

Clinical profile and spectrum of bacteriuria in patients with diabetes: An analytical study

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ABSTRACT

Introduction: Diabetes is one of the modern-day epidemics with a spectrum of complications. Urinary tract infections (UTI) are common among patients with diabetes, and often it goes unnoticed in the initial period, which can later lead to complications. This study was planned to find out the magnitude of the problem of bacteriuria among diabetics and to look for its associated factors in diabetics. **Methodology:** A hospital-based study recruiting 100 eligible diabetics consecutively over a period of one year. Socio-demographic data were collected using a semi-structured questionnaire, and clinical examinations with relevant investigations were done. Informed written consent was taken. **Results:** Bacteriuria was found in 43 out of 100 participants. Prevalence was significantly more among females (54%) as compared to males (32%). Factors like poor glycaemic control, complications like neuropathy, diabetic foot were significantly associated with bacteriuria. E Coli was the most common bacterial isolate. **Conclusion:** Urinary tract infection is common in diabetic patients, especially females, and other clinical factors like uncontrolled sugar levels also play a role.

Keywords: Bacteriuria, diabetes, UTI

Background

Diabetes mellitus (DM) is considered a modern-day epidemic, and India is labelled as the diabetes capital of the world. Changing lifestyle, food habits, and urbanization can be attributed to the increase in incidence in India.

The latest data from the International Diabetes Federation (IDF) shows that the global burden of diabetes in 2020 is more than 450 million, out of which around 77 million belong to India.^[1]

Infections are of particular concern for diabetic patients. Diabetes can slow down the body's ability to fight infections by

weakening the immune system. People with diabetes are especially prone to foot infections, yeast infections, surgical site infections, and urinary tract infections (UTIs). Studies have shown that diabetics experience worse outcomes with infections.^[2-4]

A urinary tract infection (UTI) is an infection in any part of the body's urinary system from kidneys to the urethra. It is estimated that UTI accounts for 7 million hospital visits per year along with 1 million visits to the emergency department.^[5] The peri-ureteral region is the most common portal for bacterial entry.

The relationship between UTIs and diabetes was first found in the mid 20th century. Post-mortem studies during that time aided in establishing that there is an increased occurrence of UTIs among diabetics.^[3] This risk of UTI is especially more among females due to the shorter urethra and its anatomical proximity to the anus. Also, there is a two to three-fold increase in the risk of UTI

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among females with diabetes compared to non-diabetics, and there is early upper urinary tract involvement among diabetics.^[6-9]

Many reasons can be attributed to the increased risk of UTI in DM. Diabetes causes vascular changes that lead to the ineffective blood circulation of immune cells to fight infections, and it also causes autonomic neuropathy. Diabetes can also cause bladder dysfunction leading to defective micturition and urine retention, which increases the chances of UTI.^[7,10]

In UTI bacteria is often found in urine samples (bacteriuria). If the urine contains significant bacteria, but the patient does not have any symptom, then it is labelled as asymptomatic bacteriuria.

Among diabetics, bacteriuria is often found in urine samples during routine and microbiology testing. As stated above, diabetes is an immunocompromised state, so such unattended infections can later lead to complicated UTIs. Therefore, it is vital to detect these infections early in the primary care setting routinely to prevent complications later.^[7,11] Also, knowing about the susceptibility of diabetics to bacteriuria depending upon the glycaemic control and severity of diabetes can aid primary care physicians in guiding patients' prevention. Also, it will help them to make decisions on early clinical identification followed by prompt and appropriate treatment to avoid further complications.

Keeping this in mind, the current study was planned to know the clinical and microbial spectrum associated with bacteriuria and antimicrobial sensitivity of the organisms that cause UTIs in diabetics to aid in early identification and management.

Aims Objectives

1. To study the clinico-microbiological profile of bacteriuria in diabetes.
2. To study the relationship of duration, severity, and type of diabetes mellitus with the profile of bacteriuria.

Material and Methods

One hundred diabetics (type 1 and 2) admitted to a tertiary care hospital, fulfilling the below-mentioned enrolment criteria, were included in the study. Enrolment was done consecutively for a period of one year, from October 2015 to September 2016. Males and females were enrolled equally. Those individuals, with documented evidence of diabetes or those, with fasting venous blood glucose values equal to or more than 126 mg/dl and postprandial blood sugar more than or equal to 180 mg/dl were included in the study. This research is a part of thesis research work, and ethical approval was obtained from the institutional ethical committee.

Inclusion criteria

1. Age 21 years and above
2. Both type 1 and type 2 DM.

Exclusion criteria

1. History of receiving antibiotics within two weeks prior to culture.
2. Patients on a continuous indwelling catheter.

A detailed history was taken after obtaining informed written consent from the patient, with specific reference to the duration of diabetes, type, treatment taken, adherence, symptoms related to diabetes, and its complications. History concerning Urinary tract infection like fever, dysuria, increased frequency, urgency, suprapubic pain, haematuria, and any symptoms suggestive of acute pyelonephritis like fever with chills, nausea, vomiting, and diarrhoea, was noted. Any catheterization in the past was also enquired about.

Clinical examination of all patients was done, including temperature recording, pulse rate, blood pressure, suprapubic tenderness, or palpation for any deep abdominal mass, were carried out.

For urine analysis, about 5–10 ml of the midstream urine sample was collected in a sterile container. For routine microscopy, samples were sent immediately to the laboratory, while for bacteriology, incubation was done for 1–2 days in blood/chocolate agar, and organisms were identified by looking at the nature of colonies, lactose fermentation, and other biochemical tests.

Throughout, the term bacteriuria means uncentrifuged gram-stained urine containing at least one organism per oil immersion field, correlating with a colony count of $>10^5$ CFU/ml. And the terms like non-bacteriuria or without bacteriuria mean uncentrifuged gram-stained urine that contains at least one organism per oil immersion field, correlating with a colony count of $<10^5$ CFU/ml. Antibiotics sensitivity was tested. Apart from that, complete blood counts (CBC) and Ultrasound (USG) abdomen were also done.

Collected data were entered into an excel spreadsheet, coded appropriately, and analysed using MS excel 365 and R software 4.1.0.

Non-parametric tests like the Chi-square test and parametric tests like unpaired t-test and one-way ANOVA were used to analyse the data depending upon the nature of distribution and type of data. All tests performed at a 95% Confidence interval with $P < 0.05$ was considered statistically significant.

Results

Equal number of males and females participated in the study, the majority (36%) belonged to the age group of 41–50 years. Out of the 100 enrolled, eight were type 1 diabetics and the rest 92 were type 2 diabetics. About 43 patients had bacteriuria. Prevalence was significantly more among females (54%) as compared to males (32%). ($\chi^2 = 4.93$, $P = 0.026$) [Figure 1].

As it is reflected in Figure 2, bacteriuria is progressively more common in the older age group compared to the younger age group, though this difference was not found statistically significant. ($\chi^2 = 5.54, P = 0.352$).

As reflected in Table 1, the prevalence of bacteriuria was maximum (54.4%) with 6–10 years of history of diabetes, and it is followed by a duration of up to five years and then more than ten years where prevalence was 43.7% and 18.2% respectively. This distribution was statistically significant ($P < .05$).

As it is seen from Figure 3, patients purely on insulin have the least prevalence (39.3%) of bacteriuria, and patients not on any antidiabetic medications had the maximum prevalence (50%) of bacteriuria. However, this distribution was not statistically significant ($P > .05$).

When the distribution of other complications of diabetes with bacteriuria was assessed, it was found that the presence of neuropathy and diabetic foot was significantly associated with the presence of bacteriuria. ($P < .05$) [Table 2].

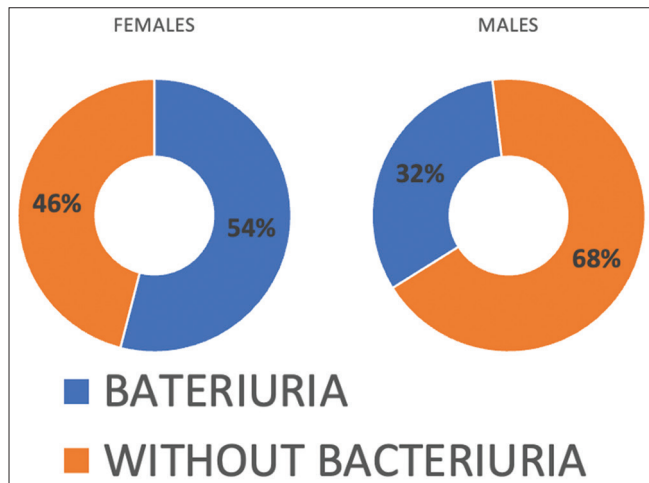


Figure 1: Gender-wise prevalence of bacteriuria among diabetics

Figure 4 shows the distribution of symptoms of UTI in patients with bacteriuria as it can be seen that 32.6% (14/43) of patients had no symptoms (asymptomatic bacteriuria). In comparison, for those with symptoms, the most common symptom was dysuria (41.9%), followed by increased frequency (39.5) and suprapubic pain (37.2%). Fever was seen in 27.9% of the cases, and the rest of the symptoms were seen in less than 15% of the patients. The point to be noted here is that the overall prevalence of asymptomatic bacteriuria among enrolled diabetics was 14% (14/100).

Regarding the assessment of signs in UTI, there was no statistical significance on evaluation of tenderness between bacteriuric ($n = 57$) and non-bacteriuric ($n = 43$) patients, for Suprapubic tenderness (19.3% vs. 32.6%), Renal Angle tenderness (14% vs. 23.3%), and Deep palpation tenderness (1.8% vs. 2.3%).

On blood investigations, the occurrence of anaemia was more among with the bacteriuria group (48.8%) as compared to the without bacteriuria group (36.8%), though this difference was not found statistically significant.

On the other hand, leucocytosis ($>12,000$) was present in 7 (12%) patients in the non-bacteriuric group, compared to 13 (30.2%) patients in the bacteriuric group. This was statistically significant for bacteriuria ($P = 0.007$).

As it is reflected, [Figure 5] those with increased HbA1C levels had a higher chance of UTI with bacteriuria. However, this distribution was not statistically significant ($P > .05$).

Table 1: Duration of diabetes with the presence of bacteriuria

	PATIENT GROUP n (%)		Total
	Without bacteriuria	With bacteriuria	
Upto 5 year	18 (56.3)	14 (43.7)	32 (100)
>5-10 year	21 (45.6)	25 (54.4)	46 (100)
>10 year	18 (81.8)	4 (18.2)	22 (100)
Total	57 (57)	43 (43)	100 (100)

$\chi^2 = 7.9, P = 0.01^*$. *Significant (with Yates correction)

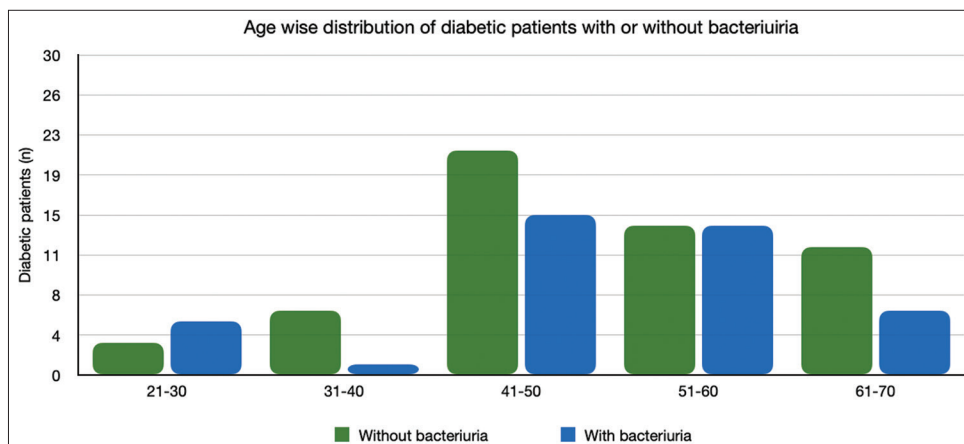


Figure 2: Age-wise distribution of diabetic patients with and without bacteriuria

Table 2: Complication of diabetes with presence or absence of bacteriuria

Complications**	Without Bacteriuria 57(%)	With Bacteriuria 43(%)	Total 100 (%)	Significance
Retinopathy	16 (48.5)	17 (51.5)	33 (100)	$\chi^2=1.45, P=0.22$
Neuropathy	20 (44.4)	25 (55.6)	45 (100)	$\chi^2=5.26, P=0.02^*$
Nephropathy	9 (45)	11 (55)	20 (100)	$\chi^2=1.46, P=0.22$
Diabetic foot	6 (27.3)	16 (72.7)	22 (100)	$\chi^2=10.16, P=0.00^*$

**Multiple responses. *Significant

Table 3: Distribution of culture isolates and antibiotic sensitivity

Culture isolate n=43	Ampicillin %	Cefuroxime %	Ceftriaxone %	Amox-clav %	Fluroquinolone %	Gentamycin %	Cotrimoxazole %
<i>E. coli</i>	52.4	20.7	12.7	30.4	40.7	6.1	41.1
<i>Enterococcus</i>	23.7	-	12.5	-	20.4	60.7	32.8
<i>Klebsiella</i>	89.7	-	13.5	15.4	-	17.8	16.7

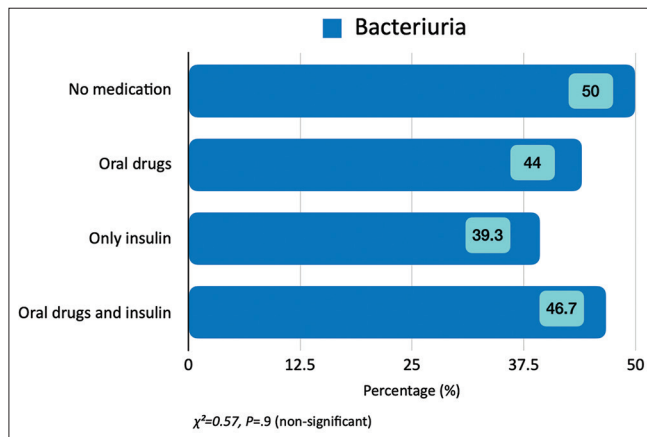


Figure 3: Type of medication for diabetics with presence or absence of bacteriuria

On urine analysis, the mean Specific gravity (SG) was 1.0356 (SD ± 0.0204) for bacteriuria (43%) and 1.027 (SD ± 0.0185) for non-bacteriuric patients (57%). The mean pH for bacteriuric patients was 6.53 (SD ± 0.57) and for non - bacteriuric patients 5.94 (SD ± 0.52). The pH values were significantly higher in the bacteriuric group.

On culture, the predominant bacteria isolated were *E. coli* (n = 31), and the next most common was *Klebsiella* (n = 7). Other organisms isolated included were *Enterococci* (n = 4), and *Pseudomonas* (n = 1). Gender-based evaluation of the causative organism also showed *E. coli* as the most common cause organism in both males (62.5%) and females (74.1%). [Table 3]

Antibiotic sensitivity, based on evaluation of urine culture, showed that the majority *E. coli* infected patients were sensitive to Ampicillin, followed by Cotrimoxazole and fluoroquinolones.

Discussion

Prevalence

The overall prevalence of bacteriuria in the present study was found to be 43% among the enrolled diabetics. This is comparable with prevalence in a study done by Shah MA,

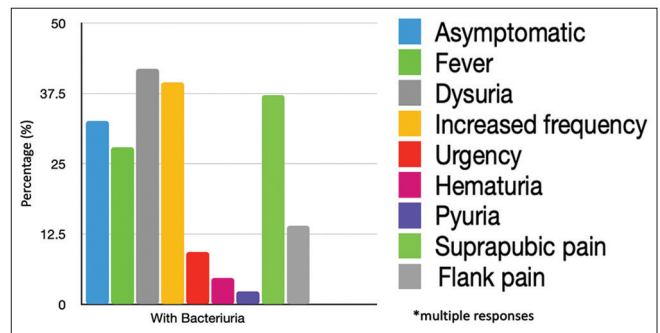


Figure 4: Symptoms of UTI in bacteriuria patients

et al. (2019),^[12] where the UTI was seen in 40.2% among enrolled diabetics.^[12] Similar findings were observed in previous studies done by Pargavi et al.^[13] (37%), Yadav et al.^[14] (38%), and Sewify et al.^[15] (35%). These comparable results may be due to similarity in criteria for labelling bacteriuria and the type of the study population.

Bacteriuria with age

There was no significant association between age and incidence of bacteriuria in the present study in diabetic patients. This was in contrast to other studies by Huvos et al.^[16] Ooi BS, et al.,^[17] O’Sullivan DJ, et al.,^[18] Vejlegaard et al.,^[19] Vigg et al.,^[20] Edward J. Boyko^[21] et al., who found significant incidence in older age group. Jaspani et al.^[22] and Zhanel et al.^[23] found no significant association with age.

Bacteriuria with gender

In this study, the incidence of urinary tract infection was found to be significantly higher in females (54%) compared to males (32%) (P < .05). These results are in line with a study done by Shah MA, et al. (2019), where prevalence among females was 54.9% and among males was 23.8%.^[12]

Many other studies like Chaudhary et al.,^[24] Ijaz et al.,^[25] Forland et al.,^[6] Ooi BS et al.,^[17] O’Sullivan DJ, et al.,^[18] Vigg et al.,^[20] Jaspani et al.,^[22] showed similar findings. The reason can be attributed to the shorter urethra and its close proximity to the perianal area.

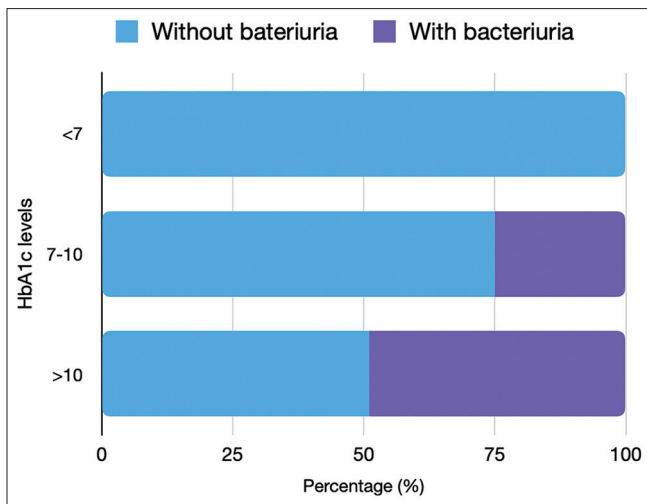


Figure 5: Glycaemic control (HbA1c levels) and presence and absence of bacteriuria

Duration of diabetes

The mean duration of diabetes in this study was six years for bacteriuric patients and nine years in patients without bacteriuria. These were similar results in studies done by Ooi BS *et al.*,^[17] Vigg *et al.*,^[20] Jaspani *et al.*,^[22] Zhanel *et al.*,^[23] who did not find any correlation with duration of diabetes in their study.

Type of treatment taken

In the present study, there was no significant correlation between bacteriuria and type treatment taken for diabetes. The majority of the patients with urinary tract infections were not willing for insulin to control blood sugars, though it was advised. Patients purely on insulin have the least prevalence (39.3%) of bacteriuria, and patients not on any antidiabetic medications had the maximum prevalence (50%) of bacteriuria. Vigg *et al.*,^[20] Jaspani *et al.*,^[22] and Zhanel *et al.*^[23] had similar observations. No significant difference in bacteriuria was noted between patients who were regular on treatment and follow-up. This shows the importance of treatment adherence on the occurrence of UTIs.

Complication of diabetes

Among complications of diabetes, diabetic neuropathy and diabetic foot ($P < .05$) were found to have a significantly higher proportion of bacteriuria in the present study. Other complications like retinopathy, nephropathy did not show a significant association for bacteriuria. A study done by Geerlings SE, *et al.*^[20] showed that the presence of longstanding complications (peripheral neuropathy, peripheral vascular disease) increased the risk of developing bacteriuria. Zhanel *et al.*^[23] found a significant association with heart disease. Vejlegaard *et al.*^[19] found an association of bacteriuria with retinopathy, heart disease, and peripheral vascular disease.

Uncontrolled diabetes and bacteriuria

The study on HbA1c showed that all patients in the bacteriuric group had HbA1c above seven, and 37 patients in the bacteriuric

group above ten. This was statistically significant for bacteriuria. Shah MA, *et al.* (2019)^[12] and Szucs *et al.*^[27] had also found a higher incidence of bacteriuria in uncontrolled diabetics. But Zhanel *et al.*,^[23] Vigg *et al.*,^[20] Jaspani *et al.*,^[22] Keane *et al.*^[28] found no significant relationship between control of diabetes and association of bacteriuria. The reason for the increased infection rate can be attributed to deprived immunity in uncontrolled diabetes and increased susceptibility of bacterial growth in glucosuria.

Microbiological profile

In this study, the following organisms: Escherichia Coli, Klebsiella, Enterococci, and Pseudomonas were isolated; of which, *E. Coli* (72%) was found to be predominant, the next being Klebsiella (16.3%). One sample contained Candida along with *E. Coli*. Studies done by Bonadio M, *et al.*^[29] had found an increased incidence of *E. coli* (54.1%) in diabetic patients with bacteriuria, the next prevalent organism being Enterococcus spp: 8.3%. Similar results with this study were seen with studies done by Zhanel *et al.*,^[23] Huvos *et al.*,^[16] O'Sullivan *et al.*,^[18] Vigg *et al.*,^[20] Szucs S, *et al.*,^[27] Geerlings SE, *et al.*,^[26] Asghar *et al.*^[30] Klebsiella was the second common organism isolated, which matches with observations by Zhanel *et al.*^[23] and Vigg *et al.*^[20] While Al-Khashmani *et al.*,^[31] in their study, found that Staphylococcus epidermidis was the most common bacterium isolated from urine in both diabetics and non-diabetics (22.4%), and *E. coli* (19%) was the second most common isolate. Other common bacterium isolates included Enterococcus fecalis (13.7%), Klebsiella pneumonia (12%), and Enterobacter sp (12%), Staph aureus (10.3%).

About half of Ecoli isolates were susceptible to Ampicillin, and around 40% each for Cotrimoxazole and fluoroquinolone, and about 30% to Amoxiclav. Studies done by Bonadio M *et al.*,^[29] and Zhanel *et al.*^[23] did correlate with the present study. In a study done by Asghar *et al.*,^[30] *E. coli* was shown to have high resistance (87%) to fluoroquinolones. The probable reasons for this variation in findings can be due to the difference in the patients' drug adherence, treatment protocols/Regimens, and the availability of drugs in the different regions.

Conclusion

In the study population:

- Asymptomatic urinary tract infection is common in diabetic patients.
- Increased incidence of Urinary tract infections in patients with long-standing high blood sugar (high HbA1c).
- Age does not affect the occurrence rate and clinical profile of UTIs.
- Diabetic drug adherence reduces the prevalence of bacteriuria among diabetics comparable to non-diabetics
- Female Diabetic patients are more prone to urinary tract infections.
- *E. coli* was the most common organism isolated in patients. Resistance to common antibiotics was observed.

Recommendation

Provision of mandatory screening at primary care setting for bacteriuria among uncontrolled diabetics to prevent future complications. Further studies can be done to explore the possible reasons (like drug adherence, irrational treatment) for the increased resistance found to a broad range of antibiotics.

Ethical approval

This study is a part of post graduate thesis work and ethical approval was obtained before the start of the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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