Original Article

Microbiologic profile and clinical practices in urinary tract infections in a tertiary care center in Southern India

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Abstract

Context: Studies reported differences in clinical profiles of urinary tract infections (UTIs) in patients with and without type 2 diabetes mellitus (T2DM). Studies on the impact of the pattern of antibiotic resistance of organisms causing UTI on actual clinical practice are lacking. **Objectives:** 1. To study the clinical and microbiologic profiles of UTIs. 2. To compare treatment given with the prevailing antimicrobial sensitivity. **Settings and Design:** This is a cross-sectional study conducted in a tertiary care hospital. **Methods and Materials:** Retrospective chart review of inpatients with UTI (N = 200, 100 each of patients with and without T2DM), aged >18 years with a positive urine culture. **Statistical Analysis:** We used the statistical package SPSS version 17. The categorical variables were analyzed by the Chi-square test. Data were considered significant if *P* value was less than 0.05. **Results:** Similar to previous Indian studies, T2DM patients with UTI had significantly more asymptomatic bacteriuria, asymptomatic bacteriuria (32% vs. 6%), previous history of UTI (25% vs. 2%), and prior catheterization (16% vs. 1%). Escherichia coli (*E. coli*) was the most common organism isolated and showed sensitivity pattern of meropenem > netilmicin > amikacin > nitrofurantoin. Ceftriaxone was the most common empirical therapy given in spite the prevailing low sensitivity of *E. coli* to it. All ASB cases were treated unlike recommendations. **Conclusions:** Ceftriaxone is the most common empirical therapy given in spite the prevailing low sensitivity of E. coli to it. Cases of ASB were treated unlike recommendations.

Keywords: Antibiotic sensitivity, diabetes mellitus, empirical treatment, urinary tract infections

Introduction

The urinary tract is the most common site of infection in type 2 diabetes mellitus (T2DM) patients.[1] A meta-analysis reported a higher point prevalence of asymptomatic bacteriuria (ASB) among T2DM, 12.2% vs. 4.5% among healthy control subjects.[2] However, a study from India found no significant difference.[3] T2DM patients have increased the prevalence of complications of UTIs such as pyelonephritis, renal abscess, emphysematous cystitis and renal papillary necrosis,[4] and UTIs caused by resistant pathogens.[5]

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The present study was conducted to compare not only the symptoms of UTI in patients with and without T2DM but also compared the resistance pattern and the treatment given by physicians.

Materials and Methods

Ethics: The study was approved by the Institutional Ethics Committee of St. John's National Academy of Health Sciences, Bangalore, India. The patients were approached and explained about the study and written informed consent was obtained before recruitment. The information obtained during the data collection was kept confidential.

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Study design

Selection and description of participants: This was a cross-sectional study conducted on 200 inpatients under the Department of General Medicine in a tertiary care hospital in Bangalore, Karnataka, India. Two hundred positive urine culture reports, 100 patients with T2DM and 100 patients without DM (Non-DM), were identified from the Department of Microbiology using the inpatient record details. All patients were aged ≥18 years and type 1 diabetes mellitus; patients with genitourinary TB and terminally ill were excluded from the study. Data were collected using a proforma including presenting complaints and symptomatology, history of UTI, previous urinary catheterization, renal complications, and other comorbidities. In addition to this, review of the inpatient treatment and investigation record was done and relevant laboratory investigation reports of serum BUN, serum creatinine, abdominal ultrasonography findings, first-line treatment for UTI given on admission, and antibiotic sensitivity patterns were collected.

Microbiological Analysis: Midstream urine samples were collected using a sterile container after clear instructions to the patients. Urine cultures yielding $\geq 10^5$ colony-forming units were further processed to identify the pathogen using biochemical tests and perform the antibiotic susceptibility testing by the modified Kirby-Bauer disc diffusion method showing colony forming units $\geq 10^5$/ml were considered significant and processed further for identification using biochemical tests. Antibiotic sensitivity was performed by the manual modified Kirby-Bauer disc diffusion method.

Statistics

Statistical analysis was done using statistical package SPSS version 17. The categorical variables were analyzed by the Chi-square test. Data were considered significant if *P* value was less than 0.05.

Results

Patients with DM consisted of 44 males and 56 females ($n = 100$), and patients without DM (Non-DM, $n = 100$) consisted of 34 males and 66 females. The mean age among DM and Non-DM was 61.4 ± 12.6 and 42.9 ± 18.2 years, respectively. Comparison of clinical characteristics between patients with and without DM is shown in Table 1. There was a significant statistical difference between the two groups with regard to asymptomatic bacteriuria, fever, and history of prior UTI and catheterization. There were five cases of pyelonephritis and two cases of hydroureteronephrosis among patients with DM but none among patients without DM.

Table 2 shows the organisms causing UTIs in the two study groups. Escherichia coli (*E. coli*) were the most common bacterial isolate from patients with and without DM. *Enterococcus, Klebsiella* spp., and *Pseudomonas* spp. were also isolated in decreasing order of frequency.

Table 1: Comparison of clinical characteristics between the two study groups.

Symptoms	DM (*n*=100)	Non-DM (*n*=100)	*P*
Fever	53	97	≤0.001
Asymptomatic Bacteriuria	32	6	≤0.001
Dysuria	14	16	0.69
Retention	6	1	0.054
Increased frequency	9	6	0.42
Abdominal pain	11	14	0.52
Vomiting	18	23	0.38
Pyuria	34	33	0.64
Previous UTI	25	2	≤0,001
Previous catheterization	16	1	≤0.001
Pyelonephritis	5	0	0.06
Hydroureteronenphrosis	2	0	0.49

P value using Chi-square test or Fishers exact test

Table 2: Organisms causing UTIs in DM and Non-DM

Organism	DM	Non-DM
E. coli	67	62
Enterococcus	9	18
Klebsiella	14	7
Pseudomonas	6	5
Coagulase Negative Staphylococcus	1	3
Candida spp.	1	2

Table 3 shows that isolates of *E. coli* from patients with DM and without DM were sensitive to the following antibiotics in decreasing order of sensitivity: meropenem (88% vs. 85%) > netilmicin (86% vs. 81%) > nitrofurantoin (75% in both study groups) > gentamicin (58% vs. 62%).

Table 4 shows that ceftriaxone was the most common drug used for initial therapy of UTIs followed by tazobactam piperacillin and ciprofloxacin in UTI patients with and without DM.

Discussion

We compared the clinical profiles of UTI and antimicrobial sensitivity of microorganisms causing UTI in patients with and without T2DM. We also studied the most common empirical therapy given by physicians. The findings of our study show that patients with DM have significantly higher asymptomatic bacteriuria (ASB), prior UTIs and prior catheterization compared to patients without DM. We also found that fever occurred significantly more frequently in patients without diabetes than patients with DM. There were five cases of pyelonephritis and two hydroureteronephrosis among T2DM patients but none among non-DM patients. The study also shows that *E. coli* is the most common organism causing UTI, and ceftriaxone is the most common empirical therapy given to UTI patients in spite low susceptibility *E. coli* and other bacterial isolated to ceftriaxone as reported by previous studies and the present study.

Several studies from India have investigated the antimicrobial sensitivity or resistance pattern of UTI causing organisms in

Table 3: Antimicrobial susceptibility pattern in the two study groups (Susceptible expressed as %)

	E. coli sensitivity		*Enterococcus* sensitivity		*Klebsiella* sensitivity		*Pseudomonas* sensitivity	
	DM	Non-DM	DM	Non-DM	DM	Non-DM	DM	Non-DM
Amikacin	57	48	0	1	9	4	6	2
Amoxcillin	3	8	43	38	0	0	0	0
Ceftaxamine	11	14	0	25	21	20	0	0
Cefotaxime	3	12	0	0	14	20	0	0
Cephalexin	3	10	0	0	14	20	0	0
Cotrimoxazole	33	20	0	25	0	0	0	0
Ceftriaxone	9	14	14	25	50	20	21	33
Ciprofloxacin	5	8	14	13	21	60	30	19
Colistin	3	8	0	13	14	0	0	25
Gentamicin	58	62	29	30	50	40	9	9
Levofloxacin	11	14	0	25	21	40	0	0
Meropenem	88	85	0	50	64	60	50	83
Netilmicin	86	81	0	25	57	60	5	5
Norfloxacin	14	14	64	37	14	40	0	0
Nitrofurantion	72	75	96	93	0	20	0	0
Piperacillin-Tazobactum	34	25	0	50	21	40	50	83
Penicillin	0	0	57	25	0	0	0	0
Tigecycline	3	2	50	19	0	0	0	0
Teicoplanin	0	0	92	87	0	0	0	0
Vancomycin	0	0	89	100	0	0	0	0

Table 4: Antibiotics used for empirical therapy

Empirical therapy	DM (%)	Non-DM (%)
Ceftriaxone	44	42
Ciprofloxacin	9	9
Meropenem	5	-
Tazobactam-piperacillin	17	7
Amikacin	-	6
Nitrofurantoin	-	2
Others	25	34

patients without DM[6-9] and patients with DM.[10,11] In addition, few Indian studies investigated clinical and microbiological profile in patients without DM[12] and patients with DM vs. patients without DM.[3,13] This is the first Indian study that studied not only the clinical and microbiological profile of UTIs in patients with and without DM but also empirical therapy for UTI in them.

Our finding that patients with T2DM had significantly higher ASB than patients without DM (32% vs. 6%) is similar to a recent meta-analysis. This meta-analysis reported a point prevalence of ASB of 12.2% among patients with DM compared to 4.5% among healthy control subjects.[2] However, a prospective study from India found no significant difference[3] and also reported a comparatively higher point prevalence of 30%.

This study found that significantly fewer patients with DM had fever than patients without DM. Similarly, a 2014 study from North Korea comparing symptoms of acute pyelonephritis in community dwelling women with T2DM vs. women without DM found that significantly fewer women with DM had symptoms of upper UTI (flank pain and costovertebral tenderness with or without symptoms of lower UTI) and lower UTI (frequency, urgency, dysuria, and suprapubic pain).[14] This is in contrast to the finding that DM patients are more vulnerable to have a more severe presentation of UTI[15] though diabetic neuropathy can cause alteration of signs. An Indian study found no difference between clinical presentation of UTI in patients with and without DM.[3] Another Indian study found no statistical difference with regard to fever, burning micturition, and vomiting though they were common presenting symptoms; this study also found that patients with DM had a significantly more increased urinary frequency, dysuria, flank pain, and hematuria and urinary incontinence.[13] Although it cannot be concluded from this study, the lack of fever in DM patients may be associated with the altered immune response in patients with DM.[16]

We found that DM patients had a significantly higher history of previous UTI than the patients without DM. A similar finding was also reported by Indian studies[13,17] and also by a Dutch study.[18] However, another Indian study did not find statistically significant difference regarding the history of previous UTI though it was reported by 27% DM patients and 18% patients without DM.[3] In our study, patients with DM also had a history of previous catheterization significantly more than patients without DM.

In this study, there were five cases of pyelonephritis and two hydroureteronephrosis among T2DM patients and none among non-DM patients though these did not attain statistical difference. This is similar to the higher prevalence of pyelonephritis reported in men and women with DM vs. men and women without.[3,19,20] Three cases of pyelonephritis were caused by *E. coli* and one each by *Klebsiella* and *Enterococcus* similar to the Indian study that reported *E. coli* as the most common organism isolated from pyelonephritis.[3] There were two cases of hydroureteronephrosis

(HUN), caused by an *E. coli* and *Klebsiella*, among patients with DM but none among patients without DM.

The present study found that *E. coli* is the most common organism isolated from patients irrespective of DM status. Similar finding was reported by previous studies.[3,7,9–13,21–23] *Enterococcus, Klebsiella,* and *Pseudomonas* were also isolated in decreasing order of frequency. These three bacteria were also isolated in the studies just quoted with a small change in the order of frequency. There were two UTI cases caused by *Candida* species in patients without DM and one in patients with DM.

This study also found that isolates of *E. coli* from patients with DM and without DM were sensitive to the following antibiotics in decreasing order of sensitivity: meropenem (88% vs. 85%) >netilmycin (86% vs. 81%)> nitrofurantoin (75% in both study groups) >gentamicin (58% vs. 62%). This antibiotic sensitivity pattern is similar to previous Indian studies.[3,6-8,11,23] This study also found decreased sensitivity of *E. coli* to aminopenicillin (amoxicillin), cephalosporins (cephalexin, cefotaxime, and ceftriaxone), quinolones (ciprofloxacin, norfloxacin, and levofloxacin), and cotrimoxazole with the sensitivities ranging from 3 to 8%, 9 to 14%, 5 to 14%, and 20 to 30%, respectively. A similar pattern of decreased the sensitivity of *E. coli* was also reported by previous Indian quoted above. The findings of these Indian studies show that nitrofurantoin can be used as empirical therapy for UTIs in patients with and without DM by physicians in primary and remote health centers. Again, the decreased sensitivity of *E. coli* to aminopenicillin and fluoroquinolones indicates that primary care physicians should not use these oral drugs for empirical treatment of UTIs. It is noteworthy that isolates of *E. coli* showed low sensitivity ranging 3–8% to colistin, which regained importance in the past few decades owing to its effectiveness in the treatment of emerging drug-resistant gram-negative bacteria.

In this study, all the UTI patients, with and without DM, were given empirical therapy irrespective of whether they were symptomatic or asymptomatic. The thirty-two cases of ASB among patients with DM and six among patients without DM were also given empirical antibiotic though there are no recommendations to treat ASB irrespective of DM status from Government of India,[24] Infectious Disease Society of America,[25] and standard reference textbook.[26] In the past, there were concerns about ASB leading to symptomatic UTI and deterioration of renal function in patients with DM.[27,28] However, those concerns have been disproved by studies with a follow-up period ranging 27 months to 6 years, conducted on patients with DM.[29,30] Moreover, the most common empirical antibiotic given to the UTI patients was ceftriaxone in spite the decreased the susceptibility of UTI causing *E. coli* to ceftriaxone or cephalosporins shown by previous studies from India. These appear to emphasize the need to update the clinicians with the antimicrobial sensitivity pattern of organisms causing UTI from recent studies and the latest studies according to which treatment of ASB has not been recommended.

In conclusion, this study found significantly higher ASB, history of prior UTIs and catheterization, and pyelonephritis among patients with DM compared to patients without DM. Interestingly, significantly fewer patients with DM had fever. All UTI patients, with and without DM, including ASB were given empirical antibiotic treatment; ceftriaxone being the most commonly used in spite recommendations not to treat ASB and decreased the sensitivity of UTI causing *E. coli* to ceftriaxone and other cephalosporins by recent studies from India.

Directions for future research: This study highlights the difference in the prevailing sensitivity of organisms to antibiotics and the actual antibiotic given by physicians to treat UITs. Future studies can be planned to study the factors underlying this difference. Again, physicians gave the same antibiotic for UTIs in patients with and without T2DM; further studies can investigate if UTI patients with and without T2DM respond to treatment the same manner or not, and future studies should focus on the etiology and culture sensitivity of UTIs in both outpatient and inpatient settings.

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Conflicts of interest

There are no conflicts of interest.

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