Original article

# Bacterial urinary tract infection and antibiotic sensitivity pattern among type II diabetic patients – A cross-sectional study from tertiary care teaching hospital in Central Lahore

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## ABSTRACT

Background: Diabetes mellitus is the fifth leading cause of death in developed countries. Risk of infections is increased in diabetic patients with urinary tract being the most common site of infection. Worldwide, the prevalence of urinary tract infections (UTI) is estimated to be around 150 million persons per year. UTI exhibit a poorer prognosis in patients of type 2 diabetes mellitus (T2DM) due to a compromise in their immune status in addition to emerging antimicrobial resistance due to widespread use of antimicrobial agents. This study aims to determine frequency of common bacterial pathogens causing UTI and antibiotic sensitivity pattern among type 2 diabetic patients. This may help to guide physicians regarding appropriate management of UTI in the local population to avoid multidrug resistance.

Patients and methods: This cross sectional study involved 215 type 2 diabetic patients admitted to Medical Unit-III of Sir Ganga Ram hospital, Lahore from 01-12-2016 to 31-05-2017. Type 2 adult diabetic patients (diagnosed for at least 1 year) of age 40-80 years, either male or female, with urine pus cells ≥5/HPF performed as baseline investigation at admission were included in the study. Further urine samples were obtained (clean catch midstream urine 10cc in two wide mouth sterile screw capped plastic jars) before starting treatment. Samples were sent for microscopy and culture. Culture results and antibiotic sensitivities were recorded. Data was analyzed using SPSS for windows version 23.0. Categorical variables like gender, organisms and antibiotic sensitivity was presented in Frequency or Percentage form. Numerical variables like age and duration of diabetes were presented as Mean± SD. Data was stratified for age, gender and duration of DM to deal with effect modifiers. Post stratification chi-square test was applied. A-value of ≤0.05 was considered significant.

Results: Total of 215 patients were included. Mean age was 63.76±10.342 years of which 164 (76.3%) were females, while 51 (23.7%) were males reflecting female predominance. Most common isolated organism in urine culture was *E. coli* (58.6%), followed by Klebsiella (20.5%), Proteus (9.3%), Pseudomonas (8.4%) and Enterococcus (3.3%) species. Most of the patients (76.7%) were sensitive to piperacillin-tazobactam followed by carbapenems (67%) and Gentamycin (56.7%), whereas 24.2% showed sensitivity to all antibiotics.

Conclusion: Females are most commonly affected among diabetic patients. The commonest isolate was *E. coli* among culture positive UTIs. *E. coli* was most sensitive to piperacillin-tazobactam and carbapenems followed by Gentamycin while least sensitive to Ceftriaxone. The results emphasize the importance of practice of urine culture and sensitivity testing in diabetic patients and cautious approach to use of commonly used antibiotic ceftriaxone and ciprofloxacin as empirical treatment for UTI despite the low sensitivity of the drug to the most prevailing organism.

Keywords: Urinary tract infection; Type 2 Diabetes Mellitus; Antibiotic sensitivity; Pathogens

## INTRODUCTION

Diabetes mellitus is one of the most challenging health issues of 21st century considering that it is among the top ten leading causes of mortality in developed countries.[1] Approximately under half a billion people worldwide are suffering from diabetes – global prevalence of diabetes in 2019 was around 9.3% (463 million people), projected to increase to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045.[2] Asian patients not only have a greater risk of developing diabetes but they also exhibit poorer prognosis.[3] The prevalence of Diabetes in Pakistan is reported to be around 11.7%.[4] Type 2 diabetes mellitus (T2DM) is a group of various disorders including several degrees of insulin resistance, improper insulin secretion, and a rise in glucose production. Patients of T2DM have a greater risk of developing infections with the urinary tract infection (UTI) being the most frequent.[5] The global

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prevalence of urinary tract infections acquired in the community is 0.7%.[6] UTIs are not only more common in type 2 diabetics but the course of disease is also more severe with greater morbidity as a result of a compromised immune system and physiological changes attributable to neuropathies involving the urinary tract.[4-7] UTIs in diabetic patients have a range of clinical presentations; from asymptomatic bacteriuria to symptomatic UTI and its complications.[7]E.coli followed by Klebsiella, Pseudomonas, *Proteus mirabilis* and Enterococcus are the most commonly implicated pathogens.[8] The susceptibility of these organism to antibiotics is variable in different regions of the world.[9,10] On account of rapidly emerging multidrug resistant (MDR) strains of the organisms to specific antibiotics following noncompliance, injudicious use of drugs, over the counter medications particularly in underdeveloped countries, health care professionals need knowledge of bacterial uropathogens and antibiotic sensitivity patterns in their respective local population regions to avoid emerging resistance to organisms due to irrational use of antibiotics. This study aims to determine frequency of common bacterial pathogens causing UTI and antibiotic sensitivity pattern among type 2 diabetic patients with the objective to guide physicians regarding appropriate management of UTI in the local population to avoid multidrug resistance.

## PATIENTS AND METHODS

This cross sectional study was performed in Medical Unit-III of Sir Ganga Ram Hospital, Lahore from 01-12-2016 to 31-05-2017. A sample size of 215 cases was taken by non-probability consecutive purposive sampling using a confidence level of 95% and a margin of error of 4%. UTI is generally asymptomatic in diabetics. Patients of both genders, aged 40- 80 years, with known Type II diabetes diagnosed for at least 1 year and found to have urine pus cells ≥5/HPF on baseline urine test at admission were included in the study report. Patients not giving consent, those with urinary catheter, already taking antibiotics or those on immunosuppressive drugs were excluded from the study. A semi-structured close-ended questionnaire was used to collect the demographic and study parameters details. Urine samples were taken using clean catch midstream urine 10cc in two wide mouth sterile screw capped plastic jars before starting treatment. Samples were sent for microscopy and culture to pathology lab of Fatima Jinnah Medical University within an hour of sample collection. Samples for culture were inoculated on Blood and Cystine-Lactose-Electrolyte Deficient (CLED) agar media. Cultures showing >$10^5$ CFUs of organisms/ml were taken as positive For each of the isolates, antibiotic susceptibility was done by Kirby Bauer disk diffusion technique and a record was made of culture results and antibiotic sensitivities. SPSS for windows version 23 was used for data entry and analysis. All the categorical variables like gender, organisms and antibiotic sensitivity were expressed as frequency or percentage. All the numerical variables like age and duration of diabetes were presented as mean ± SD.

Table 1. Frequency of UTIs in diabetic patients according to age, gender and duration of diabetes

| Characteristics | Frequency | Percentage |
|---|---|---|
| Age groups | | |
| 40 – 60 years | 96 | 44.7 |
| 61 – 80 years | 119 | 55.3 |
| Gender | | |
| Male | 51 | 23.7 |
| Female | 164 | 76.3 |
| Duration of diabetes | | |
| < 15 years | 146 | 67.9 |
| >15 years | 69 | 32.1 |

## RESULTS

During the study period, 215 patients were included, having mean age of 63.76±10.3 years. Among them 164 (76.3%) were females, while 51 (23.7%) were males. Table 1 summarizes the demographic details of study patients. The mean duration of diabetes recorded in this study sample was 12.71± 6.021 years. Out of total 215 patients, 104 (48.4%) patients had *E. coli*, 33 (15.3%) had Klebsiella, 19 (8.8%) had Pseudomonas, 14 (6.5%) had Proteus, 4 (1.9%) had Enterococcus, 4 (1.9%) had other species and 37 (17.2%) patients had no growth on urine culture (Table 2). *E. coli* exhibited greatest sensitivity to carbapenems 99% and Piperacillin-tazobactam (99%) followed by, Gentamycin 68.4%, Ciprofloxacin 52.5% and Ceftriaxone 34.5%. Klebsiella spp. showed higher sensitivity to carbapenems 99% followed by pipracillin-tazobactam 98%, Gentamycin 75.2%, Ciprofloxacin 68.3% and Ceftriaxone 40.2%.

Table 2. Frequency of microorganism causing UTI

| Microorganisms | Number | Percentage |
|---|---|---|
| *E. coli* | 104 | 48.4 |
| Klebsiella | 33 | 15.3 |
| Pseudomonas | 19 | 8.8 |
| Proteus | 14 | 6.5 |
| Enterococcus | 4 | 1.9 |
| No growth | 37 | 17.2 |
| Others (Staphylococcus) | 4 | 1.9 |
| Total | 215 | 100 |

Table 3. Antibiotic sensitivity pattern of UTI pathogens

| Antimicrobial agents | Susceptibility | *E. coli* | Klebsiella | Pseudomonas | Proteus | Enterococcus |
|---|---|---|---|---|---|---|
| Piperacillin/Tazobactam | Sensitive | 99 | 98 | 98 | 98 | 97 |
| | Resistant | 1 | 2 | 2 | 2 | 3 |
| Carbapenems | Sensitive | 99 | 99 | 99 | 98 | 97 |
| | Resistant | 1 | 1 | 1 | 2 | 3 |
| Gentamycin | Sensitive | 68.4 | 75.2 | 74.9 | 73.4 | 78.1 |
| | Resistant | 31.6 | 24.8 | 25.1 | 26.6 | 21.9 |
| Ciprofloxacin | Sensitive | 52.5 | 68.3 | 42.8 | 48.4 | 2.2 |
| | Resistant | 47.5 | 31.7 | 57.2 | 51.6 | 97.8 |
| Ceftriaxone | Sensitive | 34.5 | 40.2 | 46.7 | 68.6 | 5.5 |
| | Resistant | 65.5 | 59.8 | 52.3 | 31.4 | 94.5 |

Pseudomonas was highly sensitive to Carbapenems 99% followed by Piperacillin-Tazobactam 98%, Gentamycin 74.9%, Ceftriaxone 46.7% and Ciprofloxacin 42.8%. *Proteus spp.* also showed highest sensitivity to carbapenems 98% and Piperacillin-Tazobactam 98% followed by Gentamycin 73.4%, Ceftriaxone 68.6% and Ciprofloxacin 48.4%. Enterococci had high sensitivity to carbapenems 97% and Piperacillin-Tazobactam 97%, followed by Gentamycin 78.1%, Ceftriaxone 5.5% and Ciprofloxacin 2.2% (Table 2).

## DISCUSSION

This study was carried in diabetic patients from Lahore, Pakistan to determine the frequency of UTI and antimicrobial susceptibility pattern. Female diabetic patients showed a greater prevalence of UTI (76%) along with a significant correlation between gender and antibiotic sensitivity. Similar observations were made by Kaleemullah and coauthors in a Pakistani study and Sewify and coworkers from Kuwait.[8,12] One of the reasons for this increased prevalence reported is the anatomical differences of the urinary tract between males and females (as a shorter urethra allows easier access of bacteria to the bladder) and poor personalhygiene.[13,14] Majority of patients (55.3%) were in age group of 60-80 years which is in disagreement with other studies which have quoted majority of patients in lesser age groups. In a study from Pakistan[12] majority of patients were in the age group of 50-60 years while in another study from India[14] majority was 56-65 years. This could be due to poor hygiene, lower immunity, social and environmental factors. The commonest isolate was *E. coli* (48.4%) similar to studies from Pakistan, Ethiopia, India and Kuwait while isolates of Klebsiella 33 (15.3%), Pseudomonas 19 (8.8%), Proteus 14 (6.5%), Enterococcus 4 (1.9%) and others 4 (1.9%) vary in local and other studies.[8,12,15-17] The high prevalence of *E coli* strains can be attributed to their possession of structural virulence factors such as fimbriae, pili, flagella and secreted virulence factors such as toxins and iron-acquisition systems.[17] *E. coli* exhibited greatest sensitivity to Piperacillin-Tazobactam (99%) and Carbapenems (99%) in this study which is consistent with observation made by Kaleemullah and colleagues where *E. coli* showed a similar sensitivity to Piperacillin-Tazobactam and Imipenem (100%).[12] One study from India showed that organisms were most sensitive to Meropenem.[18] Sensitivity to Piperacillin and Carbapenems was not tested in studies from Ethiopia and Kuwait.[15,16] Piperacillin/Tazobactam had highest sensitivity towards all uropathogens in this as well as in studies from India and Pakistan.[12,18,19] In this study most uropathogens showed less sensitivity to Ciprofloxacin and ceftriaxone – the commonly used antibiotics in this region – with *E. coli* showing 52.5% and 34.5% sensitivity respectively. This is consistent with studies from Kaleemullah and associates where *E. coli* was 45.9% sensitive to Ceftriaxone and 38.9% to Ciprofloxacin as well as in studies from India and Ethiopia.[12,14,15]

The worldwide rise in the incidence of T2DM in the recent years and greater susceptibility of female diabetics to developing UTI with a worse prognosis is expected to place a significant burden on medical costs. This is further complicated with the development of antibiotic resistant strains of UTI pathogens as a result of frequent and improper antibiotic prescription to patients of UTI. There is a clear need for early culture sensitivity in diabetic patients presenting with UTI for prescription of culture specific antibiotics to decrease emergence of resistant organisms, decreasing medical cost and burden on health system resulting from repeated hospitalizations, and avoid complications due to multiple antibiotic regimes.

## CONCLUSION

Prevalence of UTI is more among T2DM females. *E. coli* remains the most common organism causing UTIs and most organisms being sensitive to piperacillin-

tazobactam and carbapenems, in contrast to commonly used antibiotics like ceftriaxone and ciprofloxacin, reflecting that antibiotic susceptibilities are changing over time. However further studies are needed to validate these results so as to guide early and judicious use of antibiotics to prevent emerging resistance to routinely used antibiotics.

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