

MICROBIOLOGIC SPECTRA AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS IN TYPE 2 DIABETIC PATIENTS WITH URINARY TRACT INFECTIONS (UTIs) – A HOSPITAL BASED STUDY

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ABSTRACT

Objectives: To determine the microbiologic spectra and their antibiotic susceptibility patterns in type 2 diabetic patients with UTIs

Materials and Methods: This descriptive cross-sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar from 1st July 2021 to 31st December 2021. Type 2 Diabetic patients with urinary tract infections were recruited in the study. Their urine cultures for sensitivities were carried out. The frequency of positive urine culture was stratified among age and gender to see the effect modifications. Antibiotic sensitivity and resistance patterns were stratified among male and female diabetic patients.

Results: Out of 150 patients, 125 were females and 25 were males. Twenty-seven (27) patients (24.3%) had positive urine cultures, out of whom 19 (70.4%) were females, and 8 (29.6%) were males. The most common organism found in females was *E.coli* (42%). Among male patients with positive urine cultures, *E.coli* was the most common organism isolated in 5 (62.51%). Cefixime had the highest resistance, with 21 (77.8%) of 25 culture-positive patients resistant to it. All the patients with positive urine cultures were sensitive to piperacillin/tazobactam, Meropenem, Doripenem, Cefepime, Aztreonam, and Tigecycline.

Conclusion: Diabetic females are more prone to UTIs with an increased prevalence of positive urine cultures as compared to diabetic men. The most common isolate was *E.coli*. The highest antimicrobial resistance was reported for Cefixime. All patients were sensitive to Meropenem, Tazobactam/Piperacillin, Aztreonam, Tigecycline, Doripenem, and Cefepime.

Keywords: Antibiotic susceptibility; Diabetes mellitus; Urine culture and sensitivity

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INTRODUCTION

Diabetes mellitus is a chronic disease affecting a large population across the globe.¹ The estimated prevalence of diabetes mellitus in Pakistan is 7 to 11% and is expected to cross 15% by the year 2030.² UTIs are a common ailment caused by bacteria. Women are considered more susceptible to urinary tract infections, with more than a 50% chance of every woman experiencing a single UTI during her lifetime.^{3,4}

UTIs, mainly asymptomatic bacteriuria, are three times higher in the diabetic population than in the average population. This finding is probably due to the excretion

of glucose in urine and neurologic dysfunction of the urinary bladder.^{5,6} Lature LH et al. concluded that the prevalence of positive urine culture among diabetic patients was 11%.⁷ *E coli*, *Klebsiella*, and *Proteus* species were isolated in 54.5%, 18%, and 18% of cases respectively.⁸ Murad MC et al. concluded that the prevalence of positive urine culture was 12% among diabetic patients.⁸ *E coli* was the most common pathogen isolated from the urine of diabetic patients in 26% and 55.1% of UTIs in Japan and India respectively.⁹ He K et al. concluded that 70.47% of diabetic patients with asymptomatic UTIs were positive in mid-stream urine cultures, while 44.1% of patients with symptomatic UTIs had positive urine cultures.¹⁰ They also concluded that the rate of a positive culture in males was lower than in females (38.2% vs. 51.2%, $p < 0.05$). Male patients were found to have fewer gram-negative infections than females (53.8% vs. 89.3%, $p < 0.001$) and more gram-positive infections than females (30.7% vs. 9.8%, $p < 0.01$).¹⁰

This study will provide local statistics on the sensitivity pattern of different bacteria, which will modify future

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recommendations and help to prevent irrational empirical use of antibiotics. Our study aims to ascertain the yield of urine culture and sensitivity (C/S) reports in diabetic patients. It will enable us to determine the common organisms grown in culture reports of both male and female diabetic patients. It will also enable us to determine the common drug sensitivities of these organisms so that in the future, patients can be started on such antibiotics even if culture reports are pending or inconclusive.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar, from Jul 1, 2021, to Dec 31, 2021. Non-probability consecutive sampling technique was used. One-hundred and fifty male and female diabetic patients with urinary tract infections on urine routine examination were recruited in the study using an 11% prevalence of positive urine culture in diabetic patients.⁷ This sample size was calculated using the WHO calculator for sample size calculation keeping a 95% confidence interval and 6% margin of error (sample size increases as margin of error decreases). Patients with a history of antibiotic intake in the last week and pregnant women were excluded from the study. The conditions mentioned earlier can act as confounders and introduce bias if included in the study.

After approval from the hospital research and ethical committee, all diabetic patients having urinary tract infections fulfilling the inclusion criteria were included in the study. Written informed consent was taken from all the patients after explaining the purpose and benefits of the study.

All information regarding the name, age, gender of the patient, and duration of diabetes was recorded on pre-designed proforma. Complete history and clinical examination of all patients were carried out. All baseline investigations were carried out, including fasting and random blood sugars.

All the data was stored in the Excel office and analyzed in SPSS (statistical package for social sciences)

version 22. Mean and standard deviations (SD) were calculated for quantitative variables like age, fasting blood glucose level, and random blood glucose level. In contrast, percentages and frequencies were calculated for categorical variables like gender and proportion of positive urine cultures and their respective sensitivities and resistance patterns. The frequency of positive urine culture was stratified among age and gender to see the effect modifications. Post-stratification, Chi-square test, was $p < 0.05$ as statistically significant.

RESULTS

Our study included 150 patients, of which 125 (83.3%) were females and 25 (16.7%) were males. The total number of patients with positive urine cultures was 27 (24.3%), out of which 19 (70.4%) were females and 8 (29.6%) were males. Out of 125 females, 19 (15.2%) had positive urine cultures, while 8 (32%) of 25 male patients had positive urine cultures. The highest number of culture-positive females was between 51 and 60, i.e., 9 (47.4%). Most of the culture-positive males, i.e. 4 (50%), were in the 61-70 age group.

The urine culture sensitivities of patients with positive urine cultures are shown in Table 1, and antibiotic sensitivity and resistance patterns of male and female patients are demonstrated in Table 2.

DISCUSSION

Women are considered more susceptible to urinary tract infections, with more than a 50% chance of every woman experiencing a single episode of urinary tract infection in her life time.¹¹ The prevalence of urinary tract infections increases with age, and its rate doubles in women aged greater than 65 years as compared to the overall rate seen in the female population.¹² The reasons for the higher rate of infection in this age group vary by health status, with certain factors like catheterization increasing the chances for infections, and pathogens are most likely responsible for this.¹³ Increased sexual activity is consid-

Table 1: Urine culture sensitivities of patients with positive urine cultures

Urine Culture			
	Gender (n)		Grand Total (n)
	F	M	
Citrobacter species	2		2
E. coli	8	5	13
Klebsiella	3	1	4
Morganella Morganii	1		1
Pseudomonas	3	2	5
Staph. aureus	2		2
Total	19	8	27

Table 2: Antibiotic sensitivity and resistance patterns of male and female diabetic patients

S#	ANTIBIOTICS	S		R	
			Female (n)	Male (n)	Female (n)
1	Ciprofloxacin	2	5	6	14
2	Levofloxacin	2	5	6	14
3	Cefixime	2	4	6	15
4	Amoxicillin	2	8	6	11
5	Co-Amoxiclav	7	17	1	2
6	Fosfomycin	7	17	1	2
7	Nitrofurantoin	8	15	0	4
8	Doxycycline	7	14	1	5
9	Cefuroxime	4	12	4	7
10	Ceftazidime	5	8	3	11
11	Co-trimoxazole	5	10	3	9
12	Amikacin	4	15	4	4
13	Gentamicin	4	17	4	2
14	Streptomycin	7	14	1	5
15	Ceftriaxone	7	11	1	8
16	Cefoperazone/sulbactam	8	16	0	3
17	Piperacillin/tazobactam	8	19	0	0
18	Meropenem	8	19	0	0
19	Doripenem	8	19	0	0
20	Cefepime	8	19	0	0
21	Aztreonam	8	19	0	0
22	Tigecycline	8	19	0	0

ered a significant risk factor for UTIs in younger women, and recurrence within six months is common.¹⁴ UTIs create a massive societal and personal burden, with many medical visits in the United States being related to them.⁴ In the United States alone, around 8 million annual UTIs have been documented.⁵

Our study indicates that almost one fourth of our patients had positive urine cultures, which is supported by many studies. One study reported that the prevalence of asymptomatic bacteriuria in diabetic patients is from 8-26%.^{15, 16} A meta-analysis was published in 2011 reporting a 12.2% prevalence of asymptomatic bacteriuria in patients with diabetes mellitus in contrast to 4.5% in healthy individuals taken as controls. Hence, we can conclude that UTIs are more common in diabetic patients than in non-diabetics.^{6, 17} This fact is also supported by an observational study conducted in the UK which found that the incidence rate of UTI was 46.9% per 1000 people with diabetes compared to 29.9% for non-diabetics.^{6, 18} An American database study in 2014 found that UTI was more common in diabetic patients of both genders than non-diabetics (9.4% vs. 5.7%), respectively.^{19, 20}

According to our study, 83.3% of our patients with

UTIs diabetics were females, and 16.7% were males, which indicates that more females with diabetes get UTIs as compared to men with diabetes. These findings are supported by a cohort study including more than 6000 patients who were part of 10 clinical trials.²¹⁻²³ A case-control study of Washington state health suggested that pyelonephritis was 4.1 times more prevalent in pre-menopausal diabetic women than in non-diabetic women.^{26, 27} Multiple explanations exist for the increased prevalence of UTIs in people with diabetes compared to non-diabetics.²⁴⁻²⁸ High glucose concentrations inside the renal parenchyma can also promote bacterial growth and proliferation, increasing the risk of complications such as emphysematous pyelonephritis.^{29, 30} Many impairments in the immune system, including innate, cellular and humoral immunity, may contribute to the pathogenesis of UTI in diabetic patients.³¹⁻³³ People with diabetes having asymptomatic bacteriuria demonstrated lower interleukin 6 and 8 levels compared to non-diabetic patients.³⁴ Autonomic neuropathy leading to dysfunctional voiding and urinary retention results in decreased bacterial clearance, contributing to bacterial growth.²⁰⁻²² Our study demonstrated that 83.3% of our patients with UTIs were females and 70.4% of our study's culture-positive patients were also females. These findings

are seconded by a study conducted in Saudi Arabia.³⁴

The highest number of culture-positive females was found between 51-60 years of age group (47.4%), while the highest number of culture-positive males (50%) was found between 61-70 years of age group. These findings are supported by a study conducted at NRI Medical College and hospital, India.³⁵ Another multicenter study conducted at 12 clinical sites spread throughout major cities of Pakistan supports these findings.²⁵

E.coli was the most isolated organism from our patient's urine cultures (48.1%), followed by *Pseudomonas* (18.5%) and *Klebsiella* (14.8%). A study conducted by Murad MC et al. had similar findings where *E.coli* was the most common organism isolated, i.e., in 54.5% of cases.³⁰ *E.coli* was also found to be the most common organism isolated, followed by *Klebsiella* in a study conducted in Kuwait.³¹

According to our study results, Cefixime had the highest resistance reported (77.8%), followed by ciprofloxacin and levofloxacin (74.1%). These findings are supported by a retrospective study conducted in Dublin from 1999 to 2009.³³⁻⁴⁰ A study conducted in Turkey suggested the same, and the reason for resistance to these antimicrobials might be the high use of these antibiotics.³⁴ Diabetic patients are more likely to harbour resistant organisms as a cause of UTIs. It also includes fluoroquinolone-resistant pathogens.^{41,42} There are several explanations for this; use of antibiotics for un-confirmed UTIs without a urine test and only based on symptoms of dysuria or peri-urethral burning, multiple courses of antibiotics, premature stopping of antibiotics after symptomatic relief, quackery, late presentation to a certified health care professional among many others. Injudicious use of urinary catheters is also a leading cause in centers where protocols and guidelines are not followed.³⁶

The cause-and-effect relationship between diabetes and its associated factors could not be studied due to its cross-sectional design. It was conducted at one center, which can lead to selection bias and affect the generalizability of the study. We also did not study the effect of confounding factors like socioeconomic class and education. Other factors like malnutrition and viral infections, e.g. HIV, which might be associated with diabetes, were not recorded. Activity, alcohol, and substance abuse consumption were also not adequately assessed.

CONCLUSION

Diabetic females are more prone to UTIs as well as an increased prevalence of positive urine cultures as compared to diabetic men. The most common isolate

was *E. coli*, followed by *Pseudomonas* and *Klebsiella*. The highest antimicrobial resistance was reported for Cefixime, followed by ciprofloxacin and levofloxacin. Most patients were found sensitive to Cefoperazone/Sulbactam, and all patients were sensitive to Meropenem, Tazobactam/Piperacillin, Aztreonam, Tigecycline, Doripenem and Cefepime.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Badshah A:	Designed the study, data collection, manuscript writing, statistical analysis
Khan A:	Manuscript writing, reference writing
Mohammad W:	Conceived the idea, final editing
Zaman R:	Data collection
Khan Z:	Literature review, data collection
Haider I:	Critical appraisal, supervision

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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