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ORIGINAL ARTICLE

Antibiotic sensitivity pattern among diabetic patients admitted with urinary tract infection.

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ABSTRACT… Objective: To determine the frequency of types of bacterial pathogens involved in urinary tract infections and antibiotic sensitivity patterns among diabetic patients in the medical units of Khyber Teaching Hospital Peshawar. **Study Design:** Cross-sectional study. **Setting:** Department of Medicine, Khyber Teaching Hospital, Peshawar. **Period:** November 9, 2022 until May 8, 2023. **Methods:** The study was conducted after the approval of the hospital's ethical committee and the written informed consent of patients. Data was entered and analyzed using SPSS. Patients aged 16 to 80 years of both genders admitted to medical units with diabetes and diagnosed with urinary tract infection were enrolled using a non-probability consecutive sampling technique. **Results:** In our study, a total of 184 patients were enrolled, with a mean age of 52.08±18.4 years. There were 42.4% male and 57.6% female patients. The most common organism isolated was E. coli in 37% of patients, followed by Klebsiella in 23.9% of patients, Pseudomonas in 6.3%, Enterococcus in 12%, and Proteus mirabilis in 10.9% of patients. The most sensitive drug was Fosfomycin in 89.1% of patients, followed by nitrofurantoin in 81.5%, imipenem in 77.1%, amikacin in 73.3%, Piperacillin/tazobactam in 69%, gentamycin in 67.9%, Trimethoprim-sulfamethoxazole in 66.8%, Amoxicillin-clavulanic acid in 59.7%, ciprofloxacin in 54.3%, ceftriaxone in 51%, and cefixime in 46.1% of patients. **Conclusion:** E. coli is the most common organism isolated in urinary tract infection in diabetics and Fosfomycin is the most sensitive drug for treatment.

Key words: Urinary Tract Infection, Diabetes, E. Coli, Fosfomycin, Antibiotic Sensitivity.

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases of the 21st century, affecting 451 million people worldwide. It is estimated that these figures will increase to 693 million people by the year 2045.[1] It contributes to the seventh leading cause of mortality in the United States.[2] In Pakistan, the prevalence of Diabetes Mellitus is estimated at around 11.7%.[3]

Urinary tract infections, or UTIs, are among the most prevalent infectious diseases worldwide, with a 0.7% prevalence in the general population.[4] Pyelonephritis and cystitis are two types of urinary tract infections (UTIs) that are distinguished by the presence of microorganisms in the urinary tract.

Escherichia coli (E. Coli), Enterococcus faecalis, Klebsiella pneumonia, Serratia marcescens, Pseudomonas aeruginosa, Staphylococcus saprophyticus, Staphylococcus aureus, and Proteus mirabilis are the most frequently occurring microorganisms linked to urinary tract infections.[5] Among these pathogens, E. coli accounts for most of the community-acquired urinary tract infections. It is most frequently isolated from clinical specimens like the blood or urine of the patient. Risk factors for developing UTIs are female gender, urinary tract structural abnormalities like vesicoureteral reflux (VUR), blockage or stricture anywhere in the ureter or urinary bladder, sexual activity, in-situ urinary catheter, and a weak immunity state such as diabetes.[6]

Patients having Diabetes mellitus are prone to various infections. UTI is one of the most frequent

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bacterial infections encountered by these patients. According to one study, the frequency of UTI in patients with diabetes was 13.8%.[7] UTIs have a more severe course of disease in diabetics as compared to non-diabetics, which is because of the weak immune system of diabetics. Neuropathies involving the urinary bladder also play a role in their susceptibility to UTIs.[3] The clinical presentation of UTIs in diabetics may vary from asymptomatic bacteriuria to symptomatic infections and their complications.

The most common bacteria isolated from diabetic patients with UTI is E. coli. Other microorganisms, less common than E. coli, that can also be found in diabetic patients with UTIs are Klebsiella, Pseudomonas, Proteus mirabilis, and Enterococcus.[8] There are regional variations in the way these microorganisms react to antibiotics.[9]

Bacterial pathogens use multiple mechanisms for developing resistance to drugs. They may alter their genetic makeup or develop resistance through the recombination of foreign DNA in their chromosomes or through horizontal gene transfer.[10] Resistance patterns of bacterial pathogens vary from one region to another region, hospital to hospital, and hospital to community. In Pakistan, the issue of antibiotic resistance is increasing day by day because of the overuse and misuse of antibiotics. Moreover, there is no systematic data available regarding antibiotic resistance in Pakistan.

Drug-resistant strains of UTIs are becoming more common in both community and medical settings, and because of the overuse of antibiotics in developing nations like Pakistan, the situation is becoming more difficult.[11] Drug-resistant strains are emerging due to patient noncompliance, over-the-counter drug use, and a lack of knowledge about bacterial uropathogens and antibiotic sensitivity patterns.

The purpose of this study is to identify antibiotic sensitivity patterns and the frequency of common bacterial microorganisms that cause UTIs in diabetic patients. This information will help physicians treat UTIs appropriately in the local population while preventing multidrug resistance.

METHODS

This cross-sectional study was carried out from November 9, 2022, to May 8, 2023, at the Khyber Teaching Hospital in Peshawar, in the Department of Medicine. The data collection method employed was non-probability consecutive sampling. Using an OpenEpi calculator, the sample size is determined with a 95% confidence level, a predicted 13.8%[7] prevalence of UTI in diabetic patients, and a 5% margin of error. A total of 184 samples were calculated.

Inclusion and Exclusion Criteria

The inclusion criteria of this study are: 1) male and female patients admitted to medical units who are diabetic and are diagnosed with UTI based on having ≥5 pus cells/HPF in baseline urine, 2) Age greater than 16 years and less than 80 years. Patients already taking antibiotics and immunosuppressive drugs were excluded from the study.

Data Collection

Data was collected after approval from hospital administration, permission from the Ethical Committee of the institution (Ref No.406/DME/KMC), and informed consent was obtained from every conscious patient and attendant of the unconscious patient after a full explanation of the study work on the questionnaire by the trainee himself.

Patients with diabetes mellitus who were admitted to the medical unit were evaluated, and those patients who met the inclusion and exclusion criteria were enrolled in this study. After fulfilling the management protocol, the data regarding UTI in diabetic patients was collected.

Before beginning treatment, urine samples from diabetic patients were collected using clean catch midstream urine (10 cc) in two wide-mouth sterile screw-capped plastic jars. Within an hour of sample collection, samples were sent to the pathology laboratory of Khyber Teaching Hospital in Peshawar for microscopy and culture.

Statistical Analysis

SPSS, version 26.0, is a statistical program used for data entry and analysis. The continuous variables, which included blood sugar levels, age, and the length of diabetes, were expressed as mean ± standard deviation. Frequencies and percentages were used to describe categorical variables such as antibiotic sensitivity, gender, and the type of diabetes mellitus bacterial pathogens. Via stratification against the frequency of pathogens isolated, effect modifiers such as age, gender, type of diabetes, and duration of diabetes were adjusted. The Chi-square test for post-stratification was applied. A P-value of less than 0.05 was considered statistically significant.

RESULTS

In our study, a total of 184 patients were enrolled, with a mean age of 52.08±18.4 years. There were 42.4% male and 57.6% female patients. The mean duration of diabetes was 7.36 ± 3.7 years. The mean blood sugar level was 256.6±47.3 mg/dl. Type I diabetes was present in 19.6% of patients, and type II diabetes was present in 80.4% of patients. The most common organism isolated was E. coli in 37% of patients, followed by Klebsiella in 23.9% of patients, Pseudomonas in 6.3%, Enterococcus in 12%, and Proteus mirabilis in 10.9% of patients. Table-I

The most sensitive drug was Fosfomycin in 89.1% of patients followed by nitrofurantoin in 81.5%, imipenem in 77.1%, amikacin in 73.3%, Piperacillin/tazobactam in 69%, gentamycin in 67.9%, Trimethoprim-sulfamethoxazole in 66.8%, Amoxicillin-clavulanic acid in 59.7%, ciprofloxacin in 54.3%, ceftriaxone in 51% and cefixime in 46.1% patients, as shown in Table-I.

Data stratification was done for age groups, gender, type of diabetes, and duration of diabetes. Tables-II,III,IV,V.

When age categorized between 16-50 years and above 50 to 80 years, Klebsiella and Pseudomonas were significantly more in patients of age 51-80 years ($p < 0.05$) whereas E. coli, Proteus mirabilis, and Enterococcus were not significant [Table-II].

E. coli, Pseudomonas, and Enterococcus were more common in females significantly ($p < 0.05$), whereas Proteus mirabilis was common in males. Pathogen Klebsiella is not significantly categorized between male and female [Table-III].

When pathogens were isolated from urine samples of diabetic patients, E. coli, Klebsiella, Pseudomonas, and Enterococcus were frequently isolated from type 2 diabetes patients compared to type 1 diabetes [Table-IV].

Klebsiella, Pseudomonas, and Enterococcus pathogens were common in patients having diabetes more than 5 years of duration compared to less or equal to 5 years duration ($p < 0.005$). E. coli and Proteus mirabilis were not significantly categorized based on duration [Table-V].

Parameters		f	%
Age (years)	Mean ± SD	52.1 ± 18.4	
Gender	Male	78	42.4
	Female	106	57.6
Type of diabetes	Type I diabetes	36	19.6
	Type II diabetes	148	80.4
RBS	Mean ± SD	256.7± 47.3	
Duration of diabetes (years)	Mean ± SD	7.36 ± 3.716	
Pathogen Isolated	E. coli	68	37.0
	Klebsiella	44	23.9
	Pseudomonas	30	16.3
	Proteus mirabilis	20	10.9
	Enterococcus	22	12.0
Sensitivity pattern	Fosfomycin	164	89.1
	Nitrofurantoin	150	81.5
	Imipenem	142	77.1
	Amikacin	135	73.3
	Piperacillin/ tazobactam	127	69
	Gentacin	125	67.9
	Trimetho-prim-sulfame-thoxazole	123	66.8
	Amoxicillin-clavulanic acid	110	59.7
	Ciprofloxacin	100	54.3
	Ceftriaxone	94	51
	Cefixime	85	46.1

Table-I. Demographic, pathogen, and pattern of sensitivity in diabetic patients presented with UTI

Pathogen Isolated	16-50 Years		51-80 Years		P-Value
	F	%	F	%	
E. coli	36	52.9	32	47.1	0.871
Klebsiella	12	27.3	32	72.7	0.021
Pseudomonas	8	26.7	22	73.3	0.025
Proteus mirabilis	12	60.0	8	40.0	0.065
Enterococcus	8	36.4	14	63.6	0.071

Table-II. Percentage of pathogen isolated when age categorized into 16-50 and 51-80 years

Pathogen Isolated	Male		Female		P-Value
	F	%	F	%	
E. coli	24	35.3	44	64.7	0.034
Klebsiella	24	54.5	20	45.5	0.92
Pseudomonas	10	33.3	20	66.7	0.031
Proteus mirabilis	14	70.0	6	30.0	0.029
Enterococcus	6	27.3	16	72.7	0.023

Table-III. Pathogen isolated from Urine samples of different gender

Pathogen Isolated	Type 1 Diabetes		Type 2 Diabetes		P-Value
	F	%	F	%	
E. coli	10	14.7	58	85.3	0.012
Klebsiella	8	18.2	36	81.8	0.014
Pseudomonas	4	13.3	26	86.7	0.011
Proteus mirabilis	8	40.0	12	60.0	0.053
Enterococcus	6	27.3	16	72.7	0.035

Table-IV. Pattern of pathogen frequency between types of diabetes

Pathogen Isolated	≤ 5 years of Diabetes		> 5 years of Diabetes		P-Value
	F	%	F	%	
E. coli	34	50.0	34	50.0	0.99
Klebsiella	30	68.2	14	31.8	0.031
Pseudomonas	4	13.3	26	86.7	0.014
Proteus mirabilis	8	40.0	12	60.0	0.063
Enterococcus	0	0.0	22	100.0	0.001

Table-V. The association between the duration of diabetes and pathogen-isolated

DISCUSSION

Diabetes Mellitus (DM) has grown to be a significant socioeconomic burden on developing nations and a global public health concern.[12] Globally, 451 million people had diabetes in 2017, and by 2045, that number is predicted to rise to over 693 million. About 26.3% of the adult population over 19 in the area has diabetes, according to the most recent national diabetes survey conducted in Pakistan.[13]

Urinary tract infections (UTIs) are among the most common medical conditions seen in all age groups with diabetes mellitus. Patients with diabetes are far more likely to get UTIs than those without the disease.[14] Serious UTIs and their aftereffects can contribute significantly to morbidity and death. Additionally, there is a correlation between UTI and increased medical expenses for treating it. One potential cause of UTI in diabetics may be hyperglycemia-induced neuropathy, which can lead to neurogenic bladder, urine stasis, and an increased risk of infection.[15] Other explanations include decreased leukocyte concentrations, decreased urine cytokines, and neutrophil activity, all of which may encourage the adhesion of microorganisms to uroepithelial cells.[16] Moreover, hyperglycemia encourages a variety of organisms to colonize and grow.[17] According to published research, the most frequent isolate is E. Coli, which is followed in frequency by enterococci, gram-positive cocci,

candida, Citrobacter, Serratia, and Klebsiella pneumoniae.[17] The purpose of this study was to ascertain how frequently pathogens were isolated from UTIs in our population of diabetic patients.

A total of 184 patients with a mean age of 52.08±18.4 years were enrolled in our study. Of the patients, 42.4% were men and 57.6% were women. The average number of years with diabetes was 7.36±3.7. A blood sugar level of 256.6±47.3 mg/dl was the average. In 19.6% of patients, type I diabetes was present, while in 80.4% of patients, type II diabetes was. The most common organism isolated was E coli in 37% of patients followed by Klebsiella in 23.9% of patients, Pseudomonas in 6.3%, Enterococcus in 12%, and Proteus mirabilis in 10.9% of patients. The most sensitive drug was fosfomycin in 89.1% of patients followed by nitrofurantoin in 81.5%, imipenem in 77.1%, amikacin in 73.3%, Piperacillin/tazobactam in 69%, gentamycin in 67.9%, Trimethoprim-sulfamethoxazole in 66.8%, Amoxicillin-clavulanic acid in 59.7%, ciprofloxacin in 54.3%, ceftriaxone in 51% and cefixime in 46.1% patients.

Of the 400 T2D patients that were studied in Peshawar, 205 (51.25%) had microbial growth. Patients suffering from UTIs were 63.26 ±12.30 years old on average. Female patients made up roughly two thirds (63.9%) of the total. HbA1c was 8.80±2.20% on average. When comparing patients with suboptimal glycemic control (178; 86.3%) to those with good control (27; 13.7%), there was a discernible increase in the number of UTI cases. Glycemic levels showed significant mean differences (HbA1c = 5.86±0.48 and HbA1c = 9.25±2.02, respectively; $P < 0.001$). The most common pathogen detected in 120 isolates (71%) was E. Coli, followed by 35 isolates of Klebsiella pneumonia Spp (K. pn), 14 isolates of Pseudomonas auregonosa (P. aeruginosa) (17.1%), 12 isolates of Enterococcus (5.85%), and 2 isolates of Candida Spp (0.98%). Ipenem, meropenem, fosfomycin, and nitrofurantoin were highly susceptible to both gram-positive and gram-negative bacteria. Sensitivity to fosfomycin was 82%.[8]

200 diabetic patients were included in a study carried out in Sudan; 121 (60.5%) of the patients were men and 79 (39.5%) were women; 193 (96.5%) of the patients had type II DM. 17.1% and 20.9% of the overall population, respectively, had bacteriuria with symptoms and no symptoms. Klebsiella pneumoniae and Escherichia coli were the most common isolates. Out of the 22 E. Col isolates, 4 out of 9 K. pneumoniae isolates, and 1 out of 5 Enterococcus faecalis isolates, 8 came from patients who had symptoms. Nitrofurantoin was sensitive in 86%, amoxicillin-clavulanic acid in 90.9%, and gentamycin in 10% of cases.[17]

In an Indian study, 181 patients with diabetes (83 men and 98 women) were enrolled. Glycosylated hemoglobin (HbA1c) > 6.5 percent with $p < 0.001$ was present in the majority of diabetics (87.14 percent) who had UTIs. In patients with diabetes, the percentage of isolates of Escherichia coli (E. coli) from urine cultures was higher (64.6%), followed by Klebsiella (12.1%) and Enterococcus (9.9%). Amikacin was sensitive to 80.7% of cases, amoxicillin-clavulanic acid in 42.6% of cases, gentamycin in 68.5%, Piperacillin- Tazobactum in 68.5% of isolates and ceftriaxone in 50% of cases.[18]

In another study, the most common pathogen was Escherichia coli (71%), which was followed in order by Proteus mirabilis (1.87%), Klebsiella pneumonia (7.48%), Staphylococcus aureus (9.35%), Candida (5.61%), and Candidaalbicans (2.80%). Imipenem and Piperacillin / Tazobactam were found to be highly sensitive to most gram-negative uropathogens, with Nitrofurantion, Ceftriaxone, Levofloxacin, Ofloxacine, Ciprofloxacin, Norfloxacin, Cefixime, Nalidixic acid, and Cephradine following closely behind. Nitrofurantion and Vancomycin were the most effective treatments for Gram-positive bacteria, with Piperacillin/Tazobactam, Imipenem, Cephradine, Ceftriaxone, Norfloxacin, and Cefixime following.[11]

Literature reviews show that E. coli is universally prevalent in all diabetic patients having urinary tract infections but sensitivity pattern varies in different populations.

CONCLUSION

In conclusion, female patients experience UTIs more frequently than male patients. Klebsiella was the second most common pathogen causing UTI in diabetic patients, after E. coli. Fosfomycin was the most sensitive drug in diabetic patients having urinary tract infections.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	Yasir Iqbal	Concetualization, Methodology, Writing original.	
3	Shah Umam	Data correction, Writing original.	
4	Ejaz Khan	Writing original.	
5	Osama Ali Khan	Visualization, Writing original.	
6	Irfan Ullah	Format analysis, Writing Review.	