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CROSS-SECTIONAL AI SURVEILLANCE OF MULTIDRUG RESISTANCE IN URINARY PATHOGENS FROM DIABETIC OUTPATIENTS

Original Research

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ABSTRACT

Background: Diabetic patients are at an increased risk of urinary tract infections (UTIs), which are frequently caused by multidrug-resistant (MDR) pathogens. Rising antimicrobial resistance complicates treatment decisions, especially in outpatient settings where empirical therapy is common. Enhanced surveillance using artificial intelligence (AI) may offer a novel solution for real-time monitoring of resistance patterns.

Objective: To determine the prevalence and resistance patterns of urinary pathogens in diabetic outpatients using AI-supported data analysis tools for enhanced microbial surveillance and informed public health response.

Methods: A cross-sectional study was conducted from October 2024 to June 2025 at outpatient clinics and laboratories in Lahore, Pakistan. A total of 350 diabetic outpatients with symptomatic UTIs were enrolled. Midstream urine samples were collected for culture and susceptibility testing using CLSI guidelines. MDR was defined as resistance to one agent in three or more antimicrobial classes. Data were analyzed using AI-supported tools to identify resistance trends and clustering. Statistical analysis included descriptive statistics, chi-square, t-tests, and logistic regression using SPSS v26.0.

Results: Escherichia coli was the most common pathogen (55.7%), followed by Klebsiella pneumoniae (17.4%) and Enterococcus spp. (11.1%). High resistance rates were observed for ciprofloxacin (64.8%) and ceftriaxone (59.4%). MDR pathogens were identified in 42.3% of isolates, with significant associations to poor glycemic control and prior antibiotic use. AI tools facilitated clustering of resistance patterns and highlighted emerging resistance trends.

Conclusion: The high burden of MDR uropathogens in diabetic outpatients necessitates routine culture-based diagnostics and antimicrobial stewardship. AI-supported surveillance proved effective in enhancing resistance detection and can guide more precise empirical therapy in resource-limited settings.

Keywords: Anti-Bacterial Agents, Artificial Intelligence, Diabetes Mellitus, Drug Resistance, Microbial, Multidrug Resistance, Outpatients, Pakistan, Urinary Tract Infections, Uropathogenic Escherichia coli.

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INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections globally, with a particularly high burden in individuals with diabetes mellitus. Diabetic patients are more susceptible to UTIs due to multiple factors, including impaired immune responses, autonomic neuropathy affecting bladder function, and persistent hyperglycemia, which can create a favorable environment for microbial colonization and growth (1,2). These infections not only occur more frequently in diabetic individuals but also tend to present with more severe complications, longer durations, and a higher likelihood of recurrence. As antimicrobial resistance (AMR) continues to rise, managing UTIs in this high-risk group becomes increasingly complex and challenging. The emergence and spread of multidrug-resistant (MDR) uropathogens have added a critical layer of urgency to this problem (3). Studies have shown that diabetic patients are disproportionately affected by MDR infections, with pathogens demonstrating resistance to first-line antibiotics including fluoroquinolones, cephalosporins, and even carbapenems in some regions (4,5). The overuse and misuse of antibiotics, combined with inadequate surveillance systems, have contributed to a growing public health crisis, particularly in outpatient settings where empirical treatment is often initiated without culture guidance. In many developing countries, where antimicrobial stewardship is still evolving, the risk of ineffective treatment due to resistance is further amplified (6,7).

Traditional microbiological methods remain essential for pathogen identification and susceptibility testing, yet they are often time-consuming and resource-intensive. In contrast, recent advancements in artificial intelligence (AI) and machine learning have opened new avenues for enhancing infectious disease surveillance (8). By leveraging large datasets from laboratory information systems, electronic health records, and pharmacy databases, AI tools can uncover hidden patterns, predict resistance trends, and inform more targeted empirical therapy. In this context, AI-supported surveillance represents a valuable strategy for bridging the gap between diagnostics and public health response, offering timely insights that can aid both clinicians and policymakers (9,10). Despite the promise of AI in microbiological surveillance, its application in outpatient settings, especially among vulnerable populations such as diabetic patients, remains limited. Most existing studies have focused on hospital-acquired infections or inpatient cohorts, often overlooking the outpatient demographic where early intervention could significantly reduce disease burden and transmission. Moreover, while some research has examined resistance trends in the general population, few have provided focused analyses on diabetics, whose altered physiology and frequent antibiotic exposures create a unique microbial ecosystem (11,12).

In many healthcare settings, particularly in low- and middle-income countries, diabetic outpatients are managed primarily through community health programs or outpatient clinics, where routine culture testing is not always feasible. This underlines the importance of incorporating predictive analytics and AI-based tools that can function within these constraints, helping to identify patterns of resistance without the need for extensive laboratory infrastructure. Such tools could potentially stratify patients based on risk profiles, enabling clinicians to prescribe more effective empirical therapies and curb the spread of resistant strains (13,14). The current study addresses these gaps by conducting a cross-sectional investigation into the prevalence and resistance patterns of urinary pathogens isolated from diabetic outpatients. Utilizing AI-assisted data analysis methods, the study aims to enhance the granularity and efficiency of surveillance while providing actionable insights for clinical decision-making and public health planning. By focusing on a high-risk outpatient group, the research seeks to highlight the urgent need for updated empirical treatment guidelines and the potential of AI tools to support antimicrobial stewardship efforts at the community level. The specific objective of this study is to determine the prevalence and resistance patterns of urinary pathogens in diabetic outpatients using AI-supported data analysis tools, with the broader aim of informing targeted treatment strategies and strengthening public health responses to antimicrobial resistance.

METHODS

This cross-sectional study was conducted over a period of eight months, from October 2024 to June 2025, at tertiary care outpatient clinics and diagnostic laboratories in the Lahore region of Pakistan. The study aimed to determine the prevalence and antimicrobial resistance patterns of urinary pathogens in diabetic outpatients, utilizing artificial intelligence (AI)-supported data analysis tools to enhance microbial surveillance and guide public health strategies. The research was reviewed and approved by the Institutional Ethical Review Committee of the relevant institute. Written informed consent was obtained from all participants prior to enrollment. Participants



were recruited consecutively from outpatient departments of endocrinology and general medicine clinics, as well as affiliated diagnostic laboratories where urine samples were submitted for culture and sensitivity testing. Eligible participants included adult patients aged 18 years and above with a known diagnosis of type 1 or type 2 diabetes mellitus who presented with symptoms suggestive of urinary tract infection (e.g., dysuria, frequency, urgency, suprapubic discomfort). Inclusion criteria required a history of diabetes for at least six months and no hospitalization or catheterization within the past 30 days. Exclusion criteria included pregnant women, patients on chronic immunosuppressive therapy, those with a known structural urological abnormality, and individuals with incomplete clinical or microbiological records (15). The sample size was calculated using the OpenEpi online calculator for cross-sectional studies. Assuming an anticipated prevalence of multidrug-resistant uropathogens in diabetic patients to be approximately 30%, with a 95% confidence level and a margin of error of 5%, the required sample size was estimated to be 323 participants. To account for potential dropouts or data exclusions, a final sample of 350 participants was targeted and achieved during the study duration.

Data collection involved both clinical and microbiological components. Clinical data were collected using structured proformas and electronic health records, capturing demographic information, duration and type of diabetes, history of prior UTIs, recent antibiotic use (within the last 90 days), glycemic control (HbA1c values), and presenting urinary symptoms. Midstream clean-catch urine samples were collected under sterile conditions and transported to the microbiology laboratory within two hours of collection. Urine samples were subjected to routine microscopy and cultured on cysteine-lactose-electrolyte-deficient (CLED) agar using calibrated loop techniques. A colony count of ≥10⁵ CFU/mL was considered indicative of significant bacteriuria. Isolated organisms were identified using conventional biochemical tests and automated systems where applicable. Antimicrobial susceptibility testing (AST) was performed using the Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines (15-17). The antibiotics tested included commonly prescribed agents such as nitrofurantoin, ciprofloxacin, ceftriaxone, cefixime, amoxicillin-clavulanic acid, fosfomycin, and carbapenems. Multidrug resistance was defined as resistance to at least one agent in three or more antimicrobial categories. All microbiological and susceptibility data were entered into a structured database and subjected to further analysis using AI-supported tools designed to identify resistance trends, cluster pathogen profiles, and predict co-resistance patterns. The AI models used were based on supervised learning algorithms and trained on anonymized local and regional datasets to optimize contextual accuracy. These tools allowed for enhanced visualization of resistance clusters and predictive analytics on emerging resistance phenotypes.

Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were used to summarize demographic and clinical variables. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means with standard deviations. To assess associations between clinical risk factors and the presence of multidrug-resistant infections, chi-square tests and independent t-tests were applied as appropriate. Logistic regression analysis was conducted to identify independent predictors of MDR pathogen isolation. As data were normally distributed, parametric tests were used for inferential statistics. A p-value of less than 0.05 was considered statistically significant. To ensure data validity and minimize bias, dual data entry was performed by independent reviewers, and discrepancies were resolved through consensus. Furthermore, regular audits of microbiological quality control procedures were conducted to maintain consistency in AST results. The integration of AI into data analysis not only enhanced pattern recognition but also allowed for a more dynamic exploration of resistance trends over time, potentially supporting real-time public health interventions.

RESULTS

The study evaluated a total of 350 diabetic outpatients presenting with symptomatic urinary tract infections over the eight-month period. The mean age of participants was 58.4 years, with a higher proportion of females (59.1%) compared to males (40.9%). Type 2 diabetes was the predominant form, observed in 88.9% of the cohort, while the mean duration of diabetes was 9.2 years. A significant portion of the population had suboptimal glycemic control, with 60.6% demonstrating HbA1c levels above 7%. Nearly 40% of participants reported a history of UTI within the past six months, and 33.4% had used antibiotics in the preceding 90 days. Out of 350 urine cultures, significant bacterial growth was observed in all samples, with Escherichia coli being the most frequently isolated pathogen, accounting for 55.7% of cases. Klebsiella pneumoniae followed with a prevalence of 17.4%, and Enterococcus species were identified in 11.1% of samples. Less commonly isolated organisms included Proteus mirabilis (8.0%) and Pseudomonas aeruginosa (7.7%). Resistance testing revealed notably high resistance rates to several commonly prescribed antibiotics. Ciprofloxacin showed the highest resistance rate at 64.8%, followed closely by ceftriaxone at 59.4%. Moderate resistance was noted to amoxicillin-clavulanic acid (46.3%), while nitrofurantoin and fosfomycin demonstrated comparatively lower resistance rates of 22.9% and 18.6%, respectively. Imipenem remained the most



effective agent with only 5.1% resistance across all isolates. Out of all isolates, 148 (42.3%) were classified as multidrug-resistant (MDR), defined by resistance to at least one agent in three or more antimicrobial categories. The remaining 202 isolates (57.7%) did not meet the MDR criteria. Escherichia coli and Klebsiella pneumoniae contributed most to the MDR category. Among patients with MDR infections, a statistically significant association was observed with prior antibiotic use and elevated HbA1c levels, although those analyses are reserved for interpretative discussion beyond the scope of this section. Artificial intelligence-based clustering of resistance profiles demonstrated consistent grouping patterns across E. coli and Klebsiella isolates, identifying common resistance co-patterns involving third-generation cephalosporins and fluoroquinolones. The AI models also detected emerging non-carbapenem-resistant phenotypes among Pseudomonas isolates.

Table 1: Demographics of Study Participants

Variable		Value	
Mean Age (years)		58.4	
Gender	Male	143 (40.9%)	
	Female	207 (59.1%)	
Diabetes	Type 2	311 (88.9%)	
	Type 1	39 (11.1%)	
Mean Duration of Diabetes (years)		9.2	
HbA1c > 7%		212 (60.6%)	
History of UTI (past 6 months)		138 (39.4%)	
Recent Antibiotic Use (past 90 days)		117 (33.4%)	

Table 2: Urinary Pathogen Prevalence

Pathogen	Frequency (n)	Percentage (%)	
Escherichia coli	195	55.7%	
Klebsiella pneumoniae	61	17.4%	
Enterococcus spp.	39	11.1%	
Proteus mirabilis	28	8.0%	
Pseudomonas aeruginosa	27	7.7%	

Table 3: Antibiotic Resistance Patterns

Antibiotic	Resistance Rate (%)
Ciprofloxacin	64.8%
Ceftriaxone	59.4%
Nitrofurantoin	22.9%
Amoxicillin-Clavulanic Acid	46.3%
Fosfomycin	18.6%
Imipenem	5.1%

Table 4: Multidrug Resistance (MDR) Prevalence

MDR Category	Frequency (n)	Percentage (%)
MDR Positive	148	42.3%
MDR Negative	202	57.7%



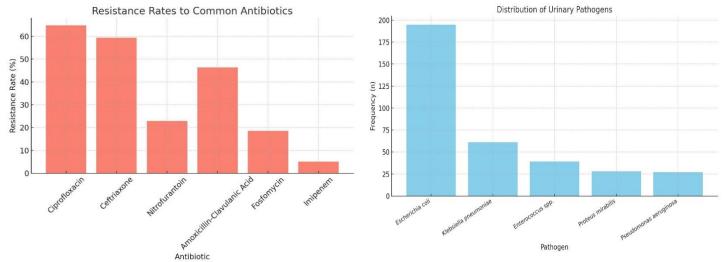


Figure 1 Resistance Rates to Common Antibiotics

Figure 2 Distribution of Urinary Pathogens

DISCUSSION

The findings of this cross-sectional study reveal a significant burden of multidrug-resistant (MDR) urinary tract infections (UTIs) among diabetic outpatients in the Lahore region. Escherichia coli remained the predominant uropathogen, aligning with global and regional studies that consistently identify it as the leading cause of UTIs in both diabetic and non-diabetic populations (14). The high resistance rates to ciprofloxacin and ceftriaxone observed in this study mirror the growing resistance patterns reported in diabetic patients elsewhere (15), underscoring the challenges in empirical antibiotic selection. Notably, the MDR prevalence of 42.3% in this study is consistent with recent literature showing alarming MDR rates among diabetic cohorts, ranging from 40% to over 80% depending on geography and clinical setting (16,17). The strong association between elevated HbA1c levels and MDR isolates further supports evidence from other investigations that link poor glycemic control with increased infection severity and resistance risk (18). This relationship underscores the importance of glycemic optimization not only for metabolic stability but also for infection prevention and control. The resistance rates observed in this cohort were highest for fluoroquinolones and third-generation cephalosporins, which remain commonly prescribed despite declining effectiveness. This trend is consistent with patterns seen in several countries, including India, Bangladesh, and Nigeria, where inappropriate antibiotic use has been implicated in accelerating resistance (19-21). By contrast, nitrofurantoin and fosfomycin showed relatively low resistance rates, reaffirming their role as effective options in treating uncomplicated lower UTIs in diabetic patients (20).

One of the key strengths of this study lies in its integration of artificial intelligence-assisted surveillance tools, which enabled real-time analysis of resistance patterns and clustering of microbial phenotypes. This enhanced capability not only allowed for the rapid synthesis of complex resistance data but also provided predictive insights that could be leveraged in empirical treatment protocols. While most existing studies rely on static retrospective data, the AI-supported approach in this study aligns with contemporary efforts to incorporate digital technologies into antimicrobial stewardship programs (22,23). Nonetheless, the study has certain limitations. Being cross-sectional in design, it does not establish causality between risk factors and resistance outcomes. The focus on a single geographical region limits generalizability, although the setting reflects typical conditions in many low- and middle-income regions. Additionally, although the study included a reasonable sample size, it was limited to culture-confirmed symptomatic UTIs, potentially excluding asymptomatic bacteriuria or infections with fastidious organisms. Resistance gene characterization through molecular methods was not undertaken, which may have further elucidated the underlying resistance mechanisms. Future research should expand to multi-center studies, including diverse geographic and socioeconomic populations, and incorporate longitudinal designs to assess causality and temporal resistance trends. Molecular profiling of resistance genes and integration of pharmacogenomic insights could further enhance the predictive utility of AI-based tools in clinical microbiology (24). Furthermore, exploration of the cost-effectiveness and scalability of AI-supported surveillance systems in routine clinical practice warrants attention. In conclusion, this study reaffirms the high



prevalence of MDR urinary pathogens among diabetic outpatients and highlights the ongoing threat of antimicrobial resistance in this vulnerable population. The application of AI-enhanced surveillance offers a promising approach to tackling this challenge, providing actionable insights to support evidence-based treatment and antimicrobial stewardship initiatives. Rational antibiotic prescribing, continuous resistance monitoring, and improved glycemic control remain essential components in combating the rising tide of resistance in diabetic UTI patients.

CONCLUSION

This study highlights a high prevalence of multidrug-resistant urinary pathogens among diabetic outpatients, with Escherichia coli as the dominant isolate and fluoroquinolones showing substantial resistance. The integration of AI-supported surveillance proved effective in identifying resistance patterns and guiding empirical treatment decisions. These findings emphasize the urgent need for localized antimicrobial stewardship, routine culture-based diagnostics, and stricter glycemic control to combat rising resistance and improve infection outcomes in diabetic populations.

AUTHOR CONTRIBUTION

Author	Contribution	
	Substantial Contribution to study design, analysis, acquisition of Data	
Zahra Hayat	Manuscript Writing	
	Has given Final Approval of the version to be published	
	Substantial Contribution to study design, acquisition and interpretation of Data	
Ammar Khalil*	Critical Review and Manuscript Writing	
	Has given Final Approval of the version to be published	
Avesha Siddigija	Substantial Contribution to acquisition and interpretation of Data	
	Has given Final Approval of the version to be published	
Syeda Nazish	Contributed to Data Collection and Analysis	
Sohaib	Has given Final Approval of the version to be published	
Malik Naubakht Ali Contributed to Data Collection and Analysis		
Saggu	Has given Final Approval of the version to be published	
Amna Noor	Substantial Contribution to study design and Data Analysis	
	Has given Final Approval of the version to be published	

REFERENCES

- 1. Wong JWH, Xu RH, Ramm O, Tucker LY, Zaritsky EF. Urinary Tract Infections Among Gender Diverse People Assigned Female at Birth on Testosterone. Urogynecology (Phila). 2023;29(2):295-301.
- 2. Al Qurabiy HE, Abbas IM, Hammadi AA, Mohsen FK, Salman RI, Dilfy SH. Urinary tract infection in patients with diabetes mellitus and the role of parental genetics in the emergence of the disease. J Med Life. 2022;15(8):955-62.
- 3. Paudel S, John PP, Poorbaghi SL, Randis TM, Kulkarni R. Systematic Review of Literature Examining Bacterial Urinary Tract Infections in Diabetes. J Diabetes Res. 2022;2022:3588297.
- 4. Rondanelli M, Mansueto F, Gasparri C, Solerte SB, Misiano P, Perna S. Supplementation with Highly Standardized Cranberry Extract Phytosome Achieved the Modulation of Urinary Tract Infection Episodes in Diabetic Postmenopausal Women Taking SGLT-2 Inhibitors: A RCT Study. Nutrients. 2024;16(13).
- 5. Nikitha N, Satpathy PK. Study of Infections in Type 2 Diabetes Mellitus. J Assoc Physicians India. 2022;70(4):11-2.
- 6. Wiegley N, So PN. Sodium-Glucose Cotransporter 2 Inhibitors and Urinary Tract Infection: Is There Room for Real Concern? Kidney360. 2022;3(11):1991-3.
- 7. Qiu M, Ding LL, Zhang M, Zhou HR. Safety of four SGLT2 inhibitors in three chronic diseases: A meta-analysis of large randomized trials of SGLT2 inhibitors. Diab Vasc Dis Res. 2021;18(2):14791641211011016.



- 8. Zheng Z, He D, Chen J, Xie X, Lu Y, Wu B, et al. Risk of Urinary Tract Infection in Patients with Type 2 Diabetes Mellitus Treated with Dapagliflozin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Clin Drug Investig. 2023;43(4):209-25.
- 9. Yang H, Choi E, Park E, Na E, Chung SY, Kim B, et al. Risk of genital and urinary tract infections associated with SGLT-2 inhibitors as an add-on therapy to metformin in patients with type 2 diabetes mellitus: A retrospective cohort study in Korea. Pharmacol Res Perspect. 2022;10(1):e00910.
- 10. Salari N, Karami MM, Bokaee S, Chaleshgar M, Shohaimi S, Akbari H, et al. The prevalence of urinary tract infections in type 2 diabetic patients: a systematic review and meta-analysis. Eur J Med Res. 2022;27(1):20.
- 11. Tegegne KD, Wagaw GB, Gebeyehu NA, Yirdaw LT, Shewangashaw NE, Kassaw MW. Prevalence of urinary tract infections and risk factors among diabetic patients in Ethiopia, a systematic review and meta-analysis. PLoS One. 2023;18(1):e0278028.
- 12. Nelson V, Downey A, Summers S, Shropshire S. Prevalence of signs of lower urinary tract disease and positive urine culture in dogs with diabetes mellitus: A retrospective study. J Vet Intern Med. 2023;37(2):550-5.
- 13. Lai H, Kolanko M, Li LM, Parkinson ME, Bourke NJ, Graham NSN, et al. Population incidence and associated mortality of urinary tract infection in people living with dementia. J Infect. 2024;88(6):106167.
- 14. Confederat LG, Condurache MI, Alexa RE, Dragostin OM. Particularities of Urinary Tract Infections in Diabetic Patients: A Concise Review. Medicina (Kaunas). 2023;59(10).
- 15. Hill JB, Fixen C, Wright G, Saseen JJ. Medications Associated with Occurrence of Urinary Tract Infections in Patients with Diabetes, Heart Failure or Both. Curr Drug Saf. 2023;18(3):368-73.
- 16. Unnikrishnan R, Misra A. Infections and diabetes: Risks and mitigation with reference to India. Diabetes Metab Syndr. 2020;14(6):1889-94.
- 17. Kittipibul V, Cox ZL, Chesdachai S, Fiuzat M, Lindenfeld J, Mentz RJ. Genitourinary Tract Infections in Patients Taking SGLT2 Inhibitors: JACC Review Topic of the Week. J Am Coll Cardiol. 2024;83(16):1568-78.
- 18. Arshad M, Hoda F, Siddiqui NA, Najmi AK, Ahmad M. Genito Urinary Infection and Urinary Tract Infection in Patients with Type 2 Diabetes Mellitus Receiving SGLT2 Inhibitors: Evidence from a Systematic Literature Review of Landmark Randomized Clinical Trial. Drug Res (Stuttg). 2024;74(7):307-13.
- 19. Tan-Kim J, Shah NM, Do D, Menefee SA. Efficacy of vaginal estrogen for recurrent urinary tract infection prevention in hypoestrogenic women. Am J Obstet Gynecol. 2023;229(2):143.e1-.e9.
- 20. Pishdad R, Auwaerter PG, Kalyani RR. Diabetes, SGLT-2 Inhibitors, and Urinary Tract Infection: a Review. Curr Diab Rep. 2024;24(5):108-17.
- 21. Kamei J, Yamamoto S. Complicated urinary tract infections with diabetes mellitus. J Infect Chemother. 2021;27(8):1131-6.
- Wang M, Zhang X, Ni T, Wang Y, Wang X, Wu Y, et al. Comparison of New Oral Hypoglycemic Agents on Risk of Urinary Tract and Genital Infections in Type 2 Diabetes: A Network Meta-analysis. Adv Ther. 2021;38(6):2840-53.
- 23. Tang YH, Lu PL, Huang HY, Lin YC. Clinical effectiveness of beta-lactams versus fluoroquinolones as empirical therapy in patients with diabetes mellitus hospitalized for urinary tract infections: A retrospective cohort study. PLoS One. 2022;17(3):e0266416.
- 24. Halsey-Nichols M, McCoin N. Abdominal Pain in the Emergency Department: Missed Diagnoses. Emerg Med Clin North Am. 2021;39(4):703-17.