

Analysis of Bacterial Uropathogens and Antimicrobial Resistance Profiles among Diabetic Patients in Al-Kut City, Iraq

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Abstract: Urinary tract infection (UTI) is a serious medical concern that results from microbial colonization and spread inside the urinary system. Because their host defenses are weakened and their urine has a high glucose content, patients with diabetes are more susceptible to bacterial UTIs. Patient treatment and infection control depend on uropathogens and their antibiograms being thoroughly and promptly examined.

Objectives: This study was performed to evaluate the prevalence of bacterial uropathogens and patterns of antibiotic resistance in individuals with diabetes in al-Kut City, Iraq

Methods: Between January 2023 and February 2024, 420 urine samples from outpatient admissions to Al-Karama and Al-Zahraa Teaching Hospitals were used in this investigation. The identification and antibiotic susceptibility tests of the causing bacteria were conducted using the fully automated VITEK 2 compact system.

RESULTS: Out of 420 urine samples from symptomatic UTI patients, 344 (81.9%) were determined to have significant growth for UTI; 292 (84.88%) of them were female patients. The Gram negative bacteria were detected in 212 (61%) of samples, while the gram positive bacteria were isolated from 123 (38%) of samples. Regardless of the sex group, E. Coli and S. aureus were the most frequently isolated uropathogens in percentage of 71.69% and 38.38%, respectively. The "resistance rates in the group of Gram-negative isolates (n=389) in decreasing order were as follows: Ampicillin 65% Cefoxitin 49% Piperacillin/tazobactam 47% < Ceftriaxone 35% < Ceftazidime and Cefepime 29% < Trimethoprim/Sulfamethoxazole 27% < Ciprofloxacin 24% Levofloxacin 23% < Nitrofurantoin 22% < Gentamicin 19% < Amikacin 18% < Imipenem 2%". On the other hand, The resistance rates in the group of Gram-positive isolates (n= 132) in decreasing order were "Oxacillin 49% < Tetracycline 46% Trimethoprim/sulfamethoxazole 45% < Levofloxacin 26% < Nitrofurantoin and Tobramycin 20% < Clindamycin 16% < , Rifampicin 11% < < Gentamicin 11% < Teicoplanin and Vancomycin 6%"

CONCLUSION: E. coli and S. aureus dominated the etiological spectrum of UTIs in AL-Kut City, Iraq. There was a relatively low resistance rate to aminoglycosides among the Gram-negative uropathogens, but significant resistance rates to "trimethoprim/sulfamethoxazole", ampicillin, and second and "third-generation cephalosporins" were detected. In the G+ group, Vancomycin, teicoplanin, and imipenem all maintained very excellent action and are suitable options for the antimicrobial therapy of complex urinary tract infections in the absence of other options.

Key points: al-Kut City, Uropathogens, Antimicrobial Resistance, Diabetes.

Introduction

One of the most frequent illnesses seen in clinical practice is “urinary tract infection (UTI)”. Due to the potential for increased morbidity as well as mortality from delayed treatment, empirical therapy for both severe and simple UTIs has been used worldwide [1, 2, 3]. Due to certain anatomical abnormalities, the infection is more common in females, those who have frequent sex, young children, the elderly, those with urinary tract abnormalities, those from low socioeconomic backgrounds, women who are pregnant, diabetics, and those with spinal cord injuries are among those who are more at risk [4]. UTI is commonly caused by “bacteria mostly by Gram-negative bacteria such as *E.coli*, *Proteus species*, *Pseudomonas aeruginosa*, *Acinetobacter species*, *Klebsiella species*, *Enterobacter species*, and *Citrobacter species*. Among Gram-positive bacteria, *Staphylococcus saprophyticus*, *Enterococcus species*, and Coagulase-negative *Staphylococcus* are common predictable spectrum of bacteria which are responsible for causing UTIs” [5,6]. A common therapy for UTIs is the use of broad-spectrum antibiotics, and the diagnosis is made on the basis of clinical judgment rather than culture and sensitivity testing. Based on the local rates of uropathogen resistance, first-line drugs are qualified for empiric treatment of UTIs. Accordingly, thresholds have been proposed for the prevalence of resistance among uropathogens in a community, above which certain strains are not advised to be treated; an antibiotic's first-line empirical treatment for UTIs should not be considered effective if its resistance exceeds 10–20% in the most probable-infecting strains [1]. Due to the prevalence of distinct strains in various parts of the world and variations in antibiotic use, the rate of antibiotic resistance varies according to geographic location [7]. The pattern of antibiotic resistance in microorganisms is constantly evolving [8, 9]. As antibiotic resistance increases globally, Elimination of urinary pathogens from the urinary tract becomes increasingly difficult, leading to long-term morbidity and high mortality rates. As a result, antibiotic resistance is emerging as a critical healthcare concern and ranks among the top priorities identified by the World Health Organization (WHO) [10,11]. Financial hardship is also brought on by antimicrobial resistance since treating resistant types of bacteria requires the use of more costly medications and further laboratory testing. [12]

Therefore, it is essential to continuously assess the effectiveness of the suggested empirical antimicrobial regimens and to conduct local resistance surveillance of uropathogens in order to guide empirical antimicrobial choices [1,13]. However, Iraq lacks a surveillance mechanism for antibiotic resistance to track community-acquired uropathogens. As a consequence, There is no regional protocol in the country for treating community-acquired UTIs appropriately.

This study's main goal was to determine the frequency of bacteria that cause urinary tract infections (UTIs) and the patterns of antibiotic susceptibility to those infections in order to create an extensive database for future use. Considering this study, it's noteworthy that not enough local research has been published on this particular issue. The trend of antimicrobial resistance is changing drastically in the current situation, and the regular emergence of novel MDR bacteria is increasing morbidity and death. The use of suitable antibiotics for the treatment of UTIs is the main emphasis of this investigation. Furthermore, our research will support relevant authorities in creating guidelines for antibiotic formularies and prescription regulations that align with the goals of the "Iraq Action Plan on Antimicrobial Resistance ". It will be easier to stop the immersed strains from spreading across the population if there is greater awareness and yearly reporting of these discoveries.

METHODS

Sample collection

Between January 2023 and February 2024, 420 midstream urine samples were taken from patients admitted to the Wassit governorate's “Al-Karama and Al-Zahraa Teaching Hospitals”. Both sexes of symptomatic patients provided samples for collection. After being delivered to the lab in a half-hour to an hour, samples were examined using a variety of standard biochemical and bacteriological techniques. Symptomatic subjects with significant bacteriuria in their urine samples were sequentially included. Exclusion was granted to those with little bacteriuria. In patients exhibiting symptoms, significant bacteriuria was characterised by the “isolation of a single organism in

quantitative counts greater than 10^2 colony-forming units (CFU)/mL from a clean-catch voided urine specimen” [14].

Using a checklist, prospective data was collected on age, sex, prior medical history, and history of antibiotic exposure within the previous three months. Using a conventional loop, 10 μ l of each Mid-stream urine sample was inoculated on standard culture medium, such as blood agar and MacConkey agar. Following a 35°C overnight incubation, the cultures were examined to check for the growth of bacteria.

The bacteria that were isolated from urine samples were identified and their antibiotic susceptibility evaluated using the VITEK 2 Compact System. A standardized saline inoculum that is suggested for VITEK identification was created using the culture plates that demonstrated the formation of substantial bacterial colonies. To identify bacteria using VITEK, we utilized specialized ID cards for both Gram-positive and Gram-negative bacteria. Special sensitivity (AST) cards were used to determine the minimum inhibitory concentrations and the results of the antimicrobial susceptibility tests (AST). The Advanced Expert System and the manufacturer's instructions (BioMérieux, France) were followed in the interpretation of the AST findings using Clinical and Laboratory Standards Institute standards.

Ethics. The study procedure was approved by the University of Wassit's College of Medicine's ethical committee.

Results

A total of 420 urine samples were submitted for analysis and culture In “Microbiology Laboratory, College of Medicine/wassit university. There were 344 (81.9%) urine samples were showing significant growth for UTI, among whom, the females were 292 (84.88%) episode. The average age (\pm SD) was 47 ± 12 years. Frequency of gender distribution of UTI cases table 1”.

Table 1: The frequency of admission and sex distribution of UTI cases admitted to “Al-Karama and Al-Zahraa Teaching Hospitals”

Sex	Frequency (%)
Male	52 (15.12)
female	292 (84.88)
Total	344 (100)

In the present study , 61.62% (n=212) of the bacteria were determined to be Gram negative, and 38.38% (n=132) to be Gram positive.

Within the Gram-negative bacteria, *E. Coli* accounted for the majority of the species (71.69%, n=152) linked to UTIs in the study group of patients (figure 1), with other gram negative bacteria coming in at 3.77%(8), *Proteus* 8.49%(18), *Enterobacter* 3.77%(8), *P.aeruginosa* 1.88%(4), and *Klebsiella species* at 10.37% (22). On the other hand, the percentage of Gram-positive bacteria was 38.38% (n=132). The most common pathogen in this group was *Staphylococcus aureus* (53%, n=70), followed by *Enterococcus faecalis* (23.48% (31). Other species of *Staphylococcus* and *Streptococcus* were diagnosed in 16.66% (n=22) and 6.81% (n=9), respectively (figure 2).

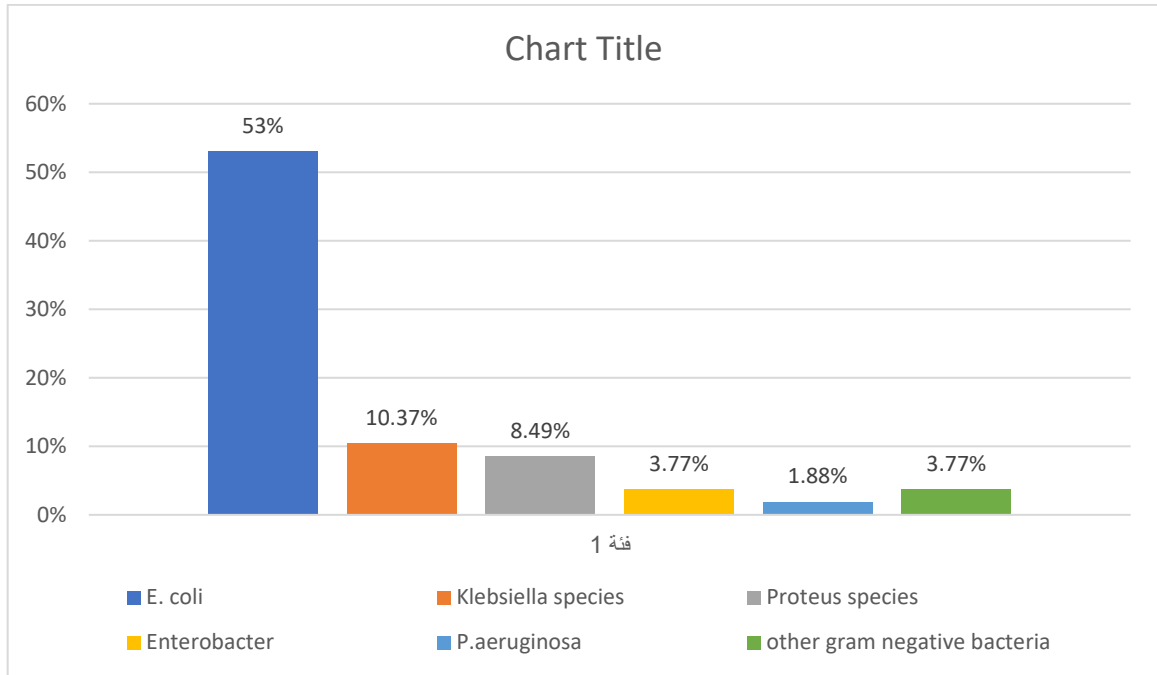


Figure 1- Percentage of Gram negative uropathogen isolated from diabetes patients

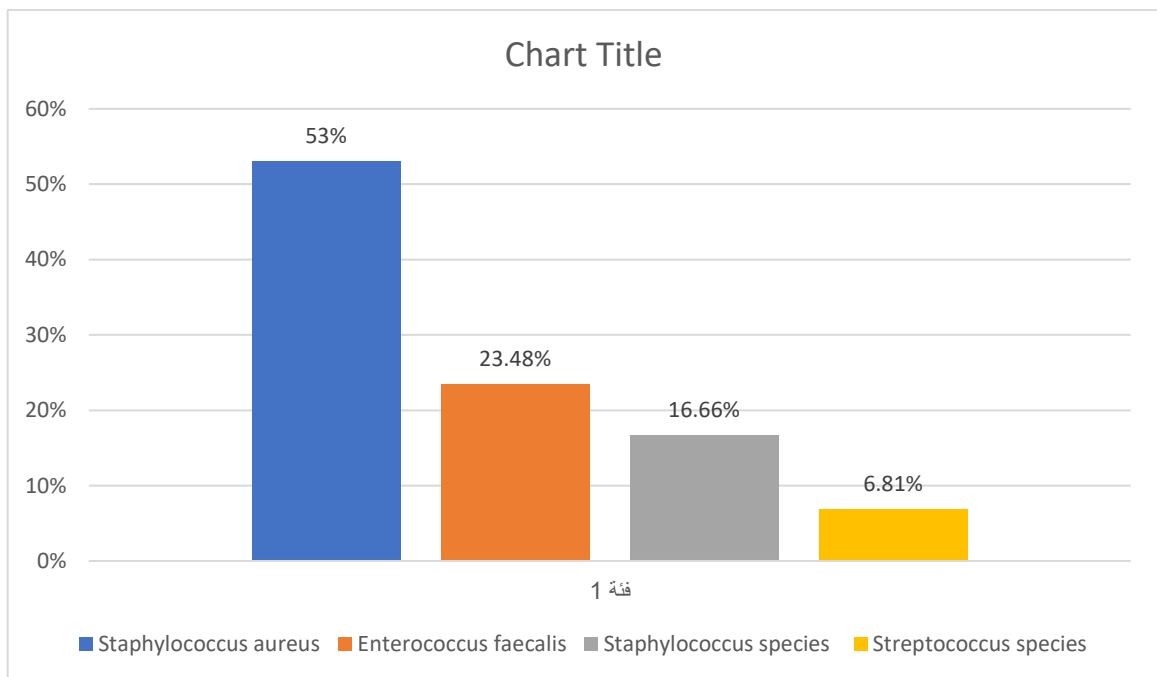


Figure 2- Percentage of Gram positive uropathogen isolated from diabetes patients

Table 2 displays the percentage (number) of common Gram-negative urine bacteria that are resistant (R) to antibiotics.

Overall, ampicillin (65%), piperacillin/tazobactam (47%), ceftioxin (49%) and ceftriaxone (35%) had the greatest rates of antibiotic resistance in Gram-negative urine pathogens, whereas imipenem (2%) and amikacin (18%) had the lowest rates. Conversely, Tetracycline (46%) and Oxacillin (49%) had the highest rates of antibiotic resistance, whereas Teicoplanin (6%) and Vancomycin (6%) had the lowest rates of resistance in Gram-positive urine bacteria. Furthermore, the rates of resistance of *E. Coli* and *S. aureus* to at least three antimicrobial drugs were 79% and 76%, respectively.

Table 2. The percent and numbers of common Gram-negative urine pathogens that are resistant (R) to antibiotics

Tested antibiotics	Overall (n= 212)	E.coli (n=152)	Klebsiella (n= 22)	Proteus (n=18)	Enterobacter (n= 8)	Pseudomonas (n= 4)
Ampicillin	129 (65)	101(66)	15 (70)	13(72)	-	-
Piperacillin/tazobactam	99 (47)	74 (49)	13 (59)	5 (28)	3 (38)	4 (100)
Ceftazidime	61 (29)	44 (29)	8 (36)	6 (33)	1 (13)	2 (50)
Cefoxitin	98 (49)	79 (52)	10(45)	9(50)	-	-
Ceftriaxone	72 (35)	57 (38)	8 (36)	5 (28)	2 (25)	-
Cefepime	62 (29)	49 (32)	6 (27)	4 (22)	1 (13)	2 (50)
Imepenem	4 (2)	3 (2)	1 (5)	0(0)	0(0)	0 (0)
Amikacin	38 (18)	29 (19)	5 (23)	2 (11)	0(0)	2 (50)
Gentamicin	40 (19)	30 (20)	6 (27)	2 (11)	0(0)	2 (50)
Ciprofloxacin	51 (24)	39 (26)	5 (23)	3 (17)	2(25)	2 (50)
Levofloxacin	49 (23)	36 (24)	6 (27)	3 (17)	2 (25)	2 (50)
Nitrofurantoin	45 (22)	30 (20)	6 (27)	6 (33)	3 (38)	-
Trimethoprim/Sulfamethoxazole	57 (27)	39 (26)	7 (32)	8 (44)	3 (38)	-

Data presented as number (percentage) ; - not tested (not included in the percentage calculations)

Table 3. The percent and numbers of common Gram-positive urine pathogens that are resistant (R) to antibiotics

Tested antibiotics	Overall (n= 132)	S. aureus (n=70)	E. faecalis (n=31)	Other staphylococci (n=22)	Streptococcus group B (n= 9)
Oxacillin	45 (49)	37 (34)	-	8 (36)	-
Gentamicin	11 (11)	9 (13)	-	2 (9)	0 (0)
Tobramycin	20 (20)	16(23)	-	4(18)	-
Levofloxacin	34 (26)	15(21)	12 (37)	4(18)	3(33)
Clindamycin	16 (16)	11(16)	-	3(13)	2 (22)
Teicoplanin	7 (6)	3 (4)	4 (13)	0 (0)	-
Vancomycin	7 (6)	3 (4)	4 (13)	0 (0)	-
Nitrofurantion	24 (20)	9 (13)	12 (37)	3(13)	-
Rifampicin	10 (11)	7 (10)	-	3(13)	-
Tetracycline	61(46)	30 (43)	16 (52)	11(50)	3(33)
Trimethoprim/sulfamethoxazole	45 (45)	31(44)	-	11(50)	3(33)

Data presented as number (percentage) ; - not tested (not included in the percentage calculations)

Discussion

Urinary tract infections (UTIs) are among the most common infections globally and should be treated seriously since they can lead to urosepsis, renal scarring, or progressive renal failure. "Antibiotics are used to treat UTIs", and the right use of empirical therapy with antimicrobial drugs has a significant role in the prognosis of the illness[17]. Geographic variations are observed in antimicrobial resistance [18, 19]. Therefore, it is essential to conduct studies like this on a regular basis to evaluate local patterns of antibiotic sensitivity to urine pathogens [20]. Therefore, the main goals of this study were to show the trends in antimicrobial resistance of the most prevalent uropathogens used in empirical treatment and to research for the etiology of UTIs. According to the

current study, women are more likely than men to get UTIs (69.8% vs. 29.2%). These findings concur with prior research indicating that women have UTIs much more frequently than males [8,1015]. Urinary tract infection (UTI) caused by bacteria that can alter the tissues of nearby structures in the urinary system. Because of their small, straight urethra and the close proximity of the urethra to the anus, females are more likely to get urinary tract infections (UTIs) due to the easy colonization of the pre-urethral area by enteric bacteria. Furthermore, after sexual activity, UTIs may occur as a result of bacteria unintentionally entering the urethra [16]. In the current investigation, 41% (n=274) of the samples had Gram positive bacteria and 59% (n=395) had Gram negative bacteria.

The current findings are consistent with those of Mahde et al. [32], who showed that 52.48% and 47.51%, respectively, of UTI patients had Gram-positive and Gram-negative bacteria. Hadi et al. (33) also noted that Gram-negative bacteria predominate in the Duhok governorate, where they are responsible for 81.3% of UTI cases, whereas Gram-positive bacteria are only responsible for 18.7% of cases in the Basra governorate. The current results were closely associated with (25) who reported that the most common microbe is *E. coli* (73.68%) and that the frequency of “Gram-negative isolates is higher than that of Gram-positive isolates. However, the results of this study contradict the findings of (26) who reported that 10% of UTI cases are caused by Gram-positive bacteria and 90% of cases are caused by Gram-negative bacteria. [24] also produced contrasting results, showing that the prevalence of staphylococci from UTIs is greater for *S. epidermidis* than for *S. aureus*, at 55.5% (10 out of 18) and 26.6% (8 out of 30), respectively. This variety might be attributed to regional variance, antibiotic overuse, which increases the virulence and invasiveness of bacterial isolates, and cultural” disparities in knowledge. As “shown in Table 4, the common isolated pathogens were *E. coli* which was the most common organism (42.2%), followed by *S. aureus* (28.33%), *E. faecalis* (12.5%) and *klebsiella* (7.2) Other bacterial pathogens were coagulase negative staphylococcus (5.8%), *proteus* (7.4%), Streptococcus group B(3.8%), *Enterobacter* (2.8%) and *pseudomonas* (07%)”. Similar comparable results were reported by Martin et al. [22], who explained that the most prevalent bacterial uropathogens were *S. aureus* (31.4%) and *E. coli* (41.9%). Moreover, the results of this investigation are consistent with those of Alhamdany [23], who noted that *E. coli* accounted for up to 55% of UTI cases and was the most common isolate. *E. Coli* is the most often identified etiological agent of urinary tract infections (UTIs), accounting for over 50% of urine isolates, according to the “Surveillance of Antimicrobial Resistance in Bulgaria [21]. *Klebsiella pneumoniae* and *Proteus* spp. come in second and third, respectively. These findings somewhat concurred with the findings of the current investigation on the dominance of *E. coli* as the primary cause of UTIs. A number of *E. coli* virulence factors, including endotoxins in all strains, adhesins (pili) and capsules found in some strains that were linked to UTIs”, and colonization factors, are responsible for the bacteria's domination. [23] The main causes of bacterial gene mutations and eventual antibiotic resistance include inappropriate use of antibiotics, overprescription of broad-spectrum antibiotics, and insufficient usage of antibiotics by patients. [34] . Antimicrobial agent resistance is seen as a major worldwide concern. The fact that the majority of UTIs are treated without bacteriological testing may be the cause of this. A better choice of antibiotics will be provided as empirical therapy for urinary tract infections (UTIs) if the patterns of antibiotic susceptibility of the causing organisms are understood.

In our investigation, 66% of the *E. Coli* isolates were ampicillin resistant. Comparing this to other research, which revealed an ampicillin resistance rate of 30% in Canada [35] and 49% in the UK [36], it is seen to be excessive. Our data also showed a significantly greater resistance to trimethoprim/sulfamethoxazole than those of other investigations, which found 11% in Canada and 16–18% in the US [35]. This variation may be explained by the fact that antibiotics are more easily obtained in our nation from pharmacies than they are in other nations due to lax regulations. Our discovery of heightened resistance to trimethoprim/sulfamethoxazole and ampicillin raises the possibility that these medications are no longer appropriate for empirical treatment of UT.

It's been demonstrated that fluoroquinolones are a viable empirical therapy for UTIs [37]. Considering that our study found that the resistance rates to ciprofloxacin and levofloxacin were

24% and 23%, respectively, this may make some sense in comparison to other antibiotics. But the growing usage of this class of antibiotics prompts worries about the likelihood of rising resistance patterns soon. Which suggested fluoroquinolones as a substitute medication for the previously advised first-line therapy in the treatment of uncomplicated UTIs [38]. Furthermore, this is consistent with the US Food and Drug Administration's most recent pronouncement. A warning that fluoroquinolones should not be used for regular respiratory tract infections or simple UTIs unless there is an appropriate alternative agent will be included to the product insert [39]. The current study demonstrate that strains of *E. Coli* that were isolated were determined to be the most sensitive to imipenem (2%). This antibiotic's high price and restricted availability in our area might account for its apparent lack of resistance.

This study's concerning conclusion was that G-uropathogens exhibited a significant level of drug resistance to cefoxitin (49%), ceftriaxone (35%), ceftazidime (29%), and piperacillin/tazobactam (47%). This research also found a significant proportion of resistance to trimethoprim/sulfamethoxazole (27%) and nitrofurantoin (22%) which is closely linked to the findings of Gupta et al (40). The widespread use of fluoroquinolone and third-generation cephalosporin medicines in UTI patients is most likely the cause of this resistance. Gentamicin and amikacin resistance levels are comparatively low (18% and 19%, respectively), which is a promising finding of this study. These findings were validated by Barlam et al. [43], who note When treating more severe or difficult UTIs or infections with few other treatment options, the aminoglycosides gentamicin and amikacin are among the best antibiotics to use parenterally or in combination. The causes of UTIs and the susceptibilities of these bacteria to antimicrobials are constantly changing, both within and across countries.[41,42]

Limitations

The study population was restricted to a single area. More illuminating information may be obtained by studying the processes by which bacteria acquire resistance in a broader cohort of people with varying medical problems from various geographic locations.

CONCLUSION:

E. coli and *S. aureus* dominated the etiological spectrum of UTIs in AL-Kut City, Iraq. There was a relatively low resistance rate to aminoglycosides among the Gram-negative uropathogens, but significant resistance rates to trimethoprim/sulfamethoxazole, ampicillin, and second and third-generation cephalosporins were detected. In the G+ group, Vancomycin, teicoplanin, and imipenem all maintained very excellent action and are suitable options for the antimicrobial therapy of complex urinary tract infections in the absence of other options.

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