Original Article

Frequency of Urinary Tract Infection, Microbial Patterns and Drug Resistance in Diabetic Patients in a Tertiary Care Unit

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ABSTRACT

OBJECTIVE: To determine the frequency of UTIs in people with diabetes and identify local bacterial flora and antibiotic resistance.

METHODOLOGY: An observational, analytical, cross-sectional study was conducted at the Medicine Ward of Jinnah Medical and Dental College Hospital (now Sohail Trust Hospital) from January-December 2020. A convenient sampling technique was applied, and the sample size was 132. Diabetic patients >18 years of age were included. Data was collected on a structured questionnaire. A urine sample was sent for culture sensitivity. Any growing flora and their sensitivity/resistance to antibiotics were recorded. All the data were analysed using SPSS version 21.

RESULTS: UTI was found in 31(23.5%) patients. Female gender, insulin therapy, and lower creatinine clearance were related to UTI, as shown by significant p values. Most common flora was E. Coli 26(84%), followed by Klebsiella 4(13%) and S. aureus 1(3%). E.Coli was 100% resistant to 3rd generation cephalosporins, 83.9% resistant to quinolones and 67.7% resistant to Penicillin (amoxicillin/clavulanic acid) and 43% resistant to aminoglycosides. Klebsiella was 100% resistant to Penicillin and quinolones and 85% to 3rd generation cephalosporin. E. coli and Klebsiella were 100% sensitive to carbapenems, nitrofurantoin and Fosfomycin, whereas S. Aureus was resistant to cloxacillin, clindamycin and clindamycin and quinolones, while sensitive to vancomycin., linezolid and aminoglycosides.

CONCLUSION: UTI was found in 23.5% of our diabetic patients; the most common organisms prevalent were E. Coli, Klebsiella and S. aureus, which was primarily resistant to Penicillins, Cephalosporins and quinolones while sensitive to nitrofurantoin, Fosfomycin and carbapenems.

KEYWORDS: Diabetes Miletus, Urinary Tract Infection, E. Coli, Antibiotic Resistance, Aminoglycosides, Quinolones.

INTRODUCTION

Diabetes Miletus is ranked as the fourth most cause of death worldwide[1]. The prevalence of diabetes in Pakistan is reported to be one in four adults (26.7%), the highest national prevalence in the world. In 2021, 33 million adults in Pakistan are living with diabetes – a 70% increase since 2019. Pakistan has the third highest number of people living with diabetes globally, after China (141 million) and India (74 million). In 2021, diabetes was responsible for 400,000 deaths in the country– the highest number in the Middle East and North Africa Region[2].

Diabetes is a multi-system disease affecting all significant organs, i.e. heart, brain, eyes and kidneys. It also increases the chances of certain infections like pneumonia, skin infections, foot ulcers and urinary tract infections. The incidence of repeated UTIs in people with diabetes is growing daily, especially in developing countries, because of a lack of diabetic control, poor hygiene and injudicious use of antibiotics. Thus, the high prevalence of diabetes is a significant burden on the health structure of the country[3].

Diabetes mellitus is a recognised risk factor for urinary tract infection (UTI). In Pakistan prevalence of UTI in people with diabetes ranges from 13-35% [3,4]. Multiple factors contribute to this high prevalence, ranging from poverty, lack of access to healthcare facilities, the self-prescription of antibiotics by the general population, and the over-prescription of antibiotics by healthcare workers without culture/sensitivity. All of this has contributed high prevalence of UTI in the diabetic population, which unfortunately leads to drug-resistant bacteria that were previously responsive to conventional antibiotics, especially beta-lactams and fluoroquinolones[5-7].

Data regarding UTI in diabetes has been studied in many countries. Most studies found gram-negative rods, Escherichia coli, proteus, Klebsiella, coagulase-negative staphylococci, enterococci, and pseudomonas, but there was marked variation in resistance patterns in different areas of the world. Data regarding drug sensitivity patterns is still limited, especially in the Asian population, with a high

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prevalence of diabetes. From the existing data, resistance to the conventionally used anti-biotics fluoroquinolones, penicillins, cephalosporin and aminoglycosides is constantly increasing, so there is a need to search for drug sensitivity patterns at the hospital level. It will help to find an alternative to these antibiotics[8-10].

Therefore, the rationale of this study was to help find local sensitivity patterns since, in clinics, it is not always possible to obtain a culture and sensitivity report for each case of UTI, especially the repeated one, because of financial constraints. Moreover, there is not enough information about the relationship between diabetic control (HbA1C), use of insulin and creatinine clearance on the occurrence of UTI. Our study aimed to fill these gaps in previous studies by identifying local bacterial and antibiotic resistance and assessing the effect of diabetic control, treatment and renal functions.

The objective of our study was to determine the frequency of Urinary tract infections in diabetic patients visiting the Medical ward and OPD of Sohail Trust Hospital and to assess the effect of age, gender, duration of diabetes, HbA1c, use of insulin/oral antidiabetics and creatinine clearance on the occurrence of UTI. We also identified the typical flora and their sensitivity and resistance to significant antibiotics, i.e. Penicillin, cephalosporin, Fluoroquinolones, Aminoglycosides, Carbapenems, Nitrofurantoin and Fosfomycin.

METHODOLOGY

It was a single-centred descriptive cross-sectional observational study conducted at the Department of Medicine, Sohail Trust Hospital Karachi (Jinnah Medical College Hospital) Korangi Karachi. The study was conducted from January - December 2020. The Convenient sampling technique was used for sample collection. All the patients of either gender admitted to the medicine ward or visiting medical OPD for treatment of diabetes, aged between 18-70 years, with a duration of diabetes mellitus for at least six months, were included. Diabetes mellitus was defined according to criteria of the American Diabetic Association as having Fasting blood glucose >126 on two occasions or HbA1C > 6.5 [11]. Patients with any structural abnormality of the urinary tract(Strictures, stones), using steroids or immunosuppressant drugs, antibiotics, and pregnancy are excluded since they are independent risk factors that can increase the prevalence of repeated and resistant urinary infections. The sample size was 132, calculated online using WHO sample size software, with a 95% confidence interval and a 5% chance of error[10]. Before starting the study ethically approved by the hospital URGC (Undergraduate Research Committee (Protocol I #: 00055/20). Researchers themselves collected data on a pre-designed questionnaire. Before the enrolment, participants were explained the details of the study and utilisation of data, the informed consent was taken from all the patients. The patients were asked simple yes/no statements or short answer questions in simple and understandable language. Qualitative variables were gender, presence of symptoms, previous H/O UTI, treatment (Insulin/Oral Antidiabetics), bacterial flora, and drug sensitivity, and quantitative variables were age, HbA1C, duration of diabetes, and creatinine clearance. After initial data collection, urine samples were sent to the hospital laboratory for D/R and culture sensitivity.

Samples were cultured on Blood agar and MacConkey agar. Antibiotic Susceptibility pattern was determined on Mueller-Hinton using Kirby –Bauer disc diffusion method. Urinary tract infection (UTI) is diagnosed with a positive urine culture with or without symptoms of UTI (dysuria, frequency and urine urgency). After collecting urine culture reports, any growing flora and their sensitivity/ resistance to all the effective antibiotics were recorded in the Performa. Data were analysed in SPSS version 21. Qualitative data are presented as frequencies/percentages, while quantitative data are presented as mean ± SD. The student T-test was applied to quantitative data, while the chi-square test was used to qualitative data. A P-value of < 0.05 is considered statistically significant.

RESULTS

UTI was found in 31(23.5%) diabetic patients; in comparison, 101(76.5%) patients had diabetes without UTI (**Figure I**). In comparing general characteristics between UTIs and non-UTI groups, we observed that females were more affected by UTI than males (p-value=0.02). Patients on insulin had a lower percentage of UTI than those on oral therapy (p value=0.045). HbA1C was also high in the UTI group (p-value = 0.042). Average Creatinine Clearance decreased in patients with UTI, as shown by significant p values (0.022). While the relationship between age, duration of diabetes and presence of symptoms was not found to be statistically significant (**Table I**)

In the culture/sensitivity report, the most common flora was E. Coli 26(84%), followed by Klebsiella 4(13%) and S. aureus 1(3%) (**Table II**).

E. coli was 65.3% resistant to Penicillin (amoxicillin/ clavulanic acid), 100% resistant to 3rd generation Cephalosporins, 84.6% to Quinolones and 42.3% to aminoglycosides. Carbapenems, Nitrofurantoin and Fosfomycin were 100% sensitive for E. coli. Klebsiella was 100% resistant to Penicillin and quinolones, 75% resistant to 3rd generation cephalosporin and 25% resistant to aminoglycosides while 100% sensitive to carbapenems, nitrofurantoin and Fosfomycin. (**Table III)**

S. Aureus isolated in only one sample was resistant to cloxacillin, clindamycin and quinolones while sensitive to vancomycin, linezolid and aminoglycosides. **(Table III)**

Figure I: Frequency of UTI

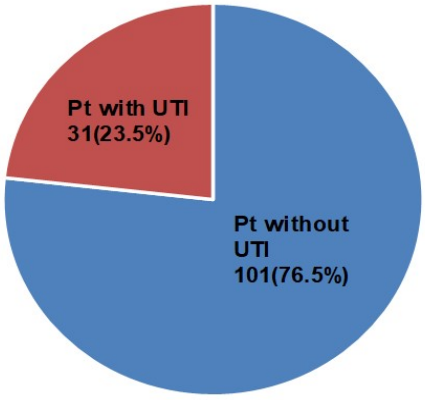

Table I: Demographic Characteristics of the Patients

Characteristics	Pt with UTI (31)	Pt without UTI (101)	P-value
Mean Age	56.74±12.85	52.60±12.43	0.110
Male Female	7 (22.6%) 24 (77.4%)	42 (41.6%) 59 (58.4%)	0.028
Mean duration of diabetes	10.71±6.07 year	9.40±6.16 year	0.301
Presence of symptoms (frequency, urgency)	12(38.7%)	32(31.7%)	0.303
On Insulin	14(45.2%)	63(62.4%)	0.045
HbA1c	9.28±1.88	7.63±2.08	0.042
Average Creatinine clearance	114.3±13.8	106.8±20.4	0.022

Table II: Frequency of Isolated Flora

Flora	N(%)
E. COLI	26(84%)
Klebsiella	4(13 %)
S. aureus	1(3%)

Table III: Frequency of Antibiotic Resistance

Flora	Antibiotic Groups	Resistance	Sensitive
E. COLI	Penicillin(Augmentin)	17(65.3%)	9 (34.6%)
	Cephalosporins (Ceftriaxone)	26 (100%)	0(0%)
	Quinolones	22 (84.6%)	4 (15.3%)
	Aminoglycosides	11(42.3%)	15(57.6%)
	Carbepenems (Imipenem)	0(0%)	26(100%)
	Nitrofurantoin	0 (0%)	26 (100%)
	Fosfomycin	0 (0%)	26 (100%)
Klebsiella	Penicillin(Augmentin)	4(100%)	0(0%)
	Cephalosporins (Cftriaxone)	3(75%)	1(25%)
	Quinolones	4(100%)	0(0%)
	aminoglycosides	1(25%)	3(75%)
	carbepenems (Imipenem)	0 (0%)	4 (100%)
	nitrofurantoin	0 (0%)	4 (100%)
	Fosfomycin	0 (0%)	4 (100%)
S. AUREUS	Penicillin (Cloxacillin)	1 (100%)	0 (0%)
	Clindamycin	1(100%)	0(0%)
	Quinolones	1(100%)	0(0%)
	Aminoglycosides	0 (0%)	1 (100%)
	Linezolid	0(0%)	1(100%)
	Vancomycin	0 (0%)	1 (100%)

DISCUSSION

Diabetes mellitus is a recognised risk factor for urinary tract infections. The incidence of repeated UTIs in people with diabetes is increasing daily, especially in developing countries, because of a lack of diabetic control, poor hygiene and injudicious use of antibiotics. In our study, we found the prevalence of UTI in people with diabetes in about 31(23.5%) patients; the other studies of the region have shown variable results ranging from 8-54%. Laway BA 2021[11] conducted a study in Kashmir and found 17% of patients had active UTIs. Ahmed S 2020[12] conducted a study in Peshawar and found 51% had culture-positive UTIs. Kumar R et al.[13] conducted a study in Sind, Pakistan, and found that 13% of the samples were culture-positive. This variation in the frequency of UTIs can be due to hygienic conditions, literacy, awareness in the community, poverty, access to healthcare facilities and diabetic control. That is why regional and hospital-based studies are essential sources to determine the local data about infection.

We also noted in our study that the occurrence of UTI was seen in females with low creatinine clearance and the use of Oral antidiabetic medications. Kande S 2021[14] conducted a study in 2021 in India and also observed that the incidence of UTI was more common in female diabetics and in patients with HbA1c of > 9%. Jha PK 2014[15] conducted a study in Nepal and observed a significant relationship between HbA1c and insulin with a low incidence of UTI.

Klinberg A et al.[16] and Raeispur M 2018[17] also observed that a high incidence of UTI was associated with elevated serum creatinine and HbA1c.

Our drug sensitivity data showed that E. coli, Klebsiella, and S. aureus were the most common organisms. We observed that both gram negatives were resistant to commonly used antibiotics like beta-lactam/lactamase (penicillins, Cephalosporins), fluoroquinolones and aminoglycosides, most of which are widely prescribed for treating UTI in general

practice. We observed that they were sensitive to Nitrofurantoin, Carbapenems and Fosfomycin. This changing trend shows the injudicious use of antibiotics, especially without drug sensitivity, leading to an alarming rate of resistance in gram-negative bacteria. The other studies in the subcontinent also show similar results. Forson AO et al.[18] conducted a study in 2020 that found that E.coli and Klebsiella were highly resistant to cefuroxime, ampicillin and gentamycin.

Nath T 2021[19] conducted a study in India that found high resistance in E.coli, Klebsiella and enterococcus to fluoroquinolones, aminoglycosides and co-amoxyclav.

Keshi L et al.[20] and Woldemariam HK et al.[5] also observed multi-drug resistance in gram-negative related urinary tract infections.

Our study observed that E.coli and Klebsiella were both sensitive to Carbapenems, nitrofurantoin and Fosfomycin, while staphylococcus was sensitive to vancomycin, linezolid and aminoglycoside. Nigussie D 2017[21] conducted a study in Turkey and observed that most gram-negative were resistant to aminoglycoside and ceftriaxone but sensitive to nitrofurantoin. A recent study conducted in India also showed high sensitivity of gram-negative infection for Carbapenems and nitrofurantoin while staphylococcus for vancomycin and linezolid[23].

Nongrum S et al.[23] and Yismaw G 2012[24] documented similar results in their studies supporting the same sensitivity pattern.

CONCLUSION

UTI was found in 23.5% % of our diabetic patients. The most common organisms prevalent were E. Coli, Klebsiella and S. aureus, which was primarily resistant to Penicillins, Cephalosporins and quinolones while sensitive to nitrofurantoin, Fosfomycin and carbapenem. This emerging resistance should be monitored frequently to observe any extension in resistance as we are recently experiencing extensive drug resistance cases of typhoid in Sindh. More studies with frequent monitoring in multiple centres are therefore recommended.

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AUTHOR'S CONTRIBUTION

Razzaque S: Major contribution in conceptualising the idea, study design, editing and supervision of the study process

Kumar A: Contribution in conceptualising the idea, study design, editing and supervision of the study process

Khan AA: Major contribution to the research proposal, data analysis, and manuscript writing.

Abid M: Major contribution to data collection and data analysis

Raza SS: Major contribution to patient selection, coordination and data collection.

Eraj R: Major contribution to data collection and writing the manuscript

REFERENCES

1. Organization WH. The top 10 causes of death. World Health Organization. 9 December 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
2. Atlas D. Demographic and Geographic Outline. Diabetes Atlas. 2021. Available from: https://www.diabetesatlas.org.
3. Zubair KU, Shah AH, Fawwad A, Sabir R, Butt A. Frequency of urinary tract infection and antibiotic sensitivity of uropathogens in patients with diabetes. Pak J Med Sci. 2019; 35(6): 1664-68. doi: 10.12669/pjms.35.6.115.
4. Ramrakhia S, Raja K, Dev K, Kumar A, Kumar V, Kumar B. Comparison of Incidence of Urinary Tract Infection in Diabetic vs Non-Diabetic and Associated Pathogens. Cureus. 2020; 12(9): e10500. doi: 10.7759/cureus.10500.
5. Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM et al. Common uropathogens and their antibiotic susceptibility pattern among diabetic patients. BMC Infect Dis. 2019; 19(1): 43. doi: 10.1186/s12879-018-3669-5.
6. Chen SL, Jackson SL, Boyko EJ. Diabetes mellitus and urinary tract infection: epidemiology, pathogenesis and proposed studies in animal models. J Urol. 2009; 182(6 Suppl): S51-6. doi:10.1016/j.juro.2009.07.090.
7. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM et al. Infectious disease society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005; 40: 643-654. doi: 10.1086/427507. Epub 2005 Feb 4.
8. Feleke Y, Mengistu Y, Enquselassie F. Diabetic infections: Clinical and bacteriological study at TikurAnbessa specialised university hospital, Addis Ababa, Ethiopia. Ethiop Med J. 2007; 45:171–9.
9. Aswani SM, Chandrashekar U, Shivashankara K, Pruthvi B. Clinical profile of urinary tract infections in diabetics and non-diabetics. Australas Med J.

2014; 7(1): 29-34. doi: 10.4066/AMJ.2014.1906.
10. Baqai R, Aziz M, Rasool G. Urinary tract infection in diabetic patients and biofilm formation of uropathogens. Infect Dis J Pak. 2008; 17(1): 7-9.
11. Laway BA, Nabi T, Bhat MH, Fomda BA. Prevalence, clinical profile and follow-up of asymptomatic bacteriuria in patients with type 2 diabetes-prospective case-control study in Srinagar. Diabetes Metab Syndr. 2021; 15(1): 455 -459. doi: 10.1016/j.dsx.2020.12.043. Epub 2021 Jan 18.
12. Ahmad S, Hussain A, Khan MSA, Shakireen N, Ali I. Diabetes mellitus and urinary tract infection: Causative uropathogens, their antibiotic susceptibility pattern and the effects of glycemic status. Pak J Med Sci. 2020; 36(7): 1550-1557. doi: 10.12669/pjms.36.7.2881.
13. Kumar R, Kumar R, Perswami P, Taimur M, Shah A, Shoukat F. Clinical and Microbiological Profile of Urinary Tract Infections in Diabetic versus Non-Diabetic Individuals. Cureus. 2019; 11(8): e5464. doi: 10.7759/cureus.5464.
14. Kande S, Patro S, Panigrahi A, Khora PK, Pattnaik D. Prevalence of uropathogens and their antimicrobial resistance pattern among adult diabetic patients. Indian J Public Health. 2021 Jul-Sep;65(3):280-286. doi: 10.4103/ijph.IJPH_14 13_ 20.
15. Jha PK, Baral R, Khanal B. Prevalence of uropathogens in diabetic patients and their susceptibility pattern at a tertiary care centre in Nepal - A retrospective study. Int J Biomed Lab Sci. 2014; 3(2): 29-34.
16. Klingeberg A, Noll I, Willrich N, Feig M, Emrich D, Zill E et al. Antibiotic-Resistant E. coli in Uncomplicated Community-Acquired Urinary Tract Infection. Dtsch Arztebl Int. 2018; 115(29-30): 494 -500. doi: 10.3238/arztebl.2018.0494.
17. Raeispour M, Ranjbar R. Antibiotic resistance, virulence factors and genotyping of Uropathogenic *Escherichia coli* strains. Antimicrob Resist Infect Control. 2018; 7: 118. doi:10.1186/s 13756-018-0411-4.
18. Forson AO, Menkah DA, Quarchie MN, Dhikrullahi SB, Olu-Taiwo M, Codjoe FS. Bacterial drug-resistance patterns and genetic diversity of bacteria-associated bacteriuria in diabetic patients in Ghana. IJID Reg. 2021; 1: 142-149. doi: 10.1016/j.ijregi.2021.10.007.
19. Nath T, Das SK, Hazra S. Pattern of uropathogens and antibiotic sensitivity in diabetes patients attending to out - Patient department and diabetes clinic of a teaching hospital: A cross-sectional study. J Family Med Prim Care. 2021; 10(10): 3638-3643. doi: 10.4103/jfmpc.jfmpc_ 71_21.
20. Keshi L, Weiwei X, Shoulin L, Xiadong L, Hao W, Junhai J et al. Analysis of Drug Resistance of Extended-Spectrum Beta-Lactamases-Producing Escherichia Coli and Klebsiella Pneumoniae in Children with Urinary Tract Infection. Saudi Med J. 2019; 40(11): 1111-1115. doi: 10.15537/smj.2019. 11.24547.
21. Nigussie D, Amsalu A. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. Turk J Urol. 2017; 43(1): 85-92. doi: 10.5152/tud.2016.86155. Epub 2017 Jan 27.
22. Jagadeesan S, Tripathi BK, Patel P, Muthathal S. Urinary tract infection and Diabetes Mellitus-Etio-clinical profile and antibiogram: A North Indian perspective. J Family Med Prim Care. 2022; 11 (5): 1902-1906. doi: 10.4103/jfmpc.jfmpc_2017_ 21. Epub 2022 May 14.
23. Nongrum S, Thaledi S, Singh VA, Narang VK, Mehta S, Garg R et al. Association of uropathogens with asymptomatic urinary tract infection in diabetes mellitus patients. Int J Curr Microbiol App Sci. 2016; 5(10): 355-61.
24. Yismaw G, Asrat D, Woldeamanuel Y, Unakal CG. Urinary tract infection: bacterial etiologies, drug resistance profile and associated risk factors in diabetic patients attending Gondar University Hospital, Gondar, Ethiopia. Eur J Exp Biol. 2012; 2(4): 889-898.