PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 12 (Deccember 2024)

Original Article

OPEN ACCESS

Sensitivity Pattern of Uropathogens in Diabetic and Non-Diabetic Patients Presenting to a Tertiary Care Hospital

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ARTICLE INFO

Keywords:
Diabetes Mellitus, Urinary Tract Infections, Antibiotic Resistance, Meropenem, Ciprofloxacin

How to Cite:
Nisar, M., Farooq, M. W., & Asadullah. (2024). Sensitivity Pattern of Uropathogens in Diabetic and Non-Diabetic Patients Presenting to a Tertiary Care Hospital: Uropathogen Sensitivity in Diabetic Patients. Pakistan Journal of Health Sciences, 5(12), 08-13. https://doi.org/10.54393/pjhs.v5i12.2243

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Received date: 25th September, 2024
Accepted date: 18th December, 2024
Published date: 31st December, 2024

ABSTRACT

Diabetes Mellitus (DM) is a prevalent global health issue, with Pakistan experiencing a high burden. Diabetic patients were more susceptible to Urinary Tract Infections (UTIs) and often exhibit greater antibiotic resistance. **Objective:** To determine the sensitivity/resistance patterns of DM and Non-DM UTI patients. **Methods:** A cross-sectional study was conducted on 208-UTI at Lady Reading Hospital, Peshawar, from January to July 2020. Patients were equally divided into DM (n=104) and non-DM (n=104) groups. **Results:** A total of 208 UTI cases were equally divided between diabetic and non-diabetic groups (104 in each). The mean age of patients was 42.49 ± 1.148 years with a male predominance 132 (63.4%). Dysuria was reported in 81 (38.9%), urinary frequency in 86 (41.3%), and fever in 41 (19.7%) patients. Significant differences were observed in antibiotic resistance patterns between diabetic and non-diabetic groups. Diabetic patients exhibited higher resistance to Meropenem 86 (78%) versus 24 (22%), p<0.001), Ciprofloxacin 95 (98%) versus 2 (2%), p<0.001), and Ceftazidime 93 (79.4%) versus 24(20.6%), p<0.001) compared to non-diabetics. Conversely, sensitivity were significantly lower in diabetic patients for Meropenem (18(18%) versus 80(82%), p<0.001), Ciprofloxacin (9(8%) versus 102(91.8%), p<0.001), and Ceftazidime (11(12.3%) versus 79(87.7%), p<0.001). No significant associations were found between age or gender and antibiotic sensitivity within either group. **Conclusion:** The study demonstrates that diabetic patients were at significantly higher risk for antibiotic-resistant UTIs, particularly against meropenem, ciprofloxacin, and ceftazidime. These findings highlight the importance of customized antibiotic therapies and better glycemic control in diabetic patients to reduce UTIs complications.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic Non-Communicable Disease (NCD) marked by persistent hyperglycemia, arising from insulin-related problems. It is a leading cause of mortality and morbidity globally, impacting individuals across all age groups, genders, and regions [1]. With increasing prevalence in both developed and developing nations, including Pakistan, diabetes is now acknowledged as a major global health concern [2, 3]. Pakistan, a populous nation in South Asia, is experiencing a growing burden of (NCDs), with DM becoming a prominent public health challenge. The diabetic population in the country has escalated from 5.2 million in 2000 to nearly 33 million by 2021 [4]. In 2016, NCDs, including diabetes, accounted for 58% of all deaths in Pakistan. Diabetes directly caused 3% of these deaths and contributed to other NCDs, such as cardiovascular diseases and hypertension [5]. Addressing the diabetes epidemic is crucial for mitigating its widespread health and economic impacts. In Pakistan, the prevalence of diabetes mellitus is reported at 26.3%, with 19.2% of individuals having known DM and 7.1% being new diagnosis. In comparison to rural regions (25.3%), the prevalence of DM is greater in urban (28.3%). Additionally, the prevalence of prediabetes is recorded at 14.4%, with 15.5% in urban and 13.9% in rural regions. Major risk factors

DOI:https://doi.org/10.54393/pjhs.v5i12.2243

associated with diabetes include being 43 years or older, a positive family history, hypertension, obesity, and dyslipidemia [6]. In comparison to individuals without diabetes, those with the condition are at a higher risk for all types of infections, including infections of the mucous membranes, lower respiratory infections, Urinary Tract Infections (UTIs), sepsis, endocarditis, as well as skin, bone, and joint infections [7]. According to the available data, urinary tract infections (UTIs) are the most common bacterial infection in patients with diabetes [8], occurring in 15.35% of cases, compared to 12.28% in individuals without diabetes [9]. The clinical profiles of diabetic patients indicate various factors that contribute to the higher incidence of UTIs in this group, such as inadequate circulation, a compromised immune system due to reduced activity of white blood cells in combating infections, and impaired bladder contractions that cause bladder dysfunction [10]. Furthermore, physiological variables such as age, gender, length of diabetes, long-term anti-diabetic medication use, and other diabetic sequelae such glycosuria and neuropathy are thought to be predisposing factors for the higher incidence of UTI in diabetics. Patients with diabetes may experience asymptomatic or symptomatic UTI, which includes urethritis, cystitis, prostatitis, pyelonephritis, and asymptomatic bacteriuria (ABU) [11]. A study carried out across 12 clinical sites in Pakistan explored the prevalence of asymptomatic UTIs in Type II Diabetes Mellitus (T2DM) patients. The findings showed that 8.08% of the patients had positive urine cultures, with a significantly higher occurrence in females (77.27%, p<0.001). The age group 40–59 years was the most common among those with positive cultures (70.45%). *Escherichia coli* was the most frequently identified pathogen (52.3%), and all bacterial isolates were resistant to Ciprofloxacin [6]. A hospital-based study conducted in Peshawar found that the disease was more prevalent in females (63.9%) and among patients with suboptimal glycemic control (86.3%) compared to those with good glycemic control (13.7%). *Escherichia coli* was the most frequently identified pathogen (71%), followed by *Klebsiella pneumoniae* (17.1%), *Pseudomonas aeruginosa* (6.83%), *Enterococcus* (5.85%), and Candida species (0.98%). Imipenem, meropenem, fosfomycin, and nitrofurantoin were highly effective against both gram-positive and gram-negative bacteria [12]. The literature indicates that *Escherichia coli* is the most common organism responsible for UTIs in both DM and non-DM patients, accounting for 50% of infections in diabetics and 43.33% in non-diabetics [9, 13]. Following this, in diabetics, *Acinetobacter* accounted for 18.33% and *Klebsiella* for 15%, while in non-diabetics, *Acinetobacter* was present in 15% and *Pseudomonas* in 12% [9]. Imipenem showed the highest sensitivity (46.66% in diabetics, 43.33% in non-diabetics). Subsequently, nitrofurantoin and cotrimoxazole each displayed a sensitivity of 20% in diabetics and 13% in nondiabetics, norfloxacin (31.66%), amikacin (20%), and gentamicin (20%) exhibited sensitivity. High resistance was observed to ciprofloxacin (98.33% in diabetics, 78.33% in non-diabetics), followed by resistance to norfloxacin (91.66%) and ampicillin (66.66%) in diabetics, and 55% resistance to both nitrofurantoin and norfloxacin in non-diabetics. Diabetic patients showed a statistically significant reduction in susceptibility, particularly to norfloxacin, ciprofloxacin, gentamicin, cefotaxime, and ampicillin. Study revealed that 100% of DM patients and 81.66% of non-DM exhibited resistance to three or more antimicrobial agents [13]. Given the growing concern about antibiotic resistance, particularly in patients with diabetes who are prone to Urinary Tract Infections (UTIs), it is crucial to understand the microbial profile and resistance patterns in this population. Existing data suggest that diabetic individuals are more susceptible to infections due to factors like compromised immunity and glycemic control. By analyzing the resistance and sensitivity of common uropathogens.

This study seeks to contribute valuable insights into the emerging resistance trends and guide future research and clinical practices in managing UTIs.

METHODS

This comparative cross-sectional, study was carried out in the Department of Medicine, Lady Reading Hospital, Peshawar from 13th January 2020 to 13th July 2020, including both diabetic and non-diabetic patients. A sample of 208 patients was selected and calculated using the openepi sample size calculator, by keeping 5% level of significance, 80% power of test and anticipated frequency of sensitivity of E.coli to ceftazidime among non-diabetics patients 50% versus in diabetic UTI patients 31.1% [14]. The sample of 208 patients then equally divide in to two group (diabetic versus non diabetic UTI patients). Each group consists of 104 UTI patients. Non-probability consecutive sampling was employed for patient selection. The inclusion criteria comprised of adults of both genders, aged 18 to 60 years, including both diabetic and non-diabetic individuals presenting with a UTI. Diabetic patients were required to have a fasting glucose level >126 mg/dL and a postprandial (2-hour) glucose level >200 mg/dL, while non-diabetic patients were to have a fasting blood sugar level <110 mg/dL. All participants exhibited a fever exceeding 98.6°F. Exclusion criteria were patients with urinary tract calculi, those receiving immunosuppressive therapy, those with urinary tract abnormalities, and patients with a history of catheterization or instrumentation. These conditions were assessed via medical history, X-ray, ultrasound, and other diagnostic methods. Ethical clearance was obtained from

DOI:https://doi.org/10.54393/pjhs.v5i12.2243

the hospital's ethical committee under reference number 198/LRH, dated 12/09/2019, and informed consent was secured from all participants after explaining the benefits and risks involved. Data collection was carried out through a thorough medical history, physical examination, and the use of pre-structured questionnaires. Numerous laboratory tests were performed, including fasting and random blood glucose, urine culture and sensitivity tests, urine dipstick examinations, and total and differential leukocyte counts using an automated blood analyzer. Urine cultures were grown on MacConkey's agar and Cystine Lactose Electrolyte Deficient (CLED) medium, supervised by a pathologist at the hospital laboratory. Additional tests such as kidney, ureter, and bladder ultrasounds, blood culture, and sensitivity tests, as well as serum urea, creatinine, and electrolyte levels, were conducted where necessary. Data were analyzed using SPSS version 25.0, with numerical variables expressed as mean ± SD and categorical variables presented as frequencies and percentages. Antibiotic resistance and sensitivity of UTI patients were stratified based on diabetic status. Diabetic status of UTI patients were stratified among age, gender, and symptom presence to evaluate the influence of these factors on. A post-stratification chi-squared test was performed by considering p-value ≤0.05 statistically significant.

RESULTS

The study includes 208 individuals presenting with urinary tract infections (UTI) were analyzed, of which 104 (50%) patients were diabetic, and 104 (50%) patients were non-diabetic. The mean age of the patients was 42.49 ± 1.148 years, with a male predominance 132 (63.4%) patients compared to females 76 (36.5%). Regarding UTI symptoms, dysuria was reported in 81 (38.9%) patients, urinary frequency in 86 (41.3%), and fever in 41 (19.7%) patients. The table 1 highlights key differences in the baseline characteristics of Diabetic (DM) and Non-Diabetic (Non-DM) patients with Urinary Tract Infections (UTIs). A significant variation in age distribution was observed, with a higher proportion of DM patients in the 31-40 and 41-50 years age group 32 (30.77%) and 43 (41.35%) and Non-DM patients predominantly in the 41-50 and 51-60 age group 45 (43.27%) patients in each. The gender distribution reveals that most of DM patients were male 85 (81.73%), while the Non-DM group had a balanced gender distribution, with 47 (45.19%) males and 57 (54.81%) females, reflecting a statistically significant difference (P-value < 0.0001). Symptomatically, dysuria was more prevalent in Non-DM patients 46 (45.5%) patients compared to DM patients 35 (33.65%), while urinary frequency was more common in DM patients 47 (45.19%). Fever was relatively balanced between the two groups, with 22 (21.15%) patients in the DM group and 19 (18.27%) patients in the Non-DM group.

Table 1: Baseline Demographic Characteristics of DM and Non-DM UTI Patients (n=208)

Baseline Characteristics	Categories	DM N (%)	Non-DM N (%)	p-value
Age	18-30	9 (8.65%)	8 (7.69%)	<0.0001
	31-40	32 (30.77%)	6 (5.77%)	
	41-50	43 (41.35%)	45 (43.27%)	
	51-60	20 (19.23%)	45 (43.27%)	
	Total	104	104	
Gender	Male	85 (81.73%)	47 (45.19%)	<0.0001
	Female	19 (18.27%)	57 (54.81%)	
	Total	104	104	
Symptoms	Dysuria	35 (33.65%)	46 (44.23%)	0.2927
	Urinary Frequency	47 (45.19%)	39 (37.50%)	
	Fever	22 (21.15%)	19 (18.27%)	
	Total	104	104	

The table 2 showed a significant difference in the antibiotic sensitivity and resistance patterns between DM and Non-DM UTI patients for Meropenem, Ciprofloxacin, and Ceftazidime. In the DM group, 86 (78%) patients were resistant to Meropenem, compared to only 24 (22%) in the Non-DM group. Similarly, 95 (98%) of DM patients were resistant to Ciprofloxacin, while only 2 (2%) of Non-DM patients exhibited resistance. For Ceftazidime, 93 (79.4%) of DM patients were resistant, compared to 24 (20.5%) in the Non-DM group. In contrast, Non-DM patients showed significantly higher sensitivity to all three antibiotics. For Meropenem, just 18 (18%) of DM patients were sensitive, compared to 80 (82%) of Non-DM patients. Likewise, 9 (8%) of DM patients were sensitive to Ciprofloxacin, while 102 (91.8%) of Non-DM patients showed sensitivity. Finally, 11 (12.3%) of DM patients were sensitive to Ceftazidime, whereas 79 (87.7%) of Non-DM patients responded positively. The p-values for all comparisons were <0.001, indicating that these differences were statistically significant, with DM patients showing higher resistance and lower sensitivity to these antibiotics.

Table 2: Antibiotic Sensitivity and Resistance Pattern of DM and Non-DM UTI Patients (n=208)

Antibiotic Pattern		DM N (%)	Non-DM N (%)	p-value
Meropenem	Resistance	86 (78%)	24 (22%)	<0.001
	Sensitivity	18 (18%)	80 (82%)	<0.001
Ciprofloxacin	Resistance	95 (98%)	2 (2%)	<0.001
	Sensitivity	9 (8%)	102 (91.8%)	<0.001
Ceftazidime	Resistance	93 (79.4%)	24 (20.6%)	<0.001
	Sensitivity	11 (12.3%)	79 (87.7%)	<0.001

The table 3 examined the relationship between age, gender, and antibiotic sensitivity patterns for DM and Non-DM patients across three antibiotics: Meropenem, Ciprofloxacin, and Ceftazidime. For DM patients, the antibiotic sensitivity patterns by age and gender do not

DOI:https://doi.org/10.54393/pjhs.v5i12.2243

show significant differences. The p-value for age was 0.771, indicating no significant association between age groups (<40 and >40 years) and antibiotic sensitivity to Meropenem, Ciprofloxacin, or Ceftazidime. Similarly, the p-value for gender was 0.56, meaning there was no statistically significant difference in antibiotic sensitivity between males and females for any of the antibiotics tested. For Non-DM patients, the p-value for age was 0.115, suggesting that there was no strong evidence of an association between age groups (<40 and >40 years) and antibiotic sensitivity. However, while the p-value was higher than 0.05 (indicating non-significance), it was still relatively close, suggesting some potential for a difference in antibiotic sensitivity by age, particularly for Ciprofloxacin, where a higher percentage of patients >40 years were sensitive. The p-value for gender was 0.551, meaning there was no statistically significant difference in antibiotic sensitivity between males and females for Non-DM patients.

Table 3: Age and Gender versus Antibiotic Sensitivity Pattern of DM and Non-DM Patients

Antibiotic Sensitivity	DM		p-value	DM		p-value
	Age N (%)			Age N (%)		
	>40 Years	>40 Years		>40 Years	>40 Years	
Meropenem	11 (61.11%)	7 (38.89%)	0.771	14 (17.5%)	66 (82.5%)	0.115
Ciprofloxacin	5 (55.56%)	4 (44.44%)		9 (8.82%)	93 (91.18%)	
Ceftazidime	5 (45.45%)	6 (54.55%)		11 (13.92%)	68 (86.08%)	
Antibiotic Sensitivity	**Gender**			**Gender**		
	Male	**Female**		**Male**	**Female**	
Meropenem	9 (50.0%)	9 (50.0%)	0.56	33 (41.25%)	47 (58.75%)	0.551
Ciprofloxacin	6 (66.67%)	3 (33.33%)		47 (46.08%)	55 (53.92%)	
Ceftazidime	5 (45.45%)	6 (54.55%)		37 (46.84%)	42 (53.16%)	

Figure 1 presented multiple bar-chart for antibiotic sensitivity patterns for DM and Non-DM patients across symptoms (dysuria, urinary frequency, and fever). For DM patients, sensitivity was highest for dysuria across all antibiotics, with lower sensitivity for fever and the lowest for urinary frequency. In Non-DM patients, sensitivity was also highest for dysuria, with more balanced sensitivity across other symptoms. Non-DM patients consistently exhibit higher sensitivity to all antibiotics compared to DM patients, with the differences being most notable for urinary frequency and fever. The chart highlights that dysuria was associated with the highest sensitivity in both groups.

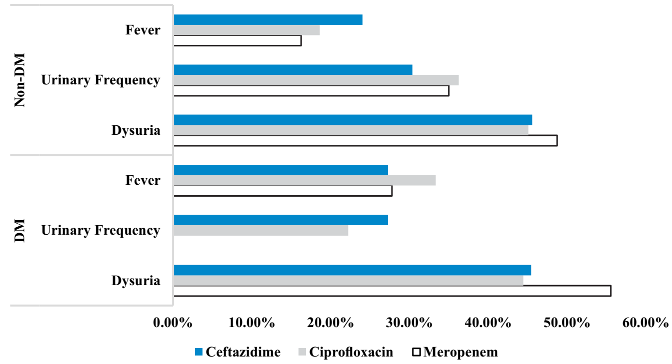

Figure 1: Multiple Bar-Chart for Antibiotic Sensitivity versus UTI Symptoms among DM and Non-DM Patients

DISCUSSION

Urinary Tract Infections (UTIs) pose a significant healthcare challenge, which was further exacerbated by the improper use of antibiotics. This study focuses on examining the sensitivity and resistance patterns of antibiotics in both Diabetic (DM) and Non-Diabetic (non-DM) patients. The results of this study showed that people with DM and those without DM have significantly different uropathogen sensitivity patterns, which has substantial therapeutic implications for the treatment of Urinary Tract Infections (UTIs) in these populations. Diabetic patients exhibited significantly higher rates of antibiotic resistance compared to non-diabetic patients, aligning with findings from Shill MC *et al.*, in 2023, which demonstrated that while Imipenem and meropenem showed 100% sensitivity against *Escherichia coli*, *Staphylococcus*, and *Klebsiella* in non-diabetic patients, their effectiveness was diminished in diabetic individuals [4, 15]. Additionally, antibiotics such as nitrofurantoin, ceftazidime, and ceftriaxone were markedly less effective in diabetic patients ($p \leq 0.0002$ to $p \leq 0.0168$). Overall, diabetic patients demonstrated lower antibiotic sensitivity, except for ciprofloxacin and levofloxacin, when compared to non-diabetic counterparts ($p < 0.05$ to 0.0001) [15]. This study revealed that significantly large amount (greater than 75%) of diabetic patients exhibited resistance to these three antibiotics, compared to much lower resistance rates in non-diabetic patients (22% for Meropenem, 20% for Ceftazidime, and 2% for Ciprofloxacin), highlighting the strong association between diabetes and antibiotic resistance. These results align with the study performed by Signing AT *et al.*, in 2020 [16]. Their study revealed a strong correlation between antibiotic resistance and diabetic status, showing significant resistance to ceftriaxone, cefixime, ceftazidime, cefotaxime, cefepime, and ciprofloxacin among diabetic patients (X^2 values ranging from 9.45 to 27.93, all with p-values < 0.01). Multidrug resistance was notably higher in diabetic patients, with 62.50% for *Escherichia coli*, 63.16% for *Klebsiella pneumoniae*, and

DOI:https://doi.org/10.54393/pjhs.v5i12.2243

78.57% for *Staphylococcus aureus*, compared to 37.50%, 36.84%, and 21.43%, respectively, in non-diabetic patients. This underscores the heightened antibiotic and multidrug resistance in diabetic UTI patients [16]. The literature suggests that inadequate glycemic control was a significant risk factor for increased antibiotic resistance [17-19]. This was supported by findings of the study, where all diabetic patients showed resistance to multiple antibiotics. Studies indicate that hyperglycemia fosters a more conducive environment for bacterial growth, leading to persistent or recurrent UTIs that require longer courses of antibiotics and result in increased resistance [18, 20, 21]. The age distribution in this study showed that diabetic patients were primarily between 31-50 years old, which was consistent with earlier findings linking older age with increased diabetes-related complications, including UTIs [22]. In contrast, non-diabetic patients were more evenly distributed between the 41-60 age groups. The observed male predominance in diabetic UTI patients diverges from the findings of other studies where females had a higher prevalence of UTIs [23, 24]. However, no significant association exist between age, gender, and antibiotic sensitivity among the study group. The study also demonstrated that diabetic patients more frequently presented with urinary frequency (45.19%) compared to dysuria (33.65%) and fever (21.15%), while non-diabetic patients were more likely to report dysuria (44.23%). Whereas literature reports high symptoms of dysuria among diabetic patients [25, 26]. The limitations of this study were single-center design, small sample size, and lack of longitudinal data, which may restrict the generalizability of the findings. The future study can conduct a randomized controlled trial to check the sensitivity pattern of diabetic patients to different antibiotic use among local population of Peshawar.

CONCLUSIONS

This study highlighted significant differences in antibiotic resistance patterns between DM and non-DM patients with UTIs. DM patients exhibited notably higher resistance, especially to meropenem, ciprofloxacin, and ceftazidime, compared to their non-diabetic counterparts. These findings, which were statistically significant, suggest that diabetic individuals face a greater challenge in effective UTI treatment due to increased resistance, potentially linked to poor glycemic control. Tailored antibiotic regimens and improved glycemic management were recommended to address these risks in diabetic patients.

Authors Contribution

Conceptualization: MN
Methodology: MN
Formal analysis: MN, AU
Writing, review and editing: MN, MWF

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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