Original Research Article

Microbiological analysis of urinary tract infection in diabetic patients

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ABSTRACT

Background: Diabetes mellitus is a predisposing condition to different infections especially the complicated urinary tract infection (UTI). The susceptibility pattern of organisms in diabetics is different from their counterparts. So, there is always a dilemma while administering empirical regimen for UTI in diabetics. The study aims to find the common organisms implicated in the UTI in diabetic patients and their sensitivity pattern.

Methods: Properly collected urine specimen from all the diabetic (cases) and non-diabetic (controls) patients included in this study was processed. Sensitivity pattern and extended spectrum beta lactamase (ESBL) production for the isolated uropathogens was noted.

Results: E. coli was the most common organism isolated from both 68 cases and 85 controls in this study. Most of UTI patients with diabetes, 46 (67.7 %) had uncontrolled blood sugar level. Diabetics are more prone for catheter associated UTI (CAUTI) and fungal UTI. Most of the E coli and Atypical E coli isolated were ESBL positive for the diabetic patients (60.5%) than that for the non-diabetes (40.4%). Antimicrobial resistance pattern was similar in both the groups with maximum patients’ sensitivity to tigecycline, colistin, fosfomycin and least susceptibility to cefixime. Both E. coli and Klebsiella also showed high resistance to the fluoroquinolones.

Conclusions: E. coli is the predominant uropathogen for both the diabetic & non-diabetic cases. But diabetics are more prone to get ESBL positive UTI. CAUTI and the fungal UTI are more common in diabetics. Diabetic condition does not affect the antimicrobial resistance pattern of uropathogens. But their rising resistance to fluoroquinolones, cephalosporins is a matter of concern while prescribing empiric regimen.

Keywords: CAUTI, Diabetes mellitus, Extended spectrum beta-lactamase positive, Fluoroquinolones, Urinary tract infection

INTRODUCTION

Diabetes mellitus is the most common endocrine diseases of this century. Urinary tract infections (UTI) are of special concern for diabetic patients as these patients have a weak immune system. The increased susceptibility to UTI is attributed to factors like impairments of host defense mechanisms such as leukocyte adherence, chemotaxis, and phagocytosis that can be impaired in diabetic patients.¹ Type 2 diabetes mellitus patients are more prone for complications of UTIs such as pyelonephritis, renal abscess, emphysematous cystitis and renal papillary necrosis, and especially the UTIs by resistant uropathogens.²,³ Urinary tract infection (UTI) is commonly caused by Gram-negative bacteria such as Escherichia coli, Klebsiella species, Enterobacter species, Citrobacter species, Pseudomonas species, Proteus species and gram-positive bacteria like Enterococcus species, Streptococcus, Candida albicans and Staphylococcus saprophyticus.⁴ Bacteruria is more common in diabetics than in non-diabetics due to a combination of host and local risk factors.⁵ Gererlings in a study showed that 23% of type-2 diabetes mellitus patients with asymptomatic bacteruria (ASB) developed symptomatic UTI within 2 months and postulated that ASB was the most important risk factor for developing
UTI in diabetic women. Controversies still persist
regarding the pathogens and treatment of UTI in
diabetics. Trends of antibiotic resistance in diabetic
associated UTI show a diverse pattern where pathogens
are increasingly developing resistance to available
antibiotics. Information regarding the prevalence,
causative agents and their response to the available
antibiotic agents will be of great help in managing and
controlling UTI in type 2 diabetes mellitus patients.
Hence a study was planned to know various uropathogens
and their drug susceptibility in diabetic patients.

METHODS

This cross-sectional prospective study was carried out in
the Department of Microbiology, IMS and SUM
Hospital, Bhubaneswar from October 2019 to December
2019. An informed consent was obtained from all the
participants. The patients included in this study were the
known diabetics on treatment or, having symptoms of
diabetes plus casual plasma sugar concentration >200
mg/dl or fasting blood sugar (FBS) >126 mg/dl, 2-hour
post load glucose >200 mg/dl during an OGGT and with
any symptom suggestive of UTI. Control subjects were
the known non-diabetic patients and FBS <100 mg/dl
with any symptom suggestive of UTI. Proper history was
collected from all the patients to rule out for any other
immunosuppressive conditions or therapy.

Clean catch midstream urine specimens from non-
catheterized patients; urine obtained after cleaning the
catheter tube with 70% alcohol in catheterized patients
were used in the study. Suprapubic aspirate when
required was collected by the clinician. Urine was
obtained in a wide mouthed container, transported and
processed in the laboratory within 30 minutes or
refrigerated at 4°C when any delay was anticipated.
The urine was cultured by streaking one loopful of the sample
by a calibrated loop on cystin-lactose-电解质-volulanic acid
(CLED) agar and plate was incubated aerobically overnight at 37°C. For direct microscopy 50
μl of well mixed uncentrifuged urine was examined under
a high-power objective. The presence of one pus
cell/7HPF was considered significant pyuria. Any
significant growth on the plate was identified based on
colony morphology, gram staining and appropriate
standard biochemical tests. Fungi were identified by
colony morphology, gram stain, germ tube test and
culture on Hi-chrome agar medium. Sensitivity was put
only for cultures showing significant bacteriuria or
candiduria. Presence of at least 3 types of
microorganisms in one urine specimen was considered as
contaminated urine and these specimens were excluded.
ESBL production by the organism was detected by using
ceftazidime (CAZ) and ceftazidime clavulanic acid
(CAC) discs on MHA plate with 0.5 McFarland standardized inoculum. An increase in zone of inhibition
by 5 mm with CAC in comparison to CAZ was
considered as ESBL positive. Susceptibility to different
antibiotics based on type of growth was performed on
Muller Hinton agar plate by standard Kirby Baur's disc
diffusion method as per the CLSI guidelines.

RESULTS

In the present study, 153 UTI patients were consecutively
enrolled of which 68 belonged to diabetic (cases) and 85
to the non-diabetic (control) population. Out of total 68
diabetic patients, 32 (47 %) were female and 36 (53 %)
were male. Of the non-diabetics 47 (55.3 %) were males
and 38 (44.7 %) were females. Males outnumbered
females in both the study and control population. The
highest number of respondents (32.4%) of diabetes was
in 61-70 years, followed by ≥71-year age group (29.4%).
Among the control population the younger age group (0-
30 Year) had the highest frequency (27.1%) followed by
61-70 years (23.5%) and ≥71-year age group, (18.8%).
The mean age among diabetic and non-diabetic patients
was 55.3±21.0 years and 53.1±22.2 years respectively
(Figure 1).

Figure 1: Distribution of respondents according to age
and gender.

Out of the diabetics, 34 (50%) were taking oral
hypoglycemic agents (OHA) and rest were on insulin.
Most of UTI patients with diabetes, 46 (67.7 %) had
uncontrolled blood sugar level. 53 (78.4%) of study
population and 43 (50.6 %) of control population were
catheterized (Table 1).

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<th>Demographic parameters</th>
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<th>Diabetes status</th>
<th>Treatment history</th>
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<td>Non catheterized</td>
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<tr>
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Table 1: Comparison of clinical characteristics between the two study groups.

OHA= Oral hypoglycemic agent
E. coli was the most common organism isolated in both diabetic (55.9%) and non-diabetic group (67.1%). Other pathogens isolated frequently in diabetics were Candida spp. (11.8%), Klebsiella spp. (8.8%) and Pseudomonas spp. (5.9%). But for non-diabetic cases the frequent organisms isolated apart from E. coli were Klebsiella spp. (11.8%) and Enterococcus spp. (5.9%). The percentage of other Enterobacteriaceae was 22.0% for diabetic group and 16.5% in controls. The no fermenters were seen in 4/68 (5.9%) and 3/85 (3.5%) for case and control population respectively. Among the gram-positive bacteria Enterococcus spp was the commonest organism isolated seen in cases and controls 1/68 (1.5%) and 5 (5.9%) respectively (Figure 2).

Figure 2: Distribution of uropathogens.

Table 2: Sensitivity (%) pattern of gram-negative pathogens.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>E. coli</th>
<th>Klebsiella spp</th>
<th>Proteus spp</th>
<th>Citrobacter spp</th>
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(CAC- Cefazidime clavulanic acid, CTR- Ceftriaxone, AMC- Amoxicillin lavalunic acid, PIT- Piperacillin Tazobactam, NET- Netilmicin, AK- Amikacin, TOB- Tobramycin, OF- Ofloxacin, NX- Norfloxacin, NIT- Nitrofurantoin, COT- Cotrimoxazole, CFS- Cefoperazone sulbactam, CFM- Cefixime, MRP- Meropenem, IC- Imipenem cilastin, TGC- Tigecycline CL- Colistin, MI- Minocycline, PB- Polymixin B, FO- Fosphomycin)
cases, all were ESBL positive (100%).

Klebsiella spp

Proteus spp. was sensitive to most of

Citrobacter spp,

etic the antibiotics. In diabetic patients

study groups,

where it was resistant to all the antibiotics. In both the

In non

(16.7 %, 45.5%)

antibiotics including nitrofurantoin excepting

groups,

non

and

(90.7%,

80.7%), fosphomycin (95.3%,80.7%)

Most of

(87.5%).

The Candida isolates here reported only when they were

clinically significant. Only 2 species i.e Candida albicans

and Candida glabrata were found in the study. The yeast
cells in urine were 8/68 (11.8%) of total cases and 4/85
(4.7%) in the control group. Most of them were on
catheters5/8 (62.5%) and had associated pyuria 7/8
(87.5%).

Most of E. coli were sensitive to tigecycline (93%,
80.7%), fosfomycin (95.3%,80.7%) and colistin
(90.7%, 89.5%), amoxicillin-clavulanate (83.7%, 84.2%)
and resistant to cefixime (93%, 77.2), ceftriaxone (79.1%,
77.2%) and ofloxacin (74.4%, 77.2%) in diabetic and
non-diabetic UTI patients respectively. In both the
groups, Klebsiella spp was overall resistant to most of the
antibiotics including nitrofurantoin excepting tigecycline
(16.7 %, 45.5%) and colistin (0% and 9.9%) respectively.

In non-diabetic UTI patients Proteus spp. was sensitive to
most of antibiotics in contrast to the diabetic patients
where it was resistant to all the antibiotics. In both the
study groups, Citrobacter spp. was sensitive to most of
the antibiotics. In diabetic patients Pseudomonas spp.
was 100% resistant to ceftriaxone, ceftazidime-clavulanic acid
and ofloxacin. But non-diabetic UTI patients this
organism showed high degree of resistance to the most
antibiotics except fosfomycin. Acinetobacter spp, was a
contributing agent only in non-diabetic cases, resistant
to common antibiotics, except tigecycline, colistin,
minocycline and fosphomycin (Table 2).

For both diabetic and non-diabetic cases the antimicrobial
resistance pattern was similar having no gross difference
seen in case of E. coli, Citrobacter spp and
Pseudomonas spp with maximum sensitivity to
tigecycline, colistin, fosphomycin and least susceptibility
to cefixime. E coli and Klebsiella showed high degree of
resistance to the quinolones (Table 2).

ESBL positive E. coli was higher in

diabetic patients (60.5%) as compared to that for

non-diabetics (40.4%). Of the two Proteus spp, isolated only
in nondiabetic cases, all were ESBL positive (100%).

Figure 3: ESBL pattern of the isolated gram negative enterobacteriaceae.

Table 3: Sensitivity (%) pattern of gram-positive pathogens in non-diabetics.

|         | V | L | Z | A | M | T | N | O | L | H | A | F | K | C | P | T | C | O | M | R | T | E |
| S.aureus (nondiabetics) | 10| 0 | 0 | NA | 10| 0 | 0 | 50| 50| NA | 10| 0 | 100| 100| 100| 10 | 0 | 50| 100| 10 |
| Enterococcus spp (nondiabetics) | 80| 10| 0 | 40| 20| 60| 40| 20| 20| 40| 80| NA | NA | NA | NA | NA | NA | NA | NA | A |
| Enterococcus spp (diabetics) | 10| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10| 0 | NA | NA | NA | NA | NA | NA | NA | A |

Enterococcus spp. had showed maximum susceptibility for linezolid, fosfomycin and vancomycin. But S. aureus is sensitive to most of the antibiotics (Table 3).

Candida glabrata isolated only in diabetic cases were sensitive to common antifungals like fluconazole, amphotericin B, voriconazole and ketoconazole while 83.3% (5/6) of them were sensitive to itraconazole. The C. albicans isolated in both the groups were 100% sensitive to amphotericin B and voriconazole. But these were the more resistant strains in diabetics than non-diabetics and sensitivity was (75%, 100%) for fluconazole, (50%, 100%) for ketoconazole and (25%, 50%) for itraconazole in both the groups respectively.

**DISCUSSION**

Women are always at a higher risk of acquiring UTI than men. Both symptomatic and asymptomatic urinary tract infection are reported to occur with increased frequency in women with diabetes.8,9,10 Microorganisms thriving at the perianal region can easily access the urethra in women due to the proximity between the two. But in this study, males’ patients outnumbered females in both the study and control population. This may be gender disparity for financially poor and illiterate people in the society for accessing health services.

The highest number (32.4%) of respondents of diabetes was in 61-70 years, followed by ≥71-year age group (29.4%). Besides other predisposing factors, research has shown that age also contributes to the risk of a diabetic patient contracting UTI. Diabetic women in the premenopausal, menopause and postmenopausal stage were found to be 4.1 times more likely to be diagnosed with pyelonephritis than those without diabetes.11 Old age facilitates muscle dystrophy and consequently affecting complete voiding. Incomplete voiding encourages colonization of the urogenital tract leading to development of UTI.12

In this study for diabetic patients E. coli was the most common (55.9 %) organism isolated, followed by Klebsiella (8.8 %) and Pseudomonas (5.9 %). But for non-diabetic controls next to E. coli (67.1%) the usual organisms were Klebsiella (11.8%) and Enterococcus (5.9%). In a similar study E. coli was the most frequent uropathogen isolated, responsible for UTI in 60.2% and 65.3% of diabetic males and females respectively and 50 and 51.4 % of non-diabetic males and females.13 Another study also reported Escherichia coli as the commonest organism for diabetic cases followed by Klebsiella spp., Proteus spp. and Pseudomonas spp.14 The reason for predominant E. coli isolation is that it can bind to the glycoconjugate receptor of the epithelial cells of human urinary tract so that it can initiate infection itself.

There is a paucity of data on the role of diabetes itself as a risk factor for the development of antimicrobial resistance of the uropathogens. In this study most of E. coli strains were sensitive to Tigecycline, Colistin, Fosfomycin and least susceptibility to Cefixime. Proteus spp. showed resistance and Citrobacter spp. sensitive to most of the antibiotics. Pseudomonas spp. is 100% resistant to ceftriazone, cefazidime clavulanic acid and ofloxacin. For both diabetic and non-diabetic cases, most of Enterobacteriaceae organisms showed high resistance to fluoroquinolones which are generally the choicest empiric regimen for UTI. This study also found decreased sensitivity of E. coli to aminopenicillins, cephalosporins, and Co-trimoxazole similar to another study.15 In contrast to ours, in a study by Simkhada et al most of the urinary isolates were sensitive to ciprofloxacin, cotrimoxazole and ceftriaxone, whereas resistance was high for ampicillin.14 This is change in sensitivity pattern over time is probably due to selection pressure due to use of these common antibiotics. As in our work another study by Srinivas et al also showed similar antimicrobial resistance pattern in both diabetic and non-diabetic groups with maximum sensitivity to meropenem and least susceptibility to ampicillin. Aminoglycosides showed a better sensitivity profile than cefoperazone-sulbactum in both diabetics and non-diabetics.13 Saber et al who demonstrated that E. coli sensitivity to carbapenems was 100 per cent in both diabetic and non-diabetic subjects.16

Out of few gram-positive organisms isolated in the present study; S. aureus was sensitive to most of antibiotics and Enterococcus spp. showed maximum susceptibility to linezolid, fosfomycin and vancomycin. In another study Enterococcus spp showed maximum susceptibility to linezolid, teicoplanin and vancomycin. All the MRSA isolates in that were sensitive to vancomycin and linezolid.13

The high rate of resistance of uropathogens to broad spectrum antibiotics in diabetes is an alarming finding, thus these antibiotics should be strictly reserved for complicated UTIs. Uncontrolled diabetes plays a major contributing factor for UTI and was 68.3% of the diabetic cases. It is supported by other studies also in which a higher frequency of UTI was noticed among diabetic patients with poor glucose control.17,18

In the present study, 53/68 (78.4%) of diabetic patients and 43/85 (50.6 %) of control population were catheterized. The morbidity and mortality of catheter associated UTI (CAUTI) increases when the affected individual is diabetic. Diabetic patients with catheters are more prone to Pseudomonas infections.19 Differentiation between colonization and infection are very important as patients with indwelling urinary catheters are liable to develop repeated episodes of bacteriuria and this may result in repeated administration of antibiotics with the emergence of highly resistant bacteria.20

Extended spectrum beta-lactamases (ESBL) positive (60.5%) E. coli including atypical E. coli isolated in diabetic patients was significantly higher compared to...
that for non-diabetics (40.4%). This maximum number of E. coli in this study as ESBL positive is supported the fact that diabetics, especially with poor control, are more prone to get ESBL positive UTI.17,21,22

Fungal UTI among diabetic population are more common in patients with prolonged hospital stay, catheterization and prolonged parenteral antibiotic use.23 In this study also diabetic patients have a higher propensity for Candiduria in urine and only Candida albicans and Candida glabrata were isolated yeasts. In another study, Fungal UTI among diabetic population was more common in patients with prolonged hospital stay, catheterization and prolonged parenteral antibiotic use.23 However to draw a better comment about pathogens especially for fungi in both the diabetic and non-diabetic UTI patients a larger sample size is required.

CONCLUSION

Diabetes is a common predisposing factor for UTIs especially for aged persons above 60 year. Diabetic patients also have a higher propensity for Candida infection in urine. E. coli is the predominant uropathogen in both diabetic and non-diabetic cases. But diabetics are more prone to get ESBL positive and catheter associated UTI. Rising prevalence of resistance to fluoroquinolones, cephalosporins is a matter of concern while prescribing empiric regimen. The high-end antibiotics (tigecycline, colistin, fosphomycin and vancomycin) are to keep reserved and not to be used empirically unless otherwise their use is warranted. Regular monitoring of the antibiotic susceptibility of uropathogens in a particular area is of key importance.

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REFERENCES


