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Clinical and laboratory profile of urinary tract infection in diabetes mellitus: A western India perspective

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Abstract
Introduction: Diabetic patients have a significantly higher rate of Urinary tract infections (UTI) and a higher severity of UTI than nondiabetic patients hence Diabetic patients require accurate UTI screening in order to receive the proper treatment and avoid complications.
Materials and Methods: A total of 100 patients with diabetes mellitus who had symptoms that suggested a urinary tract infection were examined in this prospective single-center study. Data on the presence of UTI and possible risk factors was collected, and their possible relationship was analyzed. The Institutional Ethics Committee approved the study protocol and procedures. EPI INFO statistical software was used to analyze all data.
Results: Asymptomatic bacteriuria was found in nearly 25% of Bacteriuric patients. With a significant p - value of <0.001, the majority of Bacteriuric diabetics with UTI (87.14%) had glycosylated hemoglobin (HbA1c) > 8.5 percent. Escherichia coli (E. coli) was isolated from urine culture at a higher rate (68.9%) among diabetic patients in both the bacteriuric and non-bacteriuric groups, followed by Klebsiella (17.24%) and Enterococcus (8.6 %).
Conclusion: UTIs are a common complication of diabetes mellitus. To avoid the occurrence of possible severe renal complications, it is necessary to improve the care and screening of UTIs in patients with DM. Early implementation of a strict HbA1C lowering strategy, as well as genital hygiene improvements, can help prevent symptomatic UTI in these patients.

Keywords: urinary tract infection, bacteriuria, diabetes mellitus, uropathogens

Introduction

Diabetes is the most common endocrine disease in the twenty-first century.[1] In emerging countries, such as India, changing lifestyles and urbanisation have resulted in an increase in the occurrence.[1]Diabetic patients have a significantly higher rate of Urinary tract infections(UTI) and a higher severity of UTI than nondiabetic patients, [2]which can lead to problems ranging from dysuria (pain or burning sensation during urination) to organ damage and even death owing to complicated UTI (pyelonephritis). In these patients, asymptomatic bacteriuria might progress to lower UTI (cystitis), upper UTI (pyelonephritis), and potentially severe urosepsis. Emphysematous cystitis, emphysematous pyelonephritis, renal abscesses, and renal papillary necrosis are all rare consequences of UTI that occur more commonly in type 2 diabetes patients than in the general population. [3]

Defects in the host immune defence mechanisms (such as impaired neutrophil function, decreased T-cell-mediated immune response, low levels of prostaglandin E, thromboxane B2, leukotriene B4) [4] incomplete bladder emptying due to autonomic neuropathy, and poor metabolic control are all factors that contribute to an increased infection risk in diabetic patients [5]. Pathogenic microorganisms can colonise the urinary tract if the glucose concentration in the urine is higher [6].

Diabetic patients require accurate UTI screening in order to receive the proper treatment and avoid complications. Type 2 diabetes is a risk factor for not just community-acquired UTI, but also health-care-associated UTI, catheter-associated UTI, and recurrent UTI after a kidney transplant. Furthermore, these patients are more likely to have resistant infections, such as extended-spectrum –lactamase [ESBL] producing organisms, as the cause of their UTI [7].

The aim of the study was to see if there was any association between UTI and age, gender, glycemic status, and diabetes duration; to study causative microorganisms and their drug susceptibility in both type 1 and type 2 diabetes; and to assess how many patients got clinical and microbiological cure after standard antimicrobial treatment.

Materials and Methods

Study Population and Setting

This was a prospective study conducted at the Department of Medicine at a tertiary care hospital in Gujarat. The study was carried out from June 2020 to March 2021. A total of 100 Diabetic patients were included in the study (40 males and 60 females),Following an explanation of the study procedures and consent process, participants' demographic information, such as age, gender, and body mass index, was collected.

Patients having a history of diabetes or who were undergoing diabetes therapy were also eligible to participate in the study. Patients who had received antibiotics during the previous two weeks and those who were on a continuous indwelling catheter, on the other hand, were excluded. Patients who have UTI with DM but age <12 years and pregnant women were excluded from the study. As a result, 100 patients were enrolled in a succession, regardless of their gender, diabetes duration, treatment, or treatment adherence. At the time of enrolment, each patient gave their informed consent. The Institutional Review Board gave their approval to the study protocol.

Data Collection

After obtaining the patient's consent(assent in case of <18 year), a detailed history was taken, with particular attention to the patient's duration of diabetes, type, treatment received and adherence, and symptoms related to diabetes and its complications. Burning micturition, frequency, urgency, dysuria, suprapubic pain, haematuria, and any symptoms suggestive of acute pyelonephritis, such as fever, chills, nausea, and vomiting, were all noted in relation to urinary tract infection. The patient was asked about any previous urinary tract instrumentation or catheterization. A thorough examination of all systems was performed, with particular attention paid to temperature, pulse rate, blood pressure, pedal oedema, suprapubic tenderness, costovetebral angle tenderness, and tenderness/mass on deep abdominal palpation.

The weight, height, and body mass index (BMI) of each patient were measured. Every patient was asked if they had any symptoms that pointed to a UTI (e.g., fever, urgency, dysuria, urinary frequency, suprapubic pain). 2 ml blood was taken during fasting for fasting blood glucose and 5 ml blood was taken 2 hours after meal/OGTT in oxalate/fluoride vacutainers for postprandial blood glucose, HbA1C, CBC, and Renal function test. To determine the quality of glycaemic control and haemoglobin, an Immunoturbidimetric method was used to estimate HbA1c percent, CBC was measured using impedance photometry, and renal functions were assessed using GLDH and Jaffe kinetic methods. Urine was collected as clean-catch midstream samples in sterile screw-capped, graduated, wide-mouth plastic containers and transported to the laboratory within two hours of collection.For urine microscopy, 5ml of clean catch midstream urine was centrifuged at 3000 rpm for five minutes, then viewed under a microscope, with more than five WBC per high power field being considered significant. For all diabetics, a fasting sugar, postprandial sugar, and HbA1c were measured. Urinary symptoms (dysuria, urgency, frequency, or suprapubic pain or tenderness) with or without fever at presentation or during hospitalisation were the criteria for ordering a urine culture.

Urine samples were sent to the laboratory immediately for routine testing and culture. Urine samples were cultured in Blood / Chocolate agar and Mac Conkeys agar plates at 37°C for 24 to 48 hours. Colony characteristics, lactose fermentation, and biochemical tests were used to identify the organisms.The presence of $\geq 10^5$ colony-forming units(CFU per millilitre of urine was considered significant bacteriuria. The presence of bacteria in a patient with a fever and urinary symptoms was defined as a symptomatic UTI. Bacteriuria without fever or urinary symptoms was defined as Asymptomatic Bacteriuria (ASB).

Study Group

Patients were divided into two groups based on the results of urine culture analysis: (a) patients with bacteriuria; and (b) patients without bacteriuria. Uncentrifuged gram-stained urine containing at least one organism per oil immersion field, correlating with a colony count of $>10^5$ CFU/ml, was used to identify patients with bacteriuria. Following that, the clinical and laboratory profiles of these two groups were compared.

Data Analysis

All of the data was analysed using descriptive statistics such as frequency, percentage, and the chi square test and Fisher's exact test (for categorical variables). A p value of <0.05 was considered significant. The data was analysed using EPI INFO software, which was then entered into an excel sheet.

Results

Demographic details of diabetic patients with and without bacteriuria.

The study included 100 diabetic patients who had clinical or microbiological evidence of urinary tract infection. There were 42 (42%) patients with no evidence of bacteriuria, and 58 (58%) patients with bacteriuria. Furthermore, the bacteriuria group had a significant female preponderance (p=0.029), indicating that bacteriuria is more common in female diabetics than male diabetics (72.4% vs 27.6%). In both groups, the majority of patients were between the age group of 40- 60 years of age (65.5% in bacteriuric grp and 64.3 % in non-bacteriuric grp).

Table 1: Demographic details of diabetic patients with and without bacteriuria.

	Bacteriuria (n=58)	Non-Bacteriuria(n=42)
Gender		
Male	16 (27.6%)	24 (57.1%)
Female	42 (72.4%)	18 (42.9%)
Age (in years)		
< 40	4 (6.9%)	9 (21.4%)
40-60	38 (65.5%)	27 (64.3%)
>60	16 (27.6%)	6 (14.3%)
Mean age(in years)		
Male	48.94±10.05	55.48±11.49
Female	55.52±13.21	47.33±9.66

Diabetes and UTI

Mean duration of diabetes since diagnosis was 8.71 years for bacteriuric patients (n=58) and 6.16 for non-bacteriuric patients(n=42) with a p-value of 0.011, which is statistically significant difference. Patients with duration of diabetes more than 6 years had increased chances for developing urinary tract infections. Retinopathy and neuropathy were the most frequent complication in both groups. In the bacteriuric group, diabetes foot was the most common associated complication. Bacteriuria is significantly associated with diabetic foot (p=0.0001).

Table 2: Effect of Type, Duration, Treatment and Complication of Diabetes in UTI

	Bacteriuria (n=58)	Non-Bacteriuria(n=42)	p-value
Diabetes Type			
Type 1	5 (8.62%)	4 (9.52)	0.842
Type 2	53 (91.38%)	38 (90.48)	
Duration of Diabetes			
Mean duration	8.71	6.16	
Range			
<1 year	8 (13.8)	3 (7.14)	0.767
1-5 years	8 (13.8)	8 (19.05)	
6-10 years	25 (43.1)	17 (40.48)	
11-15 years	12 (20.7)	11 (26.2)	
>15 years	5 (8.6)	3 (7.14)	
Treatment Taken For Diabetes			
Insulin	12 (20.69)	14 (33.33)	0.325
Oral hypoglycemic agents	28 (48.28)	19 (45.24)	
Both	8 (13.79)	6 (14.28)	
No treatment	10 (17.24)	3 (7.14)	
Adherent to treatment	15 (25.86)	14 (33.33)	0.416
Adherent to follow-up	10 (17.24)	6 (14.28)	0.691
Complications of Diabetes			
Retinopathy	24 (41.38)	14 (33.33)	0.413
Peripheral Neuropathy	22 (37.93)	16 (38.09)	0.987
Nephropathy	21 (36.21)	8 (19.05)	0.062
Diabetes foot	26 (44.83)	3 (7.14)	0.0001*

*Yates correction applied.

Clinical characteristics of UTI in Diabetic patients with and without bacteriuria

[Table-3] summarises the clinical characteristics of urinary tract infections in diabetic patients. Individual symptoms in bacteriuric and non-bacteriuric patients revealed that dysuria (41.34%) was the most common symptom in both groups, followed by increased frequency (37.93%) in the bacteriuric group and urgency (42.86%) in the non-bacteriuric group. Asymptomatic bacteriuria was found in 15/58 (25.86%) patients [males (26.67%) vs 11 females (73.33%)]. There was a significant difference between two group for the symptom of urgency (p=0.002) and sign of tenderness on deep palpation(p=0.031).

Table 3: Clinical characteristics of UTI in Diabetic patients with and without bacteriuria

Symptom / Sign	Bacteriuric (n=58)	Non-Bacteriuric (n=42)	p-value
Asymptomatic	15 (25.86%)	0 (0%)	0.0001
Fever	19 (32.76%)	10 (23.41%)	0.330
Dysuria	24 (41.34%)	22 (52.38%)	0.276
Increased frequency	22 (37.93%)	14 (33.33%)	0.636

Urgency	9 (15.52%)	18 (42.86%)	0.002
Haematuria	8 (13.79%)	10 (23.41%)	0.198
Pyuria	4 (6.89%)	0 (0%)	0.136
Flank pain	15 (25.86%)	7 (16.67%)	0.273
Suprapubic pain	21 (36.21%)	8 (19.05%)	0.062
Suprapubic tenderness	18 (31.03%)	8 (19.05%)	0.177
Renal angle tenderness	14 (24.14%)	5 (11.9%)	0.124
Tenderness on deep palpation	13 (22.41%)	2 (3.45%)	0.031*

* yates correction applied

Laboratory Evaluation of Diabetic Patients with and Without Bacteriuria

The evaluation of fasting blood glucose levels revealed that 56 out of 58 (96.55%) patients in the bacteriuric group and 37 out of 42 (88.09%) patients in the non-bacteriuric group had fasting blood glucose levels >126 mg/dl (p=0.101). Similarly, in the bacteriuric group 56 out of 58 patients (96.55%%) had HbA1c levels greater than 7%, compared to 38 out of 42 patients (90.48%) in the non-bacteriuric group. Furthermore, in the bacteriuric and non-bacteriuric groups, 51 (87.93%) and 24(57.14%) patients, respectively, had HbA1c levels greater than 8.5%(p=0.00045).

Table 4: control of Diabetes in patients with and without bacteriuria

HbA1c %	Bacteriuric (n=58)	Non-Bacteriuric (n=42)	p-value
<7	2 (3.45%)	4 (9.52%)	
7-8.5	5 (8.62%)	14 (33.33%)	0.002
>8.5	51 (87.93%)	24 (57.14%)	

Anaemia, defined as haemoglobin levels of less than 12 gm/dl, was found in 27 of the bacteriuric patients and 16 of the non-bacteriuric patients (p=0.399). Leucocytosis, defined as a leukocyte count of more than 12,000/cu mm, was reported in 14 (30.2%) of bacteriuric patients and 6 (12.3%) of non-bacteriuric patients (p=0.224).

Analysis of Urine Culture

E. coli was the most common causative organism in the study population (68.9%), followed by Klebsiella sp. (17.24 %). There were also six cases of Enterococcus sp., one case ofcandida, and one case of pseudomonas. E. coli was the most common causative organism in both males and females, according to gender-based analysis [Table-4].

Table 5: Gender based study on organisms

Organisms	Males with Bacteriuria (n=16)	Females with Bacteriuria (n=42)	Total patients with Bacteriuria (n=58)
Candida	0 (0%)	1 (2.3%)	1 (1.7%)
*E.*coli	10 (62.2%)	30 (71.42%)	40 (68.9%)
Enterococci	2 (12.5%)	4 (9.5%)	6 (8.6%)
Klebsiella	3 (18.75%)	7 (16.6%)	10 (17.24%)
Pseudomonas	1 (6.25%)	0 (0%)	1 (1.7%)

The sensitivity to Levofloxacin was highest among the participants in this study (95.91%). Nitrofurantoin and doxycycline were next, both with the same sensitivity (89.89%). Pseudomonas and proteus are only resistant to cotrimoxazole and are highly sensitive to nitrofurantoin, levofloxacin, doxycycline.[Table-5]

Table 6: Antimicrobial sensitivity and resistance pattern

Isolated organism		Nitrofurantoin	Co-Trimoxazole	Levofloxacin	Doxycycline
E coli n=33	S	30	32	31	30
	R	03	01	02	03
Klebsiella n=10	S	09	08	10	09
	R	01	02	00	01
Pseudomonas n=1	S	01	00	01	01
	R	00	01	0	0
Enterococci n=4	S	03	02	04	03
	R	01	02	00	01
Proteus N=1	S	01	00	01	01
	R	00	01	00	00
TOTAL =49	S	44(89.79%)	42(85.71%)	47(95.91%)	44(89.79%)
	R	05(10.25)	07(14.28%)	02(4.08%)	05(10.25%)

Discussion

In our study, Females showed higher incidence of bacteriuric UTI as compared to males. Females had shown 2.6 times higher risk of developing bacteriuric UTI(72.4% vs 27.6%). study based on administrative data from the United States population found that females had a higher incidence of UTI than males (12.9 percent vs. 3.9 percent) over the course of a year.[8] Furthermore, the female gender's predisposition for UTI has been reported in previous studies with a geographical population similar to ours [9]. The increased occurrence is linked to the anatomy of the female urinary system, specifically the short urethra and bacterial colonisation in the perianal area, rather than physio-logical changes in the body caused by diabetes [6].

In contrast to previous studies, [6, 10] we found no link between bacteriuria and age or Bacteriuria and diabetes duration. Patients who had diabetes for more than 6 years, on the other hand, had a higher risk of bacteriuria. For every ten years of diabetes duration, the prevalence of bacteriuria increases by 1.9 times [11]. Longer durations of diabetes may result in a higher prevalence of diabetic chronic complications, more frequent hospitalisation, and urinary tract catheterization, which together increase the risk of urinary tract infections [11].

In our study, the incidence of bacteriuria was higher among patients taking oral hypoglycaemic agents alone compared to those taking insulin or a combination of insulin and oral hypoglycaemic agents, which is consistent with previous findings of Simkhada R.et.al.study [12].

The majority of diabetics with UTI (87.93%) had a HbA1c of more than 8.5 %, with a p- value of 0.00045. As a result, the occurrence of UTI in diabetics appears to be linked to recent glycemic control (weeks to months). In a study of the relationship between asymptomatic bacteriuria and HbA1c, Schmitt JK *et al*. (1986) found no statistically significant link between glycemic control and UTI [13]. Vaishnav B *et al*. found a link between diabetes control and bacteriuria in uncontrolled diabetic patients,[14]while Sewify M *et al*. found no link between diabetes control and bacteriuria [6]. Uncontrolled fasting blood sugar levels and high HBA1c levels were found to be associated with an increased rate of UTI in both the bacteriuric and non-bacteriuric groups in our study. Tseng CC *et al*. (2002) observed that HbA1c levels greater than 8.1% were associated with an increased risk of UTI. Tseng CC *et al*. (2002) concluded that patients with HbA1c > 8.1 percent have a higher prevalence of UTI, which our study supports [15].

We observed that patients with neuropathy or a diabetic foot were more likely to develop bacteriuria. Other complications such as retinopathy, nephropathy, and hypertension were not significantly associated with an increased risk of bacteriuria. Similar findings about bacteriuria and long-term diabetic complications have been reported in the literature [16]. We also observed that bacteriuric patients had more symptoms of urinary tract infection than non-bacteriuric patients.

The presence of ASB is a significant risk factor for symptomatic UTIs.[15] A meta-analysis of 22 studies on ASB in DM patients found a prevalence of 12.2 percent, with females (14.2 percent) having a higher prevalence than males (2.3 percent), [16] which is similar to the current study's findings of 18.96 percent in females and 6.89 percent in males.

E. coli was found to be the most common organism in urine cultures (68.9%), followed by Klebsiella (17.24%). This finding is consistent with previous research involving diabetic patients who have bacteriuria [6, 11]. Furthermore, the majority of these organisms were susceptible to nitrofurantoin, cotrimoxazole, levofloxacin and doxycycline, indicating that these antimicrobial agents may be the best choice for treating urinary tract infections in our geographical area.

Fungal UTIs are more common in diabetic patients who have a long hospital stay, are catheterized, and use parenteral antibiotics for an extended period of time.[17]One patient in the current study had UTI caused by Candida. Other factors predisposed these patients to UTI and/or a prolonged hospital stay.

Due to study design limitations, it was not possible to establish a causal relationship between UTI in diabetics and age > 40 years. This study was conducted in a specific region, and the majority of the participants were natives of that region, so race and regional variability cannot be discussed. This study did not examine all antibiotic sensitivity and resistance.

Conclusion

Female patients had a higher risk of urinary tract infection. Patients with diabetes for more than 6 years had a higher risk of developing urinary tract infections. The propensity for developing urinary tract infection based on the type of diabetes was inconclusive in the current study. Urinary tract infection did not show any association with patient age. In diabetic patients with urinary tract infections, glycated hemoglobin A1c levels were found to be high (statistically significant). Early implementation of a strict HbA1C lowering strategy, as well as genital hygiene improvements, can help prevent symptomatic UTI in these patients. The most common organism isolated from urine culture was E.coli, and Klebsiella was the second most common organism isolated. As most of the strains were sensitive, Nitrofurantoin, Co-Trimoxazole, Levofloxacin, and Doxycycline emerged as a good antimicrobial agent for the treatment of urinary tract infections. Asymptomatic bacteriuria is seen in 25% of bacteriuric patients, so routine urine screening is recommended to prevent symptomatic UTI, particularly in patients with poor glycemic control.

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