

Urinary tract infection and Diabetes Mellitus—Etio-clinical profile and antibiogram: A North Indian perspective

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ABSTRACT

Context: A complex dysregulation of glucose homeostasis, Diabetes Mellitus (DM) is an iceberg disease with an ever-rising global (8.5%, 2018) and national prevalence (7.3% - ICMR-INDIAB study, 2017) amidst adults. Besides the micro and macrovascular complications, in virtue of diverse mechanisms that downplay the immune system culminating in an array of infections especially UTIs are commoner in routine diabetic clinics. The spectrum of UTI ranges from asymptomatic bacteriuria (ASB) to serious complications such as emphysematous pyelonephritis, renal abscesses that are encountered frequently among Diabetics in contrast with non-diabetics are being studied. **Methods and Material:** A prospective comparative cross-sectional study was conducted in 250 adult consenting participants with equal diabetics and non-diabetics with culture-proven UTI, at the Department of Internal Medicine in a tertiary care hospital of National Capital Territory (NCT) of India, after fulfilling appropriate criteria. Alongside socio-demographic details and vitals parameters, glycaemic status assessment and relevant investigations were done in either group. **Results:** Mean age of the participants was 52.18 ± 9.06 with age and gender being reasonably distributed in both the groups. Fever ($P < 0.01$), dysuria ($P < 0.01$), urgency ($P < 0.01$) and urinary frequency ($P < 0.01$) found frequently among non-diabetics wherein vomiting ($P < 0.01$) and incontinence ($P < 0.01$) relatively commoner among diabetics. *E. coli*, *Klebsiella* sp., were the most common organisms in both groups with *Proteus* sp., and *Pseudomonas* sp., higher among diabetics. Severe infection and Pyelonephritis were frequent (AOR 2.64, 95% CI- 2.01-3.27, $P < 0.05$) among diabetics. Antimicrobial sensitivity patterns were not significantly different among both groups. **Conclusions:** Primary care physicians are to be acquainted with the possibility that UTI in diabetics could exhibit relatively lesser symptoms or more severe forms of UTI at presentation and less favorable outcomes. Further validation from a larger cohort of diabetics is warranted in terms of symptomatology, diagnostic approach, and sensitivity patterns.

Keywords: Diabetes, urinary tract infections, pyelonephritis, antibiotic resistance, antibiogram

Introduction

Diabetes Mellitus is an ever-growing metabolic and endocrine disorder characterized by hyperglycemia resulting from defects in insulin secretion, action, or both and is so rampant in the western and industrialized nations as the majority of patients are visiting primary care and family medicine clinics for the

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treatment of diabetes mellitus.^[1] The recent forecast from the Global Burden of Diseases survey of 2017 estimates 462 million individuals to have been affected by type 2 DM, corresponding to 6.2% of the planet's population (4.4% aged 15–49 years, 15% aged 50–69, and 22% aged 70+ years) and a point prevalence rate of 6059 patients over 10,000 population.^[2] Patients with type 2 diabetes mellitus are at increased risk of infections, with the urinary tract being the most frequent infection site.^[3-6] Every clinician may have to familiarize themselves with the symptomatology profile of urinary tract infections (UTIs) in diabetics that may range from asymptomatic bacteriuria to cystitis, pyelitis, pyelonephritis, and urosepsis and in severe and rare cases, emphysematous pyelonephritis and cystitis, renal abscess, and renal papillary necrosis.^[7] Various impairments in the immune system, including humoral, cellular, and innate immunity may contribute to the pathogenesis of UTI in diabetic patients.^[8] Therefore, screening for UTI in diabetic patients is very important to enable bacteriuria to be properly treated and prevent the development of renal complications of diabetes and eventually severe renal damage and failure.^[9] However, controversies do exist concerning incidence, prevalence, and microbiological features of UTI in diabetics and this study aims to compare clinical, microbiological, and predisposing features of UTI in diabetics with nondiabetics.

Methodology

This was a prospective comparative cross-sectional study conducted in 250 adult consenting participants with equal diabetics and nondiabetics at the department of Internal Medicine in a tertiary care hospital of the national capital territory (NCT) of India between May 2020 and February 2021. After informed consent, basic demographic details were taken in the form of an interview schedule administered with a pretested semi-structured questionnaire and venous sample for glycemic control studies and midstream clear urine sample for urinary routine and microscopic examination, culture, and sensitivity patterns were obtained from participants attending the OPD/IPD. Patients with sterile urinary growth on two specimens, already on antibiotic therapy, and the terminally ill were excluded from the study. Urine cultures beaming 10⁵ or more colony forming units were further incubated for uropathogenic identification using biochemical tests. Drug sensitivity testing was carried out with the modified Kirby–Bauer disc diffusion method for all specimens that grew uropathogens. Institutional Ethical Committee (IEC) approval [vide VMMC/SJH/Thesis/2019-10/60] was acquired apriori and appropriate statistical analysis was done with Stata 12.0 (College Station, Texas, USA).

Results

Participants with diabetes consisted of 70 males and 55 females and nondiabetics were 81 and 34, respectively. The mean age of diabetic participants was 51.9 ± 9.1 years, whereas the mean age of their counterparts was 52.1 ± 8.6 years. Clinical history of fever, urinary urgency and frequency, and dysuria was found significantly frequent among diabetic participants, whereas

Table 1: Comparison of symptomatology of UTI among diabetics and nondiabetics

Symptoms	Nondiabetic	Diabetic	Total	p (Chi-square test)
Fever	68 (77.27)	20 (22.73)	88 (35.2)	0.000
Dysuria	51 (63.75)	29 (36.25)	80 (32.0)	0.003
Urinary urgency	65 (68.42)	30 (31.58)	95 (38.0)	0.000
Urinary frequency	38 (66.67)	19 (33.33)	57 (22.8)	0.004
Abdominal pain	29 (52.73)	26 (47.27)	55 (22.0)	0.647
Vomiting	22 (35.48)	40 (64.52)	62 (24.8)	0.008
Hematuria	13 (61.9)	8 (38.1)	21 (8.4)	0.254
Pyuria	23 (65.71)	12 (34.29)	35 (14)	0.045
Incontinence	6 (16.22)	31 (83.78)	37 (14.8)	0.000
Retention	17 (60.71)	11 (39.29)	28 (11.2)	0.229

Table 2: Predisposing factors for UTI among both groups

Risk factors	Nondiabetic	Diabetic	Total	p (Chi-square test)
BPH	12 (44.14)	15 (55.56)	27	0.541
Indwelling catheter	19 (54.29)	16 (45.71)	35	0.585
Calculi	10 (83.33)	2 (16.67)	12	0.018
Stricture urethra	0 (0)	3 (100)	3	-
Cervicitis	1 (100)	0 (0)	1	-
Overall (anyone)	24 (42.11)	33 (57.89)	57	0.175

Table 3: Isolated organism causing UTI in both groups

Organism	Nondiabetic	Diabetic	Total	P (FE test)
<i>Acinetobacter</i> sp.	2 (66.67)	1 (33.33)	3	
<i>Enterobacter</i> sp.	2 (50.0)	2 (50.0)	4	
<i>Enterococcus</i> sp.	6 (46.15)	7 (53.85)	13	
<i>Klebsiella</i> sp.	40 (63.49)	23 (36.51)	63	
<i>Proteus</i> sp.	3 (25.0)	9 (75.0)	12	
<i>Pseudomonas</i> sp.	1 (33.33)	7 (87.5)	8	
<i>Staphylococcus</i> sp.	1 (33.33)	2 (55.57)	3	0.062
<i>Citrobacter</i> sp.	0 (0)	2 (100.0)	2	
<i>Escherichia coli</i>	70 (49.30)	72 (50.7)	142	
Total	125	125	250	

vomiting and urinary incontinence were common among nondiabetics, as depicted in [Table 1].

As shown in [Table 2], a history of any predisposing risk factors was elicited and only urinary tract calculi (UTC) was found more among the nondiabetics (n = 10), considering only 2 such participants with diabetes.

In terms of recurrence of UTI necessitating hospitalization in the preceding year, 34 diabetics (27.2%) reported positively in comparison to 8 participants without diabetes (6.4%). [Table 3] lists the organisms isolated in participants from both groups. The most common organism found in urinary culture among all the participants was *Escherichia coli* (56.8%), followed by *Klebsiella pneumoniae* (25.2%). *Proteus* sp. and *Pseudomonas* sp. were found to be relatively more common among participants with diabetes.

Table 4: Antibiogram of *Enterobacteriaceae* sp. isolated

Drugs	Sensitivity-N (%)		Pearson p-value	
	Diabetics	Nondiabetics	Chi ²	
Cefotaxime	46 (48.42)	64 (58.18)	1.95	0.162
Cefotaxime + Clavulanic acid	56 (58.95)	76 (69.09)	2.28	0.130
Cefuroxime	43 (45.26)	42 (38.18)	1.05	0.305
Amikacin	80 (84.21)	93 (84.55)	0.00	0.947
Amoxicillin	24 (25.26)	39 (35.45)	2.48	0.115
Ciprofloxacin	44 (46.32)	48 (43.64)	0.14	0.701
Nitrofurantoin	60 (63.16)	66 (60.0)	0.21	0.643
Nalidixic acid	67 (70.53)	78 (70.91)	0.00	0.95
Piperacillin + Tazobactam	74 (77.89)	93 (84.55)	1.49	0.222
Cefoperazone + Sulbactam	83 (87.37)	95 (86.36)	0.04	0.832
Imipenem	88 (92.63)	105 (95.45)	0.73	0.391
Meropenem	88 (92.63)	108 (98.18)	3.74	0.053
Netilmicin	72 (75.79)	85 (77.27)	0.06	0.803
Colistin	90 (94.74)	110 (100)	5.93	0.015

Table 4 depicts the antimicrobial sensitivity patterns in both groups in the decreasing order of sensitivity: Colistin (95% vs 100%) > Meropenem (93% vs 98%) > Cefoperazone/Sulbactam (87% vs 86%) > Amikacin (84% vs 85%) > Piperacillin/Tazobactam (78% vs 85%).

Discussion

Not surprising that over recent years, data from epidemiological studies theorize that asymptomatic bacteriuria (ASB) to pyelonephritis is a common occurrence among diabetic women than in those without diabetes.^[10] No negative outcomes have been reported by diverse prospective cohort studies to ASB, even though women and elderly with ASB do have heightened chances of developing symptomatic UTI.^[11,12] The current study attempted to compare the clinical and microbiological profiles of UTI in diabetics and nondiabetic patients from a tertiary care hospital in a tropical Asian country. As aforesaid, women are expected to suffer from UTIs, due to short urethra, stout body type, and other anatomical factors, but in this study, there was a mild male predominance (60.8%). This could be because the neurogenic bladder and benign prostatic hyperplasia (BPH) were common among the male participants, not to mention the surpassing mean age (52.18 ± 9.06) of the participants in both groups. The age and gender were comparable in both groups. The prevalence of bacteriuria increased 2.1 folds for every decade of diabetes, probably secondary to autonomic neuropathy and the resultant incomplete emptying of the bladder making it a suitable ground for infection; however, it requires further follow-up studies for confirmation. Few studies^[13,14] opined that diabetics on oral hypoglycemic agents were at higher risk of UTI, although such a correlation was not observed in this study. Systemic hypertension and tuberculosis were the most common medical ailments in both groups.

Identifying early and specific symptoms and signs of a common infectious ailment in a primary care setting with constrained resources becomes imperative to avoid any disastrous aftermath. In terms of symptoms, subjects without diabetes reported “fever” to be frequent, wherein diabetics had “vomiting” and “retention,” etc., to be commonly associated with UTIs. Only a few studies^[15-17] devoted their attention to the symptomatology of UTIs in comparison of diabetics and nondiabetics and they concluded that fever followed by dysuria be consistent with both groups. It is enlightening that one need not expect diabetics to showcase fever when they suffer from UTIs of any severity, making it imperative for GPs/Clinicians to actively screen for the same to initiate empirical therapy at the earliest. 64 men and 31 women failed to show any symptoms shown in [Table 1], reiterating the aforesaid. Not surprisingly, “indwelling urethral catheter” was found to be the most common identified predisposing factor for UTI among both diabetics and nondiabetics followed by benign prostatic hypertrophy (BPH) as in agreement with the previous studies.^[16,17]

Thirty-one participants reported having had recurrent UTI in the past year of which 24 were diabetics and 7 were participants without diabetes. Alongside national studies,^[16,18] a 2014 Dutch registration database-based retrospective data analysis by Schneeberger *et al.*^[19] found that patients with diabetes more often received longer and more potent initial treatment than patients without diabetes, thus making it a pressing issue for the family physicians to follow such patients with high risk to recognize and treat them at the earliest.

Most of the participants with no diabetes had plenty of leucocytes (>100 cells/HPF), wherein the count of “50–100” pus cells strata were comparable in both groups. There is a huge difference of opinion among the published literature on the usefulness of pus cells in the diagnosis and grading of severity of UTI among diabetics and the general population. There was a significant difference among participants with diabetes and nondiabetics in terms of urinary nitrite test, i.e., diabetic participants have more false-negative nitrite results than their counterparts. Sixty-eight participants (46 diabetics and 22 nondiabetics) had findings suggestive of acute pyelonephritis and were managed accordingly. A study conducted^[20] for the comparison of pyelonephritis among diabetics and nondiabetics reported that pyelonephritis was common among the elderly and diabetics and especially they presented with severe infection at presentation and consequently had poor outcomes in terms of residual renal function.

In agreement with the previous studies,^[14-17,21,22] *Escherichia coli* (56.8%), followed by *Klebsiella pneumoniae* (25.2%) were the most common organisms isolated from both groups, whereas *Proteus* sp. and *Pseudomonas* sp. were found to be relatively more common among participants with diabetes. The antimicrobial resistance pattern was similar in participants of both the groups with maximum sensitivity to Colistin and minimum sensitivity to Amoxicillin. This is in agreement with the other Indian^[15-17,21,23-25]

and South Asian studies.^[18,26-28] Diabetics had relatively lesser symptoms and more severe forms of UTI at presentation and less favorable outcomes. Further validation from a larger cohort of diabetics is warranted in terms of symptomatology, diagnostic approach, and sensitivity patterns to reinforce the findings of our study.

Conclusion

The world is being challenged with a pandemic of the ever-rising prevalence of Diabetes Mellitus, with almost nearly 40 million Indians with a major chunk across the nation remaining unaware of the disease management and related complications. Urinary urgency (38%) was the most consistent symptom related to UTI among all the participants followed by fever (35.2) and dysuria (32%). 75 of 125 diabetic participants had their glycated hemoglobin of more than 8%. The most common organism found in urinary culture among all the participants was *Escherichia coli* (56.8%), followed by *Klebsiella pneumoniae* (25.2%). *Proteus* sp. and *Pseudomonas* sp. were found to be relatively more common among participants with diabetes. There was no significant difference in antibiotic sensitivity patterns among both groups. Clinicians need to choose empirical regimens in treating an uncomplicated UTI at outpatient strata. This study illustrates symptomatology, microbiota, and their spectrum of antibiotic that may bolster primary care clinicians in accomplishing a prompt working/empirical diagnosis and thus appropriate treatment could be administered. However, further validation from a larger cohort of diabetics is warranted in terms of symptomatology, diagnostic approach, and sensitivity patterns.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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