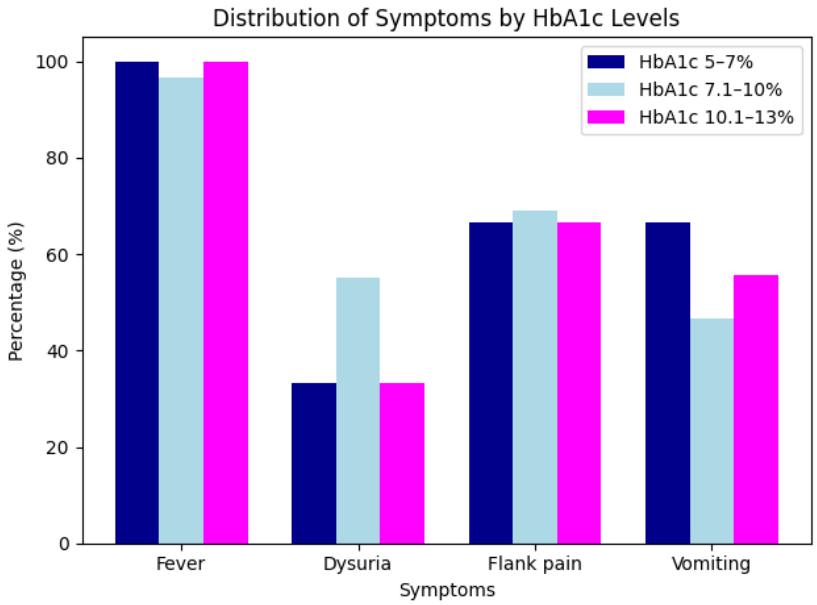

Image 2- **Frequency of Symptoms Across Different HbA1c Categories**

Table 4 - **Microbiological Profile of Urine Culture Isolates**

Organism	**Percentage**
Acinetobacter	1.43%
E.coli	48.57%
Klebsiella	10.00%
MDR *E.coli*	11.43%
MDR *Klebsiella*	1.43%
Mixed	7.14%
Nil	18.57%
Pseudomonas	1.43%

Table 4 presents the distribution of urine culture isolates among the study participants. Escherichia coli was identified as the predominant pathogen, accounting for 48.57% of positive cultures. This was followed by multidrug-resistant (MDR) E. coli (11.43%) and Klebsiella species (10%). Mixed bacterial growth was detected in 7.14% of samples, while 18.57% of cultures showed no bacterial growth. Less frequently isolated organisms included Acinetobacter, MDR Klebsiella, and Pseudomonas species, each representing 1.43% of cases.

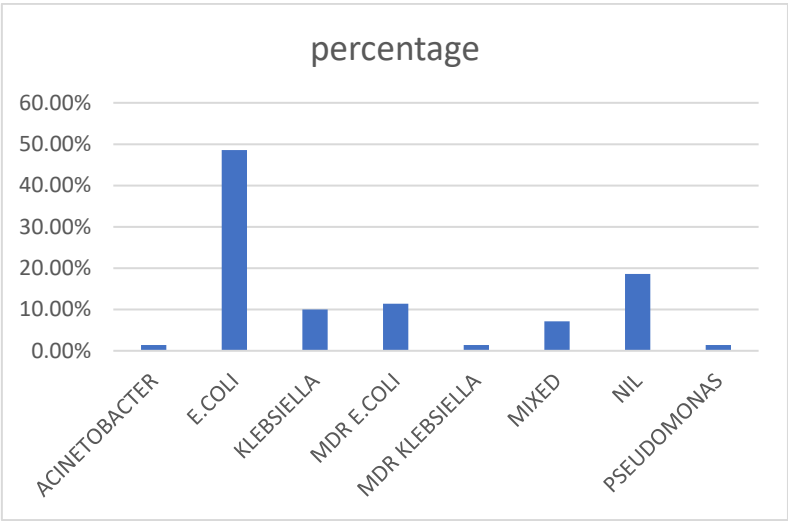

Image 3 - **Microbiological Profile of Urine Culture Isolates**

DISCUSSION

In the present study, the distribution of symptoms across different HbA1c categories highlighted variations in the clinical presentation of acute pyelonephritis (APN) among diabetic patients. While differences in symptom prevalence were observed across glycaemic categories, no statistically significant association was identified between HbA1c levels and individual symptoms. Fever was the most frequently reported symptom across all HbA1c categories, reflecting its role as a predominant clinical manifestation of APN irrespective of glycaemic status. Dysuria showed a relatively higher prevalence among patients with HbA1c levels between 7.1-10%, whereas flank pain demonstrated comparable distribution across all groups. Vomiting was observed more frequently among patients with HbA1c 5-7% and 10.1-13% compared to the intermediate group. These findings suggest heterogeneity in symptom presentation rather than a consistent increase in symptom burden with worsening glycaemic control.

Asymptomatic bacteriuria (ASB) was identified in 29% of women with type 2 diabetes. Factors associated with a higher likelihood of ASB included older age, the presence of macroalbuminuria, lower body mass index, and a history of urinary tract infection within the past year. No clear relationship was found between current HbA1c levels and the occurrence of ASB (Geerlings SE et al., 2000).[17]

Certain infections are seen more frequently in individuals with diabetes, and some are found almost exclusively in this group. Additionally, various infections tend to present with greater severity and carry a higher likelihood of complications in diabetic patients (Joshi N et al.,1999).[16]

The present study revealed that Escherichia coli was the most frequently isolated uropathogen, accounting for 48.57% of positive urine cultures. This finding is consistent with previous studies reporting E. coli as the predominant causative agent of urinary tract infections (UTIs) due to its strong adherence properties and virulence factors. A considerable proportion of isolates were identified as multidrug-resistant (MDR) E. coli (11.43%), highlighting the growing concern of antimicrobial resistance among common uropathogens. Klebsiella species constituted 10% of isolates, while mixed bacterial growth was observed in 7.14% of cases, suggesting possible polymicrobial infections. Notably, 18.57% of urine samples showed no bacterial growth, which may be attributed to prior antibiotic use or non-bacterial causes of symptoms. Rare isolates included Acinetobacter, MDR Klebsiella, and Pseudomonas species (each 1.43%), reflecting their occasional but clinically important role in complicated UTIs.

The overall prevalence of urinary tract infection was 75.4%. The most frequently identified organisms included Escherichia coli (25.6%), Enterococcus species (18.7%), and Klebsiella species (8.1%). The majority of isolates showed good susceptibility to nitrofurantoin (80.8%), gentamicin (76.8%), and amikacin (72.1%), while high resistance rates were observed with cefpodoxime (77.6%), cefixime (70.8%), and cefadroxil (65.0%) (Kande S et al., 2021).[20]

Bonadio M et al., 2006, found that Most patients presented with asymptomatic UTI. Isolation rates of E. coli, Enterococcus, and Pseudomonas species were similar between diabetic and non-diabetic women and men, with the exception of Pseudomonas in men, which was more common in the non-diabetic group ($p \leq 0.02$). Comparable patterns were also seen in catheterized patients. No significant difference in antimicrobial resistance to ampicillin, nitrofurantoin, cotrimoxazole, or ciprofloxacin was observed between groups.[18]

Prompt identification and appropriate management of urinary infections in individuals with diabetes may reduce the need for nephrectomy. The use of CT imaging has enabled the development of a classification system based on renal gas patterns in patients with emphysematous pyelonephritis. In addition, specific risk factors have been recognized to help guide clinical decision-making (Pontin AR et al., 2009).[21]

Kumar S et al., 2014, study concluded that Individuals with diabetes who develop pyelonephritis often experience a more severe clinical course. Patients with emphysematous pyelonephritis (EPN) tend to have worse treatment outcomes compared to those with non-emphysematous pyelonephritis (NEPN). Although mortality rates are similar between the two groups, the need for nephrectomy is substantially higher in EPN cases. The presence of shock or altered mental status at the time of presentation is associated with a poor prognosis in EPN.[22]

The findings of the present study underscore the importance of maintaining a high index of suspicion for acute pyelonephritis in patients with diabetes, even when urinary symptoms are mild. Early diagnosis, appropriate antimicrobial therapy, and optimal glycaemic control are essential to prevent complications. Patient education focusing on hydration, glycaemic management, and early medical consultation for urinary symptoms may significantly reduce morbidity associated with APN in the diabetic population.

Limitation of the study

Its single-center design and small sample size may limit the generalizability of the findings. The cross-sectional nature of the study precludes establishing a causal relationship between HbA1c levels and clinical severity of acute pyelonephritis. HbA1c was assessed at a single time point, which may not reflect long-term glycaemic variability. The absence of a

significant association between HbA1c categories and symptoms may be due to limited statistical power. Additionally, potential confounding factors such as prior antibiotic use, diabetic complications, and comorbid conditions were not fully accounted for. The study also did not evaluate treatment outcomes or long-term renal prognosis, limiting its clinical applicability. Future multicenter, longitudinal studies with larger sample sizes and comprehensive clinical and microbiological assessments would help strengthen and extend these findings.

CONCLUSION

The present study aimed to evaluate the symptom presentation, clinical profile, and common causative organisms of acute pyelonephritis among diabetic patients across different HbA1c categories. Although variations were observed in the frequency and pattern of symptoms, among different glycaemic groups and microbiological profile of urine culture, these differences were not found to be statistically significant.

The lack of significance may be attributed to the limited sample size and the cross-sectional design of the study. Hence, further research with a larger sample size and longer follow-up period is recommended to better understand the relationship between glycaemic control and the clinical course of acute pyelonephritis in diabetic patients.

Ethical Consideration: Study was conducted after getting approval from ethical committee KMCT Medical College, Mukkam, Kozhikode, Kerala

Declaration:

Conflicts of interests: The authors declare no conflicts of interest.
Author contribution: All authors have contributed in the manuscript.
Author funding: Nill

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