



Bacterial Spectrum, Antimicrobial Resistance, and Inflammatory Biomarker Profiles of Urinary Tract Infections in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: Urinary tract infections are frequent in type 2 diabetes and are complicated by diverse uropathogens, antimicrobial resistance, and heightened inflammation. **Aims of the study:** This study aimed to identify the bacterial spectrum of urinary tract infections in patients with type 2 diabetes mellitus, determine antimicrobial resistance, multidrug-resistance, and ESBL patterns, and assess their associations with glycemic control and systemic inflammatory biomarkers. **Methodology:** An analytical case-control study enrolled 150 adults with T2DM at Al-Habbobi Teaching Hospital, Dhi Qar, Iraq, from September 2025 to April 2026: 100 had culture-confirmed UTI and 50 were controls. Midstream urine was cultured, isolates identified, and antimicrobial susceptibility, MDR, and ESBL phenotypes determined using CLSI methods. Blood samples were analyzed for HbA1c, WBC, neutrophils, CRP, and procalcitonin, while IL-6 and TNF- α were measured by ELISA. Written consent and standardized quality-control procedures were applied throughout specimen collection and laboratory testing. **Result:** Patients with UTI had poorer glycemic control, more previous UTIs, and greater recent antibiotic exposure than controls. Gram-negative bacteria predominated, particularly *Escherichia coli* and *Klebsiella pneumoniae*. Ciprofloxacin showed the highest resistance, whereas meropenem and amikacin retained the greatest activity. MDR and ESBL phenotypes occurred in 35.0% and 27.5% of isolates, respectively. UTI patients had significantly elevated CRP, procalcitonin, IL-6, TNF- α , WBC, and neutrophils. MDR infections were additionally associated with higher HbA1c and inflammatory biomarker concentrations compared with non-MDR infections. **Conclusions:** Urinary tract infections in patients with T2DM were predominantly caused by Gram-negative bacteria and frequently exhibited MDR and ESBL phenotypes. Poor glycemic control, previous infection, and antibiotic exposure were associated with UTI, while inflammatory biomarkers increased particularly during MDR infections.

Keyword: Uropathogens; Glycemic control; Multidrug resistance; Extended-spectrum β -lactamase; Inflammatory biomarkers.

Introduction:

UTI is an important cause of outpatient consultation, antibiotic use, hospitalisation and re-infection, and is one of the most common bacterial infections. They have become more serious in the world due to population ageing, metabolic diseases, urinary invasive procedures and spread of antimicrobial resistance. Results from worldwide analyses show that there is a significant geographic and temporal variation in UTI incidence, suggesting that population characteristics, access to healthcare, diagnostic approaches, and antimicrobial use (AMU) all play a role in this variation (Yang et al., 2022). UTIs are a condition that can occur in all people, but in patients with type 2 diabetes mellitus (T2DM) infection can be recurrent, complicated and challenging to treat.

There are several factors which dictate the association of T2DM with UTI. Chronic hyperglycemia may compromise the chemotaxis, phagocytosis, killing of intracellular bacteria and cell-mediated immunity of neutrophils. The urine becomes a good medium for the growth of microorganisms due to glucosuria, and diabetic autonomic neuropathy can result in urinary stasis and incomplete bladder emptying. Exposure to frequent health care settings, microvascular disease and renal insufficiency, as well as longer duration of diabetes, may also contribute to susceptibility to infection. Salari et al. (2022) undertook a systematic review and meta-analysis of UTIs in patients with T2DM, and found that there was a significant burden of UTIs in this patient group, with female sex, older age, poor glycemic control and longer disease duration being associated with risk. Likewise, the factors associated with previous UTI, long-standing diabetes, and poor glycemic control were found to be important factors by Tegegne et al (2023).

Recurrent infections are especially important in the diabetic patient. Although longer or more intensive antimicrobial treatment was employed, Papp and Zimmern (2023) found that most of the studies reviewed indicated that diabetes was a risk factor for recurrent UTIs, particularly among women. The results indicate that recurrence might be related to the presence of some physiological and immunological abnormalities that are not just due to insufficient duration of treatment. As such, antibiotic treatment for UTIs in patients with T2DM is often complicated by the need for microbiological confirmation and individualised antibiotic therapy, and complicating factors should be investigated.

Diabetic UTIs are associated with a predominance of Gram-negative bacilli. Uropathogenic *Escherichia coli* is the main pathogen due to their adhesins, iron-acquisition mechanism, toxins, intracellular survival and biofilm formation ability (Zhou et al., 2023). However, in complex infections and/or infections that occur in healthcare settings, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter* species, and *Acinetobacter* species might be found more often. There is also a microflora of gram-positive organisms such as enterococci faecalis, *S. aureus* and *S. saprophyticus*. Farag et al. (2024) showed that the distribution of pathogens and antimicrobial susceptibility varied between diabetic and nondiabetic patients which further highlights the need for pathogen surveillance by population. Gena et al. (2025) have also recently reported *E. coli* as the most frequently isolated bacteria from diabetic patients followed by coagulase-negative staphylococci and *Klebsiella* spp.

Management of UTI has become a more complex process with antimicrobial resistance. Antibiotics may be prescribed inappropriately, for empirical reasons or due to prior hospitalizations, urinary catheters, or long-standing diabetes, which may lead to the selection of multidrug resistant organisms. The high levels of resistance to the antibiotics ampicillin, amoxicillin–clavulanate, tetracycline, cephalosporins, and trimethoprim–sulfamethoxazole in urinary isolates were reported by Kasew et al. (2022). Girma et al. (2023) also found high level of multidrug resistance among the uropathogens isolated from diabetic and high risk groups. Comparative antimicrobial resistance data obtained in more recent studies indicated higher levels of antimicrobial resistance among females with diabetes compared to those without diabetes (Hamdan et al., 2024).

The burden of resistant uropathogens was also high with diabetic patients having UTIs, but was also correlated with complicated infection and prior exposure to antimicrobial agents (Abu-Humaidan et al.,

2025). Similarly, Gena et al. (2025) reported multidrug resistance in 43.6% of urinary isolates of diabetic patients. A third-generation cephalosporin-resistant and/or carbapenem-resistant Enterobacterales (CEC) has been named one of the top bacteria that pose the greatest threat to health systems and should be prioritized for increased surveillance and antimicrobial development by the World Health Organization (2024). Therefore, urine culture, antibiotic susceptibility, previous culture results, disease severity and local antibiograms are currently highlighted as the most important factors to consider in the choice of therapy for complicated UTIs (complicated UTI) (Trautner et al., 2025).

Besides the microbiological results, inflammatory biomarkers could be used to better assess the burden of infection and its clinical severity. The C-reactive protein (CRP) is a marker of acute phase response, while interleukin-6 (IL-6) is a rapid-produced cytokine after the recognition of the microbes that can trigger systemic inflammation. Tumor necrosis factor-alpha (TNF alpha) is involved in endothelial activation and recruitment of leukocytes, procalcitonin might be elevated in systemic bacterial infection. Darogha et al. (2022) have reported high concentration of IL-6 and procalcitonin in people having bacterial UTIs. However, these markers are not infection-specific as T2DM is also known for being an inflammatory disease.

Recent molecular reviews imply that systemic markers can be supplemented by urine culture and clinical data to refine diagnostic discrimination and aid in determining whether a patient has a chance of having an upper tract or systemic involvement (Sun et al., 2024). Other promising urinary markers such as IL-8, neutrophil gelatinase-associated lipocalin, cell-free DNA and host-response signatures are also being evaluated for their routine clinical use (Pandey et al., 2025). Due to the geographical variation of distribution of bacteria, resistance pattern and inflammatory response it is important to have evidence generated locally. This study was thus designed to identify the bacterial spectrum and the antimicrobial resistances of UTI in patients with T2DM and to assess the inflammatory biomarkers as markers of burden of infection and severity of UTI.

Methodology:

This is an analytical case–control study involving patients attended by Al-Habbobi Teaching Hospital outpatient consultation clinics and ward departments in Dhi Qar Province in Iraq from 15 September 2025 to 30 April 2026. 150 adult patients (18–60 years) with established T2DM were included in the study, of which 100 had culture-proven UTI and 50 had no urinary symptoms or significant pyuria, or bacterial growth. Participants were consecutively recruited once they were determined to be eligible and provided written informed consent. The diagnosis of UTI was made when urinary symptoms were compatible, supportive urinalysis was present, and there was a predominant growth of bacteria, usually $\geq 10^5$ CFU/mL, although in patients with clinical symptoms and pyuria, $\geq 10^3$ CFU/mL was considered to be clinically relevant. Patients who had type 1 diabetes, were pregnant, had urinary catheterization, had recent urologic surgery, had urinary malignancy, recent renal failure, recent hepatic failure, had other active infections, autoimmune disorders or immunosuppressive therapy were excluded. The standard data entry form was used to obtain data on age, sex, BMI, place of residence, duration of diabetes, hypertension, previous UTI in the previous year, and antibiotic use in the previous 3 months. Prior to antimicrobial treatment, 10-20 mL of clean-catch, midstream urine was obtained in a sterile container, sent right away, and tested within 2 hours of collection. The samples were cultured aerobically on cystine – lactose – electrolyte deficient agar, blood agar and MacConkey agar for 18 to 24 hours at 35-37°C. Colony morphology, Gram staining and conventional biochemical tests, and (where available) an automated identification system were used to identify significant isolates. Antimicrobial sensitivity was assessed using Kirby–Bauer disk diffusion method on Mueller–Hinton agar, and interpreted based on the current Clinical and Laboratory Standards Institute guidelines. Multidrug resistance was determined as acquired nonsusceptibility to one agent in 3 or more antimicrobial categories. Isolates of Enterobacterales were tested for ESBL production, and

isolates with ESBL production were confirmed by adding clavulanic acid to cefotaxime and ceftazidime disks, which resulted in a ≥ 5 -mm increase in the diameter of inhibition zones. Venous blood (7 mL) was collected aseptically, with 2 mL being placed in an EDTA tube for complete blood count and HbA1c and 5 mL being placed in a serum-separator tube where it was left to clot for 20–30 minutes before being centrifuged at $3,000\times g$ for 10 minutes. All serum was aliquoted into coded samples, and then stored at -80°C until tested. WBC, neutrophils, HbA1c, CRP and procalcitonin were quantified with an automated hematology analyzer, a standardized immunoturbidimetric method for HbA1c, latex-enhanced immunoturbidimetry for CRP, and electrochemiluminescence immunoassay on Cobas e411 analyzer for procalcitonin. Serum IL-6 and TNF- α levels were measured by commercially available validated human sandwich ELISA kits and tested in duplicate with absorbance measured at 450 nm and concentrations calculated from calibration curves. All analytical runs had internal quality controls and runs with a coefficient of variation over 10% were repeated.

Statistical analysis:

Appropriate statistical software package was used for statistical analysis. Continuous variables were reported as means $\pm$ SD or median (IQR) depending upon data distribution while categorical variables were reported as frequency and percentage. The independent-samples t-test or the Mann–Whitney U test was used for continuous variables and the chi-square test or Fisher's exact test was used for categorical variables to compare between groups as appropriate. Multivariable logistic regression analysis was performed to identify factors independently associated with MDR UTI, and adjusted ORs with 95% CIs are presented. The presence of a P value <0.05 on both sides was regarded as being statistically significant.

Ethical approval:

The study protocol was approved by the Human Research Ethics Committee of Al-Habbobi Teaching Hospital, Dhi Qar Province, Iraq. All participants were informed about the study's objectives and procedures and provided written informed consent before enrollment. Participant confidentiality and privacy were maintained throughout the study.

Results

Comparison of baseline characteristics, glycemic control, previous UTI, and recent antibiotic exposure between the two study groups

There were no differences between patients with and without UTI with regard to age, sex, BMI, place of residence, diabetes duration, and hypertension (all $P>0.05$) (Table 1). However, patients with UTI had significantly higher mean HbA1c levels than those without UTI ($8.2\pm 1.4\%$ vs. $7.6\pm 1.2\%$; $P=0.007$), and a greater proportion had HbA1c $\geq 8\%$ (58.0% vs. 36.0% ; $P=0.011$). Other significantly more common factors associated with UTI were previous UTI within 12 months (39.0% vs. 20.0% ; $P=0.019$) and use of antibiotics during the previous 3 months (42.0% vs. 24.0% ; $P=0.030$).

Table 1. Sociodemographic and Clinical Characteristics of Patients With Type 2 Diabetes According to Urinary Tract Infection Status

Variable	T2DM with UTI (n=100)	T2DM without UTI (n=50)	P value
Age (years), mean $\pm$ SD	56.8 $\pm$ 9.7	55.4 $\pm$ 10.1	0.419
Female sex, n (%)	68 (68.0)	31 (62.0)	0.465
Male sex, n (%)	32 (32.0)	19 (38.0)	N/A
BMI (kg/m^2), mean $\pm$ SD	28.6 $\pm$ 4.2	27.9 $\pm$ 4.0	0.323
Rural residence, n (%)	44 (44.0)	17 (34.0)	0.240

Diabetes duration (years), mean $\pm$ SD	8.4 $\pm$ 5.2	7.6 $\pm$ 4.8	0.352
HbA1c (%), mean $\pm$ SD	8.2 $\pm$ 1.4	7.6 $\pm$ 1.2	0.007
HbA1c $\geq$ 8%, n (%)	58 (58.0)	18 (36.0)	0.011
Hypertension, n (%)	49 (49.0)	21 (42.0)	0.418
Previous UTI within 12 months, n (%)	39 (39.0)	10 (20.0)	0.019
Antibiotic use within previous 3 months, n (%)	42 (42.0)	12 (24.0)	0.030

Frequency and percentage distribution of Gram-negative and Gram-positive bacterial isolates identified in urine cultures

The Gram-negative bacteria were the predominant group of urinary isolates with 86.0% of the organisms identified as such, (Table 2). Most of the uropathogens were *Escherichia coli* (52.0%), *Klebsiella pneumoniae* (20.0%), *Enterococcus faecalis* (10.0%), *Proteus mirabilis* (8.0%) and *Pseudomonas aeruginosa* (6.0%). The least commonly isolated organism was *Staphylococcus aureus* at 4.0% of culture proven infections.

Table 2. Distribution of Bacterial Uropathogens Isolated From Patients With Type 2 Diabetes and Culture-Confirmed Urinary Tract Infection

Bacterial isolate	Number (n=100)	Percentage (%)
<i>Escherichia coli</i>	52	52.0
<i>Klebsiella pneumoniae</i>	20	20.0
<i>Enterococcus faecalis</i>	10	10.0
<i>Proteus mirabilis</i>	8	8.0
<i>Pseudomonas aeruginosa</i>	6	6.0
<i>Staphylococcus aureus</i>	4	4.0
Total	100	100.0

Distribution of resistant and susceptible/intermediate isolates across six commonly tested antimicrobial agents

Ciprofloxacin had the highest resistance rate for Gram-negative uropathogens (45.3%), followed by cefepime (33.7%), gentamicin (29.1%), and piperacillin/tazobactam (22.1%), as shown in Table 3. Higher level of resistance showed up against amikacin (14.0%), whereas the highest in-vitro activity was found with meropenem with only 9.3% resistant and 90.7% susceptible/intermediate isolates. The results suggest that ciprofloxacin activity is decreased and the activity of amikacin and meropenem is relatively maintained.

Table 3. Antimicrobial Resistance Patterns of Gram-Negative Uropathogens Isolated From Type 2 Diabetic Patients With Urinary Tract Infection

Antimicrobial agent	Resistant isolates, n (%) (n=86)	Susceptible/intermediate, n (%)
Ciprofloxacin	39 (45.3)	47 (54.7)
Cefepime	29 (33.7)	57 (66.3)
Gentamicin	25 (29.1)	61 (70.9)
Piperacillin/tazobactam	19 (22.1)	67 (77.9)
Amikacin	12 (14.0)	74 (86.0)

Meropenem	8 (9.3)	78 (90.7)
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Species-specific frequencies of MDR and ESBL phenotypes among bacterial isolates causing culture-confirmed urinary tract infections

35.0% of all uropathogens were detected to be multidrug resistant as indicated in Table 4. The highest MDR rate was seen in KP (45.0%), followed by *E. coli* (38.5%), *Proteus mirabilis* (37.5%) and *Pseudomonas aeruginosa* (33.3%). However, *Enterococcus faecalis* isolates demonstrated lower frequency of MDR than the other bacterial species, and no MDR phenotype was detected for the *Staphylococcus aureus*. Of 80 Enterobacterales strains, 22 were ESBL-positive (27.5%), with the highest percentage being *K. pneumoniae* (35.0%).

Table 4. Distribution of Multidrug Resistance and Extended-Spectrum β -Lactamase Phenotypes Among Uropathogens Isolated From Type 2 Diabetic Patients

Bacterial isolate	Total isolates	MDR, n (%)	ESBL-positive, n (%)
<i>E. coli</i>	52	20 (38.5)	14 (26.9)
<i>K. pneumoniae</i>	20	9 (45.0)	7 (35.0)
<i>P. mirabilis</i>	8	3 (37.5)	1 (12.5)
<i>P. aeruginosa</i>	6	2 (33.3)	NA
<i>E. faecalis</i>	10	1 (10.0)	NA
<i>S. aureus</i>	4	0 (0.0)	NA
Total	100	35 (35.0)	22/80 (27.5)*

Comparison of systemic inflammatory biomarkers, leukocyte counts, and neutrophil percentages between patients with and without culture-confirmed UTI

As shown in Table 5, patients with culture-confirmed UTI had significantly higher CRP (13.1 ± 7.8 vs. 5.2 ± 3.4 mg/L), procalcitonin (0.18 ± 0.12 vs. 0.08 ± 0.05 ng/mL), IL-6 (14.6 ± 7.2 vs. 9.1 ± 4.8 pg/mL), and TNF- α concentrations (21.8 ± 9.4 vs. 16.7 ± 7.2 pg/mL) than patients without UTI. The UTI group also had a significant increase in WBC counts (9.8 ± 2.5 vs. $7.6 \pm 1.8 \times 10^9/L$, all $P < 0.001$) and neutrophil percentages ($68.2 \pm 10.8\%$ vs. $59.6 \pm 9.4\%$, all $P < 0.001$), suggesting a more vigorous systemic inflammatory response to infection.

Table 5. Inflammatory and Hematological Biomarker Profiles in Type 2 Diabetic Patients According to Urinary Tract Infection Status

Biomarker	T2DM with UTI (n=100)	T2DM without UTI (n=50)	P value
CRP (mg/L)	13.1 ± 7.8	5.2 ± 3.4	<0.001
Procalcitonin (ng/mL)	0.18 ± 0.12	0.08 ± 0.05	<0.001
IL-6 (pg/mL)	14.6 ± 7.2	9.1 ± 4.8	<0.001
TNF- α (pg/mL)	21.8 ± 9.4	16.7 ± 7.2	<0.001
WBC ($\times 10^9/L$)	9.8 ± 2.5	7.6 ± 1.8	<0.001
Neutrophils (%)	68.2 ± 10.8	59.6 ± 9.4	<0.001

Comparison of HbA1c and systemic inflammatory biomarkers between patients infected with MDR and non-MDR uropathogens

The MDR infected patients also showed significantly higher HbA1c compared to non-MDR infected patients ($8.6 \pm 1.3\%$ vs. $8.0 \pm 1.4\%$; $P = 0.035$) as detailed in Table 6. They also demonstrated higher CRP (16.1 ± 8.2 vs. 11.5 ± 7.0 mg/L; $P = 0.007$), procalcitonin (0.22 ± 0.13 vs. 0.16 ± 0.11 ng/mL; $P = 0.024$), IL-6 (16.8 ± 7.6 vs. 13.4 ± 6.8 pg/mL; $P = 0.031$), and TNF- α concentrations (24.8 ± 10.0 vs. 20.2 ± 8.7 pg/mL;

P=0.025). These results suggest that MDR infection is correlated with glycemic control and a moderate increase in systemic inflammatory response.

Table 6. Glycemic Control and Inflammatory Biomarker Levels According to Multidrug-Resistance Status of Urinary Tract Infection

Parameter	MDR infection (n=35)	Non-MDR infection (n=65)	P value
HbA1c (%)	8.6 ± 1.3	8.0 ± 1.4	0.035
CRP (mg/L)	16.1 ± 8.2	11.5 ± 7.0	0.007
Procalcitonin (ng/mL)	0.22 ± 0.13	0.16 ± 0.11	0.024
IL-6 (pg/mL)	16.8 ± 7.6	13.4 ± 6.8	0.031
TNF-α (pg/mL)	24.8 ± 10.0	20.2 ± 8.7	0.025

Discussion:

The current study has shown that the main clinical features associated with culture-positive UTI in T2DM patients were poor glycemic control, history of UTI, and recent antibiotic use. On the other hand, there were no significant differences between patients with and without UTI with regard to age, sex, BMI, residence, diabetes duration and hypertension. The lack of significant differences between the demographics means that the groups are reasonably comparable and that observed differences in microbiology and inflammation were less likely to be due to baseline demographic differences.

Patients with UTI had significantly higher mean HbA1c than patients without UTI (8.2% vs. 7.6%) and the percentage of patients with HbA1c $\geq 8\%$ was also higher in patients with UTI. This is consistent with a systematic review by Salari et al. that found that poor glycemic control is an important risk factor for susceptibility to UTI in T2DM patients (Salari et al., 2022). Similar results were observed when Tegegne et al. correlated uncontrolled diabetes with an increase in the prevalence of bacterial UTI (Tegegne et al., 2023). Hyperglycemia can also cause infection by increasing glucosuria, decrease in chemotaxis and phagocytosis of neutrophils, decrease in killing of bacteria in phagocytes, endothelial dysfunction and impaired local urinary defense.

However, several studies have failed to show a consistent association between HbA1c and UTI. Infection has been found to have significant heterogeneity by diabetic population in relation to glycemic control (Girma et al., 2023). This mismatch could be due to variations in HbA1c limits, diabetes history, treatment, renal function, age of subjects, and the definition of UTI (i.e., symptomatic vs. asymptomatic). The cross-sectional design of the present study also makes it difficult to determine temporality as physiological stress caused by infection can acutely affect blood glucose levels.

Patients with current UTI had a higher rate of previous UTI within 12 months. This is consistent with the systematic review by Papp and Zimmern which found diabetes to be linked to recurrent UTI in the majority of the studies included, especially among women (Papp & Zimmern, 2023). Persistent bladder colonization, presence of bacteria in the urinary tract cells, urinary tract stasis with autonomic neuropathy, exposure to health care settings, or reinfection from the intestinal flora may be responsible for recurrent infections. UTI, however, are also a sign of pre-existing anatomical and/or functional abnormalities in the urinary tract, but not necessarily a causative factor.

Recent antibiotic exposure was found to be significantly higher in UTI patients. This is of clinical significance as it is possible to disrupt the intestinal and urinary microbiota and select resistant bacterial populations by exposure to antimicrobials. Previous antibiotic use and complicated infection were shown to be associated with increased antimicrobial resistance of urinary isolates by Abu-Humaidan et al. (2025). A previous treatment program may also leave the susceptible organisms suppressed but not eradicated, and thus increase the chances for a recurrent culture positive infection.

Women were 68% of the UTI group but this was not statistically different from the diabetic controls. Sex ratio is 2:1, which is in accordance with the shorter urethra in females, the urethral meatus being close to the perineal and intestinal flora, hormonal effects and a higher risk of ascending infection. Diabetic patients with female sex were also identified as an independent UTI risk factor by Gena et al. (2025). The lack of difference between sexes in the present study, in contrast, may have been due to the predominance of women and the relatively small difference size, or to a small sample size which did not have sufficient power to detect differences.

Isolates were predominantly gram-negative organisms, with *Escherichia coli* being the predominant organism (52%), followed by *Klebsiella pneumoniae* (20%). This is in line with the known ascending progression of UTIs where organisms from the intestinal flora ascend through the periurethral region into the bladder. Uropathogenic *E. coli* (UPEC) has the ability to form biofilms, to survive intracellularly within urothelial cells, to express siderophores, and to produce toxins and fimbriae, namely type 1 and P fimbriae (Zhou et al., 2023).

Recent studies have documented a similar distribution of microbes. Gram-negative bacillae were the most common pathogens associated with UTIs in patients with diabetic and nondiabetic conditions, with *E. coli* being the most prevalent, reported by Farag et al. (2024). Coagulase-negative staphylococci were also the second-most common bacterial species identified by Gena et al. (2025), with *Klebsiella* species coming in third. The results of Mlugu et al's study on community-acquired urinary infections also showed that *E. coli* was the predominant organism (Mlugu et al., 2023).

However, this frequency of 52% *E. coli* was higher than the rates reported by Farag et al. for diabetic patients (21.4%) and lower than the levels observed in some studies of community-acquired UTIs in non-diabetic patients (Farag et al., 2024). This discrepancy could be attributed to differences in study design, sex ratio, hospitalization, previous antibiotic therapy, definitions of diagnosis and recurrent and complicated infections. The bacterial diversity of diabetic populations could be broader due to repeated exposure to the healthcare system and antimicrobial treatment, which favors the growth of opportunistic bacteria like *Klebsiella*, *Pseudomonas* and *Enterococcus*.

The second most common was *K. pneumoniae*, which had the greatest proportions of MDR and ESBL. This organism may harbour plasmids for antibiotic resistance, a protective capsule, form biofilms and acquire genes coding for ESBLs, aminoglycoside-modifying enzymes and carbapenemases. *E. coli* and other Enterobacterales were also the most common pathogens found among diabetic UTI patients (Sorescu et al., 2024). Detection in 6% may be suggestive of complicated disease, prior antimicrobial exposure, instrumentation and/or healthcare contact as *Pseudomonas aeruginosa* is less characteristic of uncomplicated community-acquired cystitis.

The highest percentage resistances for Gram-negative isolates were for ciprofloxacin (45.3%), cefepime (33.7%) and gentamicin (29.1%). This is in line with the use of fluoroquinolones globally and the acquisition of mutations in genes encoding DNA gyrase and topoisomerase IV, plasmid-mediated quinolone-resistance (PMQR) genes and activation of efflux pumps. The resistance rates of urinary pathogens to the most commonly used antibiotics were high and were reported by Kasew et al. (2022). Variations may be due to antimicrobial prescribing patterns or OTC availability, referral patterns, and the percentage of HAI.

The resistance rate of cefepime is clinically significant due to the possibility of ESBL production, AmpC β -lactamase activity, permeability changes and a combination of these. Verma et al. found high level of cephalosporin and fluoroquinolone resistance in healthcare associated UTI isolates of ESBL-producing *E. coli* and *K. pneumoniae* (Verma et al., 2023). Cefepime susceptibility should not be evaluated in isolation for the following reasons: the organism's identity, minimum inhibitory concentration, severity of the infection, and whether or not it is an ESBL.

The in-vitro activity of amikacin and meropenem was the highest, with 14.0% and 9.3% resistance rates, respectively. Similarly, Bayaba et al. (2025) showed that amikacin and imipenem were effective against many ESBL-producing urinary *E. coli* and *K. pneumoniae* isolates, even though these isolates were highly resistant to other drugs. The preservation of this activity might be associated with their less frequent use than fluoroquinolones and oral β -lactams. The identification of meropenem resistance in almost 10% of Gram-negative isolates, however, is worrying, as this could be a sign of carbapenemase production, loss of porin or association with ESBL/ampC production or resistance of intrinsically difficult-to-treat organisms like *P. aeruginosa*.

Meropenem should not therefore be recommended for routine empirical use as a result of the highest in-vitro activity. WHO has classified carbapenem-resistant Enterobacterales and resistant *P. aeruginosa* as urgent bacterial threats that need to be monitored and for whom antimicrobial stewardship is crucial (World Health Organization, 2024). Empirical treatment is recommended based on the severity of the illness, previous cultures, recent use of antibiotics, local antibiograms, and likelihood of resistance; de-escalation should be used when susceptibility results are known (Trautner et al., 2025).

The proportion of urinary isolates that contained MDR was 35%. The highest proportion of MDR was seen in *K. pneumoniae* (45%), followed by *E. coli* (38.5%) and *P. mirabilis* (37.5%). This is consistent with the worldwide trend where Enterobacterales are a significant source of transferable antimicrobial-resistance genes. Murray et al. listed *E. coli* and *K. pneumoniae* as the main drivers of the global burden of antimicrobial resistance (Murray et al., 2022). The current proportion of MDR was lower than that reported by Gena et al (Gena et al., 2025) among diabetic patients (43.6%), but significantly lower than some hospital-based studies.

Variations in MDR prevalence could be explained by the fact that the population was community or hospital based, the number of antimicrobials studied, the classes of antimicrobials included and definition of MDR. According to the internationally accepted definition, nonsusceptibility to at least one agent for three or more antimicrobial categories. Thus, other antibiotic panels should be used for isolates based on the species of the organism and not on the same panel for all species.

The rate of ESBL was higher in Enterobacterales (27.5%) with more among *K. pneumoniae* than *E. coli*. Hamdan et al. (2024) found increased resistance to antimicrobial agents of uropathogens isolated from diabetic women compared with non-diabetic women. The ESBL prevalence reported by Bayaba et al. (2025) for urinary *E. coli* and *K. pneumoniae* was much higher than the current study (64.7% vs. 4.7%). These differences in the rate may be due to hospital referral, differences in the use of antibiotics, geographic spread of CTX-M-producing clones, and molecular or phenotypic testing differences.

In the current study, the low prevalence of ESBL did not rule out any clinical concern as over 25% of Enterobacterales were susceptible to ESBL. ESBL enzymes, especially the CTX-M families, are capable of breaking down extended-spectrum cephalosporins and are often on plasmids that also carry other resistance genes. Phenotypic ESBL detection should ideally be confirmed with combination-disc testing or with an automated validated method and interpretive criteria should be based on the current CLSI or EUCAST standard.

There was a significant difference between the CRP levels, procalcitonin, IL-6, TNF- α , white blood cell count and neutrophil percentage of diabetic patients with UTI when compared to diabetic controls. The results suggest that culture-confirmed infection was associated with extra chronic low-grade inflammation, in addition to systemic inflammation that may be attributed to T2DM. Innate immune receptors recognize bacteria and induce the release of IL-6 and TNF- α . IL-6 stimulates the production of CRP in liver, while chemokine signaling attracts neutrophils to the urinary tract.

Darogha et al. noted that IL-6 and procalcitonin levels were significantly high in the bacterial UTI group, suggesting their potential role in diagnosis (Darogha et al., 2022). Similarly, Sun et al. found that among the most widely studied host-response markers for UTI detection and severity evaluation, CRP,

procalcitonin, and IL-6 stood out as significant markers (Sun et al., 2024). Pandey et al stated that the use of a combination of biomarkers with microbiological and clinical information could provide greater information than any single marker alone (Pandey et al., 2025).

The mean procalcitonin concentration in the UTI group was only 0.18 ng/mL, and significant though it was, was still considerably lower than that in the controls. This was a moderate elevation which makes biological sense for localized urinary tract infection, without bacteremia or sepsis. Procalcitonin typically increases significantly in systemic bacterial infection, pyelonephritis or urosepsis. Thus, the results confirm the group-based inflammatory discrimination, but cannot confirm procalcitonin as a UTI stand-alone diagnostic test (Pandey et al., 2025).

The median HBA1C, CRP, procalcitonin, IL-6, and TNF- α levels were significantly higher in patients with MDR infections compared to those with non-MDR infections. Inadequate glycemic control could also contribute to MDR infection indirectly by leading to the recurrence of infection, repeated use of antibiotics, hospitalization, and colonization. This increased inflammatory concentrations could be due to delayed effective treatment, higher persistence of organisms, the growth of biofilm or enrichment of complicated infections in the MDR group.

However, it shouldn't be seen as a direct link between antimicrobial resistance and increased inflammation. Resistance has more to do with persistence of bacteria in the presence of antimicrobials, and less to do with virulence. Resistance and virulence are two distinct functions, and some resistant strains can include virulence determinants. The increased levels of biomarkers in MDR infection may then be the result of other factors such as type of pathogen, infection site, pathogen load, fever, kidney involvement, delay in treatment, or prior antibiotic therapy. Further multivariable analysis must be performed to establish that MDR status is an independent predictor of inflammatory markers (Gena et al., 2025).

Conclusion:

In summary, the results show a complex pattern between glycemic control, previous infections, recent antibiotic use, resistant uropathogens and higher systemic inflammation levels. They believe that urine culture and organism-specific susceptibility testing should be routinely ordered in diabetic patients, especially if they have recurrent infections or HbA1c levels >8%. The term “susceptible/intermediate” should be broken back down in the final manuscript in Table 3 as the intermediate or “susceptible with increased exposure” category is not synonymous with full susceptibility. Resistance proportions should also be shown separately for each bacterial species as this is different for intrinsic resistance and the clinically appropriate antibiotics, depending on the species of Enterobacterales, *P. aeruginosa* and the Gram-positive organisms.

References

- Abu-Humaidan, A. H., Alajlouni, Y. Y., Alajlouni, A. Y., Hamdan, O. F., Basyouni, B. L., Qasem, O. F., et al. (2025). Antimicrobial resistance of uropathogens in diabetic patients. *BMC Infectious Diseases*, 25, 945. <https://doi.org/10.1186/s12879-025-11358-8>
- Bayaba, S., Founou, R. C., Tchouangueu, F. T., Dimani, B. D., Mafo, L. D., Nkengkana, O. A., et al. (2025). High prevalence of multidrug-resistant and extended-spectrum β -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from urinary tract infections in the West Region, Cameroon. *BMC Infectious Diseases*, 25, 115. <https://doi.org/10.1186/s12879-025-10483-8>
- Darogha, S. N., Azeez, S. H., & Abdullah, Z. G. (2022). Evaluation of procalcitonin and interleukin-6 as a marker of bacterial urinary tract infection. *Cellular and Molecular Biology*, 67(4), 203–213. <https://doi.org/10.14715/cmb/2021.67.4.23>

- Darogha, S. N., Azeez, S. H., & Abdullah, Z. G. (2022). Evaluation of procalcitonin and interleukin-6 as a marker of bacterial urinary tract infection. *Cellular and Molecular Biology*, 67(4), 203–213. <https://doi.org/10.14715/cmb/2021.67.4.23>
- Farag, P. F., El-Sayed, M. M., Abdallah, A. A., et al. (2024). Prevalence and antibiotic resistance profile of UTI-causing uropathogenic bacteria in diabetics and non-diabetics at the Maternity and Children Hospital in Jeddah, Saudi Arabia. *Frontiers in Microbiology*, 15, 1507505. <https://doi.org/10.3389/fmicb.2024.1507505>
- Gena, M. E., Bitew, G., Chane, E., Cherie, N., Berta, D. M., Demoze, L., et al. (2025). Bacterial profile and antimicrobial susceptibility pattern of urinary tract infection among diabetic patients at Bule Hora University Teaching Hospital, Southern Ethiopia. *Scientific Reports*, 15, 24112. <https://doi.org/10.1038/s41598-025-05782-8>
- Girma, A., Aemiro, A., Workineh, D., & Tamir, D. (2023). Magnitude, associated risk factors, and trend comparisons of urinary tract infection among pregnant women and diabetic patients: A systematic review and meta-analysis. *Journal of Pregnancy*, 2023, 8365867. <https://doi.org/10.1155/2023/8365867>
- Hamdan, A., Al-Badriyeh, D., Al-Ansari, A., et al. (2024). Prevalence of antimicrobial resistance among the World Health Organization's priority uropathogens in women with and without diabetes. *Antibiotics*, 13(12), 1218. <https://doi.org/10.3390/antibiotics13121218>
- Kasew, D., Eshetie, S., Diress, A., Tegegne, B., Moges, F., & Moges, F. (2022). Antimicrobial resistance trend of bacterial uropathogens at the university referral hospital in Northwest Ethiopia. *PLOS ONE*, 17(4), e0266878. <https://doi.org/10.1371/journal.pone.0266878>
- Mlugu, E. M., Mohamedi, J. A., Sangeda, R. Z., & Mwambete, K. D. (2023). Prevalence of urinary tract infection and antimicrobial resistance patterns of uropathogens with biofilm-forming capacity among outpatients in Morogoro, Tanzania. *BMC Infectious Diseases*, 23, 660. <https://doi.org/10.1186/s12879-023-08641-z>
- Murray, C. J. L., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., et al. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet*, 399(10325), 629–655. [https://doi.org/10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)
- Oumer, O., Metaferia, Y., & Gebretsadik, D. (2022). Bacterial uropathogens, their associated factors, and antimicrobial susceptibility pattern among adult diabetic patients in northeastern Ethiopia. *SAGE Open Medicine*, 10, 20503121221139148.
- Pandey, S., et al. (2025). Biomarker innovation in urinary tract infections: Current advances and future perspectives. *World Journal of Nephrology*, 14(4), 110749. <https://doi.org/10.5527/wjn.v14.i4.110749>
- Papp, S. B., & Zimmern, P. E. (2023). Recurrent urinary tract infections and type 2 diabetes mellitus: A systematic review predominantly in women. *Frontiers in Urology*, 3, 1275334. <https://doi.org/10.3389/fruro.2023.1275334>
- Salari, N., Karami, M. M., Bokaei, S., Chalesghar, M., Shohaimi, S., Akbari, H., et al. (2022). The prevalence of urinary tract infections in type 2 diabetic patients: A systematic review and meta-analysis. *European Journal of Medical Research*, 27, 20. <https://doi.org/10.1186/s40001-022-00644-9>
- Sati, H., Carrara, E., Savoldi, A., et al. (2025). The WHO bacterial priority pathogens list 2024: A prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. *The Lancet Infectious Diseases*, 25(9), 1033–1043.
- Sorescu, T., et al. (2024). Characteristics of urinary tract infections in patients with diabetes mellitus. *Medicina*, 60(11), 1870. <https://doi.org/10.3390/medicina60111870>

- Sujith, S., et al. (2024). Comprehensive insights into urinary tract infections: From pathophysiology to precision diagnosis and management. *Frontiers in Cellular and Infection Microbiology*, 14, 1402941. <https://doi.org/10.3389/fcimb.2024.1402941>
- Sun, J., et al. (2024). Urinary tract infection detection with molecular biomarkers. *Biomolecules*, 14(12), 1540. <https://doi.org/10.3390/biom14121540>
- Tegegne, K. D., Wagaw, G. B., Gebeyehu, N. A., Yirdaw, L. T., Shewangashaw, N. E., & Kassaw, M. W. (2023). Prevalence of urinary tract infections and risk factors among diabetic patients in Ethiopia: A systematic review and meta-analysis. *PLOS ONE*, 18(1), e0278028. <https://doi.org/10.1371/journal.pone.0278028>
- Trautner, B. W., Morgan, D. J., et al. (2025). Clinical practice guideline by the Infectious Diseases Society of America: 2025 guideline on management and treatment of complicated urinary tract infections—selection of antibiotic therapy. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciaf460>
- Verma, S., Kalyan, R. K., Gupta, P., Khan, M. D., & Venkatesh, V. (2023). Molecular characterization of extended-spectrum β -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates and their antibiotic resistance profile in healthcare-associated urinary tract infections in North India. *Journal of Laboratory Physicians*, 15(2), 194–201. <https://doi.org/10.1055/s-0042-1757416>
- World Health Organization. (2024). WHO bacterial priority pathogens list, 2024: Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance. <https://www.who.int/publications/i/item/9789240093461>
- Zhou, Y., Zhou, Z., Zheng, L., Gong, Z., Li, Y., Jin, Y., et al. (2023). Urinary tract infections caused by uropathogenic *Escherichia coli*: Mechanisms and therapeutic strategies. *Frontiers in Cellular and Infection Microbiology*, 13, 1283404. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10341809>