

Prevalence and antibiogram of uropathogens among Jordanian patients with chronic kidney disease

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ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) poses a worldwide health issue that greatly heightens the risk of infections, especially urinary tract infections (UTIs), which are often caused by antibiotic-resistant pathogens. The purpose of this research was to examine the occurrence, and responsiveness of bacterial strains from UTI patients with chronic kidney disease in Jordan.

Materials and Methods: A cross-sectional study was carried out with 150 participants, comprising 100 individuals with CKD and 50 as control. Urine samples were collected, cultured, and bacterial isolates were examined through biochemical assessments, and tests for antimicrobial susceptibility.

Results: Among 107 bacterial isolates, a significant number (85%) were identified as Gram-negative, with the most common being *Escherichia coli* (30%) and *Klebsiella pneumoniae* (18.7%). Gram-positive bacteria made up 15% of the isolates, including *Enterococcus faecalis* and *Staphylococcus saprophyticus*. There was a notable resistance to norfloxacin (59.4%) and ciprofloxacin (56.1%), whereas colistin was the most effective, showing 94.5% susceptibility. Multidrug resistance (MDR) was widespread, particularly in *E. coli*, which had the highest MDR rate at 82.2%.

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Conclusion: The study emphasizes the predominance of Gram-negative bacteria, along with alarming rates of antibiotic resistance in CKD patients with UTIs. The findings of the study highlight the importance of customized antibiotic treatments and strong antimicrobial stewardship initiatives to effectively address UTIs in this vulnerable group.

Keywords: Antibiotic resistance; Chronic kidney disease; Gram-negative bacteria; Jordan; Multidrug resistance; Urinary tract infection

INTRODUCTION

Chronic kidney disease (CKD) is characterized by kidney damage or an Estimated Glomerular Filtration Rate (eGFR) below 60 mL/min/1.73 m² that lasts for at least three months, irrespective of the cause. CKD involves a gradual decline in kidney function, ultimately necessitating renal replacement therapies like dialysis or a kidney transplant. Kidney damage is identified through pathological abnormalities found via imaging tests or renal biopsies, irregularities in urine sediment, or elevated urinary albumin excretion rates (1). With over 10% of adults worldwide suffering from CKD, this condition is a major global health concern with significant regional variations in epidemiology. Chronic kidney diseases can lead to weakened immunity, anemia, poor nutrition, inflammation, vitamin deficiencies, and a diminished quality of life. Other comorbidities, such as diabetes mellitus and hypertension, are common in patients with CKD, which increases morbidity and financial burden. Additionally, individuals on long-term hemodialysis have weakened immune systems and are more vulnerable to infections including urinary tract infections (UTIs) (2).

UTIs are a leading cause of death for individuals with end-stage renal disease (ESKD) and are a major reason for hospital admissions among patients with CKD at all stages. The risk of infection increases as the disease progresses to more advanced stages (3). It is widely recognized that CKD elevates the risk of complex UTIs. Factors such as increased comorbidity, compromised immunity in CKD patients, and notably, the growing occurrence of UTIs due to antibiotic-resistant uropathogens, significantly influence the clinical progression and outcomes of UTIs in this specific group (1, 4). Additionally, UTIs are commonly observed in patients following kidney transplantation, particularly in kidney transplant recipients. However, there is a notable lack of studies examining the clinical features of UTIs in patients with CKD. Understanding the prevalent bacterial species and their resistance profiles is critical for

guiding empirical antibiotic therapy in this high-risk group of patients (5). Moreover, one of the most prevalent types of hospital-acquired and community-acquired bacterial infections are UTIs, which can present a variety of clinical manifestations ranging from asymptomatic bacteriuria or simple cystitis to potentially fatal forms of urosepsis.

UTIs are prevalent infections caused primarily by uropathogenic *Escherichia coli* (UPEC), which accounts for approximately 80% of UTIs. Less common pathogens include *Proteus mirabilis*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Enterobacter* spp., and Gram-positive bacteria such as *Streptococcus* spp. (6). In the United States, the annual prevalence of physician-diagnosed UTIs exceeds 10% in females and 3% in males, with more than 60% of females experiencing a UTI at some point in their lives. The individual risk of infection relies on several factors, including age, sexual activity, family history, medical comorbidities, and an individual's history of UTI (7). The fast increase of medication resistance among Gram-negative organisms, particularly UPEC, renders treatment of UTIs increasingly difficult (7). Additionally, according to the World Health Organization, antimicrobial resistance (AMR) is one of the top ten global health concerns and a significant and expanding public health issue worldwide. It is also a social and economic issue with an increasing impact. Numerous international and local public health action plans, initiatives, and guidelines recommend starting empirical treatment based on local patterns of antibiotic resistance, highlighting the significant importance of this work (8).

In a study from UK, it was observed that 38% of the public thought antibiotics are effective against most types of cough or colds and 43% did not know that antibiotics influence normal microbial flora (9). Some studies in Sweden and Malaysia, revealed that majority of participants were unaware of differences between viral and bacterial infections, and ignorantly used antibiotics against common cold (10, 11). Similarly, in the Arab world, around two thirds of the Jordanian community were found to believe

that antibiotics cure common cold and cough (12) whereas around half of the participants in a study from Kuwait had low knowledge on use of antibiotics and antibiotic resistance (13). In Jordan, community pharmacies are the most common pharmaceutical facilities and provide a wide range of prescription and nonprescription medicines, as well as cosmetics, skincare products, and medical equipment. Being easily accessible, many patients seek medical advice from pharmacists before visiting a physician (14), leading to higher dispense of non-prescription antibiotics, and thus its misuse among Jordanian public is very high (15).

Since little is known about patient's awareness and knowledge toward antibiotics use and resistance in different socio-economic areas in Jordan. Also, lesser studies from Middle East investigated and compared awareness, attitude and knowledge about antibiotics use and antibiotic resistance among the public residing in affluent and deprived areas. To address these gaps, the present study was aimed to investigate the prevalence and antibiotic sensitivity profile of bacteria responsible for causing urinary tract infections among patients with CKD in Jordan.

MATERIALS AND METHODS

Ethical considerations. This study was approved by Faculty of Graduate studies, Zarqa University. The research was conducted in compliance with the Helsinki Declaration's principles. Ethical approval was obtained from the Institutional Review Boards (IRB) of both Zarqa University (IRB/ZU/2025/51) and the Al-Bashir hospital IRB Committee (IRB/AL-BH/2025/10496) ensuring adherence to all necessary ethical standards.

Study design. This study used a descriptive cross-sectional design to determine the prevalence, antimicrobial sensitivity, treatment, and management of the bacterial profile causing UTIs among patients with CKD in Jordan.

Enrolled patients. A total of 100 urine samples were collected from allured patients aged (18 to 87 years) visiting the dialysis center at Al-Bashir Hospital, Amman. Moreover, 50 control samples were collected from participants who didn't have CKD or UTI infections. The required sample size was calcu-

lated using the formula for estimating proportions in cross-sectional studies:

$$n = \frac{z^2 \cdot p \cdot (1 - p)}{d^2}$$

Where:

n = required sample size

Z = Z statistic for 95% confidence level (1.96)

p = Estimated proportion (use 0.5 in absence of prior data)

d = margin of error (0.05)

Sample collection. Samples were collected from May 1, 2025, to the end of June 2025. A total of 100 samples were collected using sterile specimen containers labeled with each participant's name and ID. In addition, 50 samples were collected from the control group using sterile specimen containers similarly labeled with the participant's name and ID.

Demographic data. Two forms were filled out for each participant: the first was a specific questionnaire containing name, file number, gender, age, feeding, clinical history, laboratory tests, and current treatment with antibiotics. The second was the consent form.

Assessment criteria. The assessment criteria were established to ensure a systematic, objective, and transparent evaluation of the research components. These criteria outline the key elements used to assess the validity, relevance, and quality of the study, including methodological rigor, data integrity, and the significance of the findings. Each criterion is defined by specific indicators to guide the assessment process and maintain consistency across evaluations.

Inclusion and exclusion criteria. For the CKD patient group, participants were included if they had a confirmed diagnosis of CKD, presented with symptoms suggestive of urinary tract infection (UTI) such as painful urination, increased frequency or urgency of urination, and fever, and aged between 18 and 87 years. Participants were excluded if they had undergone renal transplantation, were receiving immunosuppressive therapy for other medical conditions, or had taken antibiotics within 48 hours prior to urine sample collection.

For the control group, individuals were included if they were between 18 and 87 years of age and had no

clinical history or current symptoms of CKD or UTI. Individuals were excluded if they had any diagnosed renal disease, recent or ongoing UTI, antibiotic use within the previous two weeks, or any chronic medical condition that could potentially affect urinary microbiota composition or renal function.

Antimicrobial susceptibility discs. Antimicrobial susceptibility profile of the GNB and GPB was performed using a panel of antibiotic discs (MAST Group Lt, UK), including piperacillin–tazobactam (PTZ/TZP) (150-300 µg/mL), ceftriaxone (CRO) (80-160 µg/mL), amikacin (AMK) (20-30 µg/mL), gentamicin (GEN) (5-10 µg/mL), ciprofloxacin (CIP) (2-4 µg/mL), norfloxacin (NOR) (1-2 µg/mL), colistin (CST/COL) (2-3 µg/mL), vancomycin (VAN) (20-40 µg/mL), linezolid (LZD) (15-25 µg/mL), trimethoprim–sulfamethoxazole (SXT/TMP-SMX) (1-2 µg/mL-40-60 µg/mL), amoxicillin (AMX) (>100 µg/mL), ampicillin (AMP) (>100 µg/mL), and nitrofurantoin (NIT) (>100 µg/mL). The susceptibility of the bacterial isolates to these antibiotics was determined and interpreted according to the relevant clinical laboratory standards. Bacterial isolates were standardized to a 0.5 McFarland turbidity and inoculated evenly onto Mueller–Hinton agar. Antibiotic-impregnated discs were placed on the surface, and the plates were incubated at 35-37°C for 16-18 h. After incubation, the zones of inhibition around the discs were measured and interpreted using CLSI (2023) guidelines to classify bacteria as Susceptible, Intermediate, or Resistant (16).

Culture media. All media including Cysteine-Lactose-Electrolyte-Deficient (CLED) agar, MacConkey agar, Mueller Hinton agar and blood agar were procured from Guangdong Huankai Biology Sci. & Tech. Co., Ltd, China and prepared in accordance with the manufacturer's instructions. For blood agar preparation, 5% sheep blood was added.

Sample processing. Clean-catch midstream urine specimens were collected from the participants using leak-proof sterile plastic containers to ensure sample integrity. Using spread plate technique, the urine samples were inoculated onto CLED agar (HI Media, India), MacConkey agar and blood agar using a calibrated wire loop (0.001 mL). The inoculated media was incubated at 37°C for 18-24 hours, after which colony counts was performed. A bacterial growth of

$\geq 10^5$ colony-forming units (CFU)/mL was considered indicative of significant bacteriuria. Bacterial identification was carried out using a combination of colony morphology, Gram staining, and standard biochemical tests, following established microbiological protocols. The plates were checked for bacterial growth after 24, 48, and 72 hours, then biochemical tests were performed on samples.

Biochemical tests. Various biochemical assays were employed to differentiate between Gram-negative and Gram-positive bacteria like Indole Test, Catalase Test, Oxidase Test, Bile Esculin Test, Triple Sugar Iron (TSI) Test, and Mannitol Salt Agar (MSA) Test, as described in Bergey's manual (17) and as briefly mentioned in Table 1.

Antimicrobial susceptibility testing using disc diffusion method. Antimicrobial susceptibility testing was conducted using the disc diffusion method in accordance with the guidelines of the Clinical Laboratory and Standards Institute (CLSI, 2023) (16). For large lipopeptide molecules like colistin, we, FMDR, performed the Colistin Broth Disk Elution (CBDE) method as approved and described by the CLSI M100 (33rd Edition, 2023) guidelines. Commercially prepared colistin disks were eluted in cation-adjusted Mueller-Hinton broth to determine minimum inhibitory concentrations (MICs).

In brief, several fresh colonies of Gram-negative and Gram-positive aerobic bacteria were obtained following a 48-hour incubation period and subsequently inoculated into 2 ml of Mueller-Hinton broth, adjusting the turbidity to match the 0.5 McFarland standard. Cotton swabs were employed to evenly distribute the bacterial cells in three dimensions on Mueller-Hinton agar plates, after which antibiotic discs were placed on the surface. The plates were then incubated at 37°C for 48 hours. The zones of inhibition surrounding the antibiotic discs were measured using a millimetric ruler, and the results were interpreted based on the guidelines recommended by CLSI (2023) (16).

Statistical analysis. Analysis of the data was done with SPSS version 25. The presentation of qualitative data, including UTI, will take the shape of frequency and percentage. Quantitative data, including age, will be expressed as mean $\pm$ standard deviation (SD). To determine whether the diagnosis of high-prev-

Table 1. Biochemical characteristics for *E. coli*, *K. pneumoniae*, *S. saprophyticus*, *E. faecalis*, *P. mirabilis* and *P. aeruginosa*.

Bacteria	Catalase	Oxidase	Bile Esculin	TSI (Slant/Butt, H ₂ S, Gas)	Indole	MSA Growth & Fermentation
<i>E. coli</i>	Positive	Negative	Negative	A/A, Gas+, H ₂ S-	Positive	No growth/No fermentation
<i>K. pneumoniae</i>	Positive	Negative	Negative	A/A, Gas+, H ₂ S-	Negative	No growth/No fermentation
<i>S. saprophyticus</i>	Positive	Negative	Variable	K/A, H ₂ S±	Negative	Growth/ Fermentation (yellow)
<i>E. faecalis</i>	Negative	Negative	Positive	K/A, H ₂ S-	Negative	Growth/Weak or no fermentation
<i>P. mirabilis</i>	Positive	Variable	Positive	K/A, Gas+, H ₂ S+	Positive	No growth/No fermentation
<i>P. aeruginosa</i>	Positive	Positive	Negative	K/K or NC, H ₂ S-, Gas-	Negative	No growth/No fermentation

alence bacteria is associated with other categorical characteristics, a chi-square test will be utilized. A P-values of less than 0.05 was considered statistically significant.

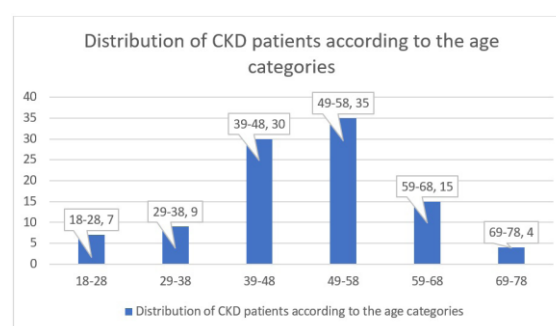
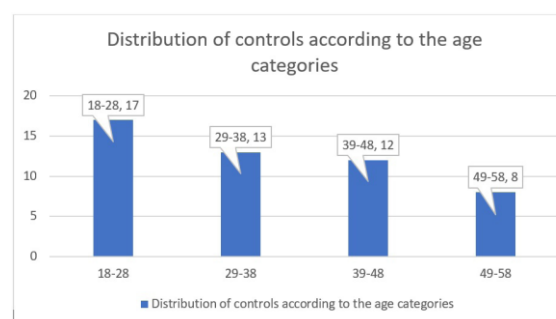
RESULTS

Sociodemographic data. Data from a total of 150 participants were analyzed, comprising 100 patients with CKD and 50 control participants. The mean age of CKD patients was 48.80 years, with a standard deviation of 11.51. In contrast, the control group had a mean age of 58.00 years and a standard deviation of 11.19. A greater proportion of CKD patients were aged between 49 and 58 years (n = 35, 35%) compared to the control group (n = 8, 16%). Conversely, a higher proportion of participants aged between 18 and 28 years was observed in the control group (n = 17, 34%) than among CKD patients (n = 7, 7%). Regarding gender distribution, males were more prevalent in both groups, with 55 (55%) males among CKD patients and 29 (58%) males in the control group. Females constituted 45 (45%) and 21 (42%) of the CKD and control groups, respectively. Detailed sociodemographic data are provided in Table 2 and Figs. 1 and 2.

Classified isolated bacteria according to Gram stain. In this study, Gram staining was conducted on all collected bacterial isolates to categorize them as either Gram-positive or Gram-negative. Among the 107 bacterial isolates, 16 isolates (15%) were identified as Gram-positive, whereas 91 isolates (85%) were classified as Gram-negative. This distribution suggests a higher prevalence of Gram-negative bacteria in the tested samples. The differentiation achieved through Gram staining was instrumental in directing subsequent microbiological analyses and antibiotic

Table 2. Sociodemographic features of CKD patient and control groups

Variables	Control	CKD Patients
Age		
Mean	58.00	48.80
49-58, n (%)	8 (16)	35 (35)
18-28, n (%)	17 (34)	7 (7)
Sex, n (%)		
Male	29 (58)	55 (55)
Female	21 (42)	45 (45)
Total	50 (100)	100 (100)


Fig. 1. Distribution of CKD patients according to the age categories.

Fig. 2. Distribution of controls according to the age categories.

susceptibility testing, given that Gram-negative bacteria are frequently associated with elevated levels of antimicrobial resistance and more severe clinical outcomes. There was significant difference in the distribution of Gram-negative versus Gram-positive bacteria among the isolates, with the predominance of Gram-negative bacteria being statistically significant ($P < 0.0001$).

Biochemical results for *E. coli*, *K. pneumoniae*, *S. saprophyticus*, *E. faecalis*, *P. mirabilis* and *P. aeruginosa*. This analysis presents the biochemical profiling results for six clinically significant bacterial species: *E. coli*, *K. pneumoniae*, *S. saprophyticus*, *E. faecalis*, *P. mirabilis*, and *P. aeruginosa*. The biochemical tests revealed distinct metabolic patterns that serve as reliable biomarkers for species identification. *E. coli* and *K. pneumoniae* demonstrated characteristic lactose fermentation capabilities, with *E. coli* showing positive indole test results and *K. pneumoniae* exhibiting urease activity. The Gram-positive cocci *S. saprophyticus* and *E. faecalis* were differentiated by their coagulase and bile-sculin hydrolysis patterns, respectively. *P. mirabilis* displayed strong urease production and swarming motility, while *P. aeruginosa* was identified by its oxidative metabolism and positive cytochrome oxidase reaction as shown in Table 2.

These biochemical profiles provide a robust framework for microbial identification in clinical laboratories. The clear differentiation between species based on metabolic characteristics has important implications for accurate diagnosis and appropriate antimicrobial therapy selection. The results align with established microbiological standards, confirming the reliability of conventional biochemical methods for bacterial identification despite the increasing availability of molecular techniques.

Classification of isolated bacteria. This analysis examined the relationship between bacterial species and growth outcomes across 150 clinical samples. The cross-tabulation revealed a perfect correspondence between specific bacterial species and their growth characteristics, with each species exclusively appearing in one growth category: *E. coli* and *K. pneumoniae* were exclusively Gram-negative (45 and 28 cases respectively), *S. saprophyticus* and *E. faecalis* were exclusively Gram-positive (6 and 10 cases respectively), while *P. mirabilis* and *P. aeruginosa*

showed only Gram-negative results (13 and 5 cases respectively). The chi-square test yielded a highly significant result ($P < 0.001$), indicating an extremely strong association between bacterial species and their growth characteristics were expressed in Fig. 3. These findings reflect the dominance of Gram-negative bacteria, particularly members of the Enterobacteriaceae family, as the primary causative agents in the studied infections. Accurate classification of bacterial types was essential for evaluating infection patterns and guiding appropriate antimicrobial therapy.

The correlation between patients CKD and controls group. The statistical analysis involved 150 valid cases, with no missing data, divided between two groups: patients and controls. A chi-square test was performed to assess the association between these groups and the studied categorical variable. The analysis revealed a highly significant relationship ($P < 0.001$), indicating a strong statistical difference between patients and controls as shown in Fig. 4.

The correlation between sex and age. The result was conducted on 100 valid cases to evaluate the association between sex and age using chi-square testing. These results suggest that the distribution of the sex and age is not significantly different across the groups studied as shown in Fig. 5, $P = 0.588$.

The association between sex and bacterial growth outcomes categorized as no growth, Gram-negative, and Gram-positive. A cross-tabulation and Pearson's chi-square test were conducted to determine whether sex influences bacterial growth patterns. The results showed no statistically significant association between gender and bacterial growth outcomes ($P = 0.855$). Males and females exhibited similar distributions across all growth categories, with "Gram negative" being the most frequent outcome for both groups (51 cases in males, 40 in females) as shown in Fig. 6. These findings suggest that gender does not play a significant role in determining bacterial growth outcomes in this study.

Correlation between sex and the type of bacterial infection. The cross-tabulation table displays the frequency counts of infections for each sex. For example, among males, *E. coli* and *K. pneumoniae* were the most common infections (25 and 15 cases respectively), while among females, *E. coli* (20 cas-

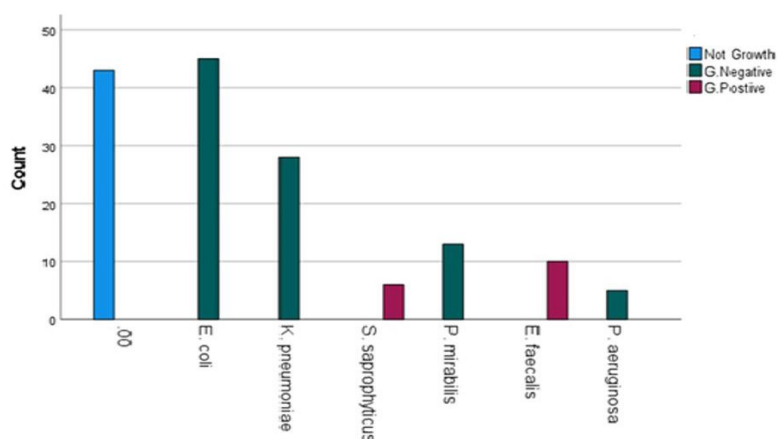


Fig. 3. Distribution of bacterial type Among 150 patients.

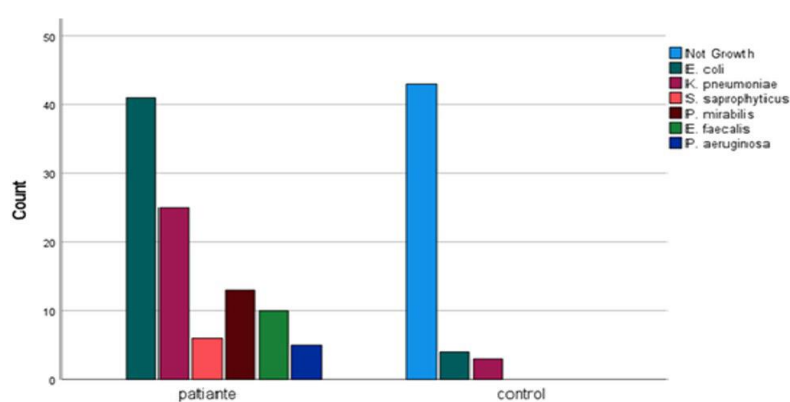


Fig. 4. Distribution of bacterial type according to patients CKD and controls group.

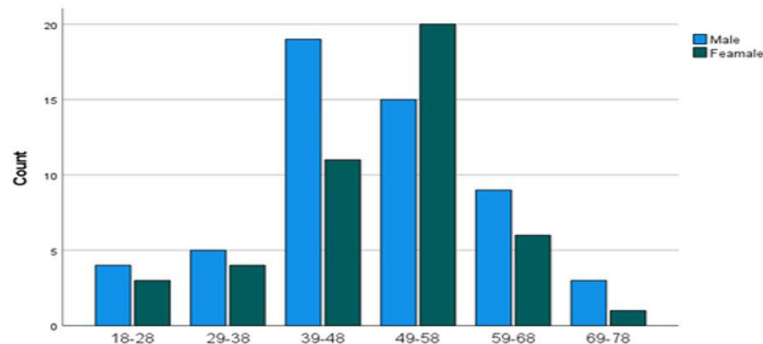


Fig. 5. Distribution of sex and age according to patients CKD and controls group.

es) and *K. pneumoniae* (13 cases) were also the most prevalent. The total sample size was 150 cases, with 84 males and 66 females.

The chi-square test results indicate that there is no statistically significant association between gender and the type of bacterial infection. This suggests that the distribution of bacterial infections does not

significantly differ between males and females in this sample was expressed in Fig. 7, $P = 0.948$.

Association between age and the distribution of bacterial infections. The results revealed a significant association between age and infection distribution ($P < 0.001$), with middle-aged groups (39-58

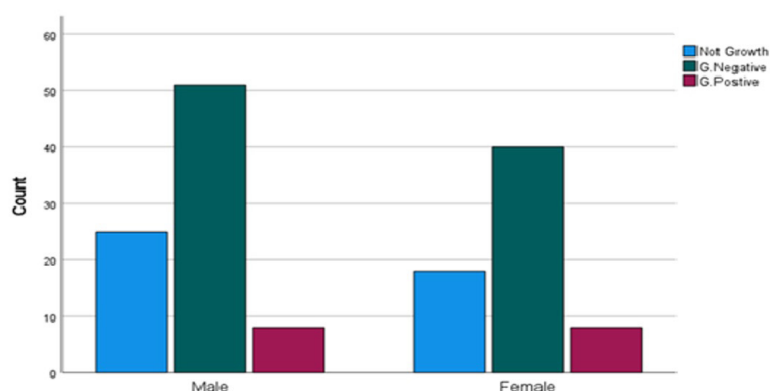


Fig. 6. Distribution of sex and bacterial growth outcomes categorized as No Growth, G. Negative, and G. Positive according to patients CKD and controls group.

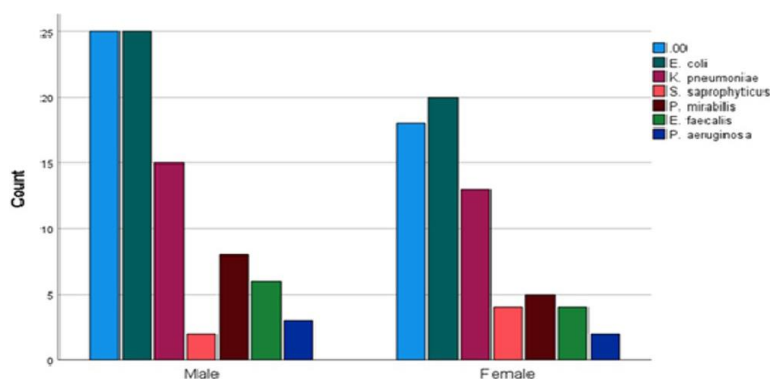


Fig. 7. Distribution of sex and the type of bacterial infection according to patients CKD and controls group.

years) showing the highest infection rates. *E. coli* and *K. pneumoniae* were the most prevalent across all age groups as shown in Fig. 8. These results suggest that age may be an important factor in bacterial infection epidemiology.

Antibiotic susceptibility and resistance profiles of *E. coli* isolates. Among 45 *E. coli* isolates, colistin (97.7%, $P < 0.001$), amikacin (86.6%, $P < 0.001$), and piperacillin/tazobactam (75.5%, $P=0.002$) showed high and statistically significant susceptibility rates. Gentamicin had moderate susceptibility (68.8%, $P=0.021$). Ceftriaxone (40%, $P=0.263$), ciprofloxacin (46.6%, $P=0.764$), and norfloxacin (42.2%, $P=0.423$) showed lower susceptibility with no significant differences as shown in Table 3.

Antibiotic susceptibility and resistance profiles of *K. pneumoniae* isolates. Among twenty-eight *K. pneumoniae* isolates, colistin (92.8%, $P < 0.001$) and amikacin (82.1%, $P = 0.001$) showed high and

statistically significant susceptibility. Piperacillin/tazobactam (60.7%, $P=0.332$) and gentamicin (64.2%, $P=0.157$) had moderate susceptibility. Lower susceptibility was seen with ceftriaxone (35.7%, $P=0.108$), ciprofloxacin (39.2%, $P=0.210$), and norfloxacin (32.1%, $P=0.049$), with norfloxacin showing borderline significance are expressed in Table 3.

Antibiotic susceptibility and resistance profiles of *P. aeruginosa* isolates. Among five *P. aeruginosa* isolates, amikacin demonstrated complete susceptibility ($P=0.031$). Piperacillin/tazobactam and colistin exhibited 80% susceptibility ($P=0.375$). Gentamicin, ciprofloxacin, and norfloxacin displayed susceptibility rates ranging from 40% to 60% ($P=1.000$). Ceftriaxone exhibited the highest resistance, with an 80% resistance rate, as shown in Table 3.

Antibiotic susceptibility and resistance profiles of *P. mirabilis* isolates. In the analysis of 13 *P. mirabilis* isolates, amikacin and colistin demonstrat-

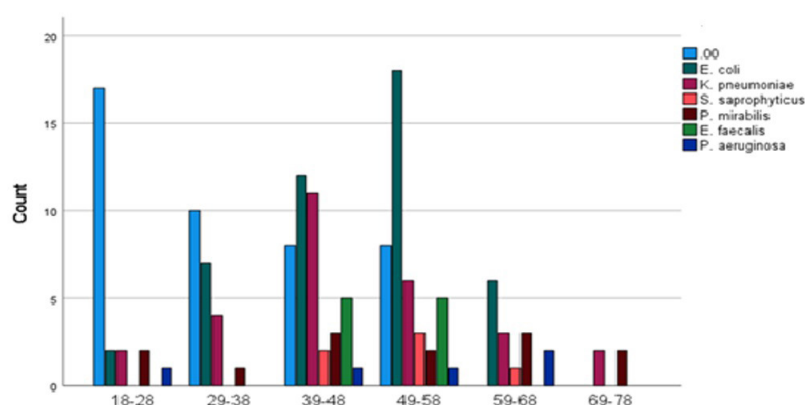


Fig. 8. Distribution of age and the type of bacterial infection according to patients CKD and controls group.

Table 3. Antibiotic susceptibility and resistance patterns of bacterial isolates

Gram-negative		PTZ	CRO	AMK	GEN	CIP	NOR	CST
<i>E. coli</i> N=45	Sustainability	34	18	39	31	21	19	44
	Percentage %	75.5	40	86.6	68.8	46.6	42.2	97.7
	Resistance	11	27	6	14	24	26	1
	Percentage %	24.5	60	13.4	31.2	53.4	57.8	2.3
	P-value	0.002	0.263	<0.001	0.021	0.764	0.423	<0.001
<i>K. pneumoniae</i> N=28	Sustainability	17	10	23	18	11	9	26
	Percentage %	60.7	35.7	82.1	64.2	39.2	32.1	92.8
	Resistance	11	18	5	10	17	19	2
	Percentage %	39.3	64.3	17.9	35.8	60.8	67.9	7.2
	P-value	0.332	0.108	0.001	0.157	0.210	0.049	<0.001
<i>P. aeruginosa</i> N=5	Sustainability	4	1	5	3	2	2	4
	Percentage %	80	20	100	60	40	40	80
	Resistance	1	4	0	2	3	3	1
	Percentage %	20	80	0	40	60	60	20
	P-value	0.375	0.375	0.031	1.000	1.000	1.000	0.375
<i>P. mirabilis</i> N=13	Sustainability	11	8	12	11	6	7	12
	Percentage %	84.6	61.5	92.3	84.6	46.1	53.9	92.3
	Resistance	2	5	1	2	7	6	1
	Percentage %	15.4	38.5	7.7	15.4	53.9	46.1	7.7
	P-value	0.022	0.581	0.006	0.022	1.000	1.000	0.006
Gram-positive		VAN	LZD	TMP-SMX	AMX	AMP	NIT	
<i>S. saprophyticus</i> N=6	Sustainability	6	6	4	3	2	5	
	Percentage %	100	100	66.6	50	33.4	83.3	
	Resistance	0	0	2	3	4	1	
	Percentage %	0	0	33.4	50	66.6	16.7	
	P-value	0.016	0.016	0.688	1.000	0.688	0.219	
<i>E. faecalis</i> N=10	Sustainability	9	10	3	8	9	8	
	Percentage %	90	100	30	80	90	80	
	Resistance	1	0	7	2	1	2	
	Percentage %	10	0	70	20	10	20	
	P-value	0.021	0.002	0.344	0.109	0.021	0.109	

ed the greatest susceptibility, with a rate of 92.3% ($P=0.006$). Piperacillin/tazobactam and gentamicin also exhibited high susceptibility, each at 84.6% ($P=0.022$). Ceftriaxone was found to have a moderate susceptibility rate of 61.5% ($P=0.581$), whereas ciprofloxacin and norfloxacin showed lower susceptibility rates of 46.1% and 53.9%, respectively ($P=1.000$) (Table 3).

Antibiotic susceptibility patterns of *S. saprophyticus* isolates. In case of six *S. saprophyticus* isolates, both vancomycin and linezolid demonstrated complete susceptibility, with a P-value of 0.016. Nitrofurantoin exhibited a high susceptibility rate of 83.3% ($P=0.219$). In contrast, trimethoprim, amoxicillin, and ampicillin had lower susceptibility rates of 66.6%, 50%, and 33.4%, respectively, with no significant differences observed, as detailed in Table 3.

Antibiotic susceptibility profiles of *E. faecalis* isolates. In the study of 10 *E. faecalis* isolates, linezolid demonstrated complete susceptibility at 100% ($P=0.002$). Both vancomycin and ampicillin exhibited 90% susceptibility ($P=0.021$). Amoxicillin and nitrofurantoin each had an 80% susceptibility rate ($P=0.109$), whereas trimethoprim showed the lowest susceptibility, with only 30% ($P=0.344$) (Table 3).

Prevalence of multidrug resistance among bacterial isolates. This section examines the prevalence of MDR among various bacterial species isolated during the study. MDR is resistance to multiple antibiotic classes and represents a significant challenge for clinical management and public health. MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories by Magiorakos et al. (18). Among the test isolates, *E. coli* exhibited the highest MDR rate at 82.2%, with resistance mainly to CRO, CIP, and NOR, approaching statistical significance ($P=0.066$). *K. pneumoniae* and *P. mirabilis* showed MDR rates of 71.4% and 69.2%, respectively, with similar resistance patterns involving CRO, CIP, and NOR. *P. aeruginosa* demonstrated a 60% MDR rate, characterized by strong resistance to these antibiotics, though without statistical significance ($P=1.000$). In contrast, *S. saprophyticus* showed a lower MDR prevalence of 33.3%, with resistance primarily to AMP, AMX, and TMP. *E. faecalis* had the lowest MDR rate at 10%,

with resistance related to TMP, AMP, and VAN, nearing significance ($P=0.070$) (Table 4).

DISCUSSION

CKD is recognized as a significant global public health challenge, particularly in low- and middle-income countries. Kidney failure is associated with several risk factors, including glomerulonephritis, urolithiasis, diabetes mellitus, hypertension, and polycystic kidney disease (1, 3). Like individuals with acquired immune deficiencies, those with CKD and renal failure may exhibit increased susceptibility to infections (3). Furthermore, metabolic abnormalities leading to secondary immunological alterations affecting various immune components render chronic renal failure a risk factor for urinary tract infections (UTIs) (2). Although evidence on this topic is limited, some studies suggest that the prevalence of UTIs in CKD patients may be comparable to that in the general population (19). In contrast a study identified notably high prevalence of UTI-causing bacteria among individuals with chronic kidney disease, at 15.8% (20). In this study, the prevalence of bacterial growth was high in males (84%) compared with females (66%). In contrast to our findings, several previous studies documented high prevalence of UTI in females compared with males (21). This could be attributed to the reason that pathogen has to travel a shorter distance to the bladder since the females' urethral tubes are shorter. Numerous other studies have reported varying rates of UTIs in CKD patients (1, 2, 4).

The age distribution of UTI prevalence observed in this study aligns with global trends but highlights unique patterns in CKD populations. Our findings revealed that middle-aged CKD patients (49-58 years) had the highest UTI incidence (35%), contrasting with the Nepalese study (22), where young adults (21-30 years; 28.8%) were the most affected. This divergence likely reflects the cumulative impact of CKD-related immunosuppression and comorbidities (e.g., diabetes, hypertension) in older adults, which elevate UTI risk (23).

The analysis of the distribution and antibiotic resistance patterns of uropathogens within our CKD cohort has revealed significant disparities between Gram-negative (85%) and Gram-positive (15%) bacteria, which carry important clinical implications.

Table 4. Prevalence of multidrug-resistant (MDR) isolates among different bacterial species.

Bacteria	Number of Isolates that negative for MDR s	Number of MDR Isolates	MDR Percentage (%)	P-value
<i>E. coli</i>	8	37	82.2 %	0.066
<i>K.pneumoniae</i>	8	20	71.4 %	0.289
<i>P. aeruginosa</i>	2	3	60 %	1.000
<i>P. mirabilis</i>	4	9	69.2 %	0.362
<i>S. saprophyticus</i>	4	2	33.3 %	0.637
<i>E. faecalis</i>	9	1	10 %	0.070
Total	35	72	76.3 %	

Gram-negative pathogens, notably *E. coli* (30%) and *K. pneumoniae* (18.7%), were predominant among the isolates, exhibiting alarmingly high resistance rates to fluoroquinolones (ciprofloxacin: 56.1%) and cephalosporins (ceftriaxone: 49.4%). This resistance is likely attributable to frequent antibiotic exposure and ESBL production in this vulnerable population. These findings surpass the resistance rates reported in general UTI studies from Nepal (22) and are consistent with global trends indicating increasing Gram-negative resistance in CKD patients (6). Notably, *P. aeruginosa* (4.6%) and *P. mirabilis* (8.7%) exhibited concerning resistance profiles, particularly in catheter-associated infections. In contrast, Gram-positive isolates, primarily *E. faecalis* (10%) and *S. saprophyticus* (6%), demonstrated distinct resistance mechanisms, including emerging vancomycin resistance (6.3%) in *E. faecalis*, which contrasts with the staphylococcal predominance observed in non-CKD populations (22).

The high efficacy of linezolid (100%) against Gram-positive isolates provides a valuable treatment option, while colistin (94.5% sensitivity) remains crucial for MDR Gram-negative infections. These findings underscore the need for CKD-specific antimicrobial guidelines that account for the unique resistance patterns in this population, emphasizing culture-guided therapy and infection prevention strategies to combat the growing threat of antimicrobial resistance in CKD-related UTIs (24). The distinct microbiological profile of UTIs in CKD patients highlights the importance of regular local surveillance to inform empirical treatment choices and stewardship programs in nephrology practice.

E. coli was the most common bacterial uropathogen reported in this study. This result is consistent with earlier research conducted in Nepal that shows 50-80% of isolates were *E. coli* (25). *P. aeruginosa*

and *S. saprophyticus* were the lowest isolated uropathogens. The findings of this study highlight a high prevalence of Gram-negative bacteria (85%), particularly *E. coli* (30%) and *K. pneumoniae* (18.7%), as the leading causes of UTIs in CKD patients in Jordan. This aligns with global trend where *E. coli* remains the predominant uropathogen in both general population and CKD patients (20). However, the alarming resistance rates to fluoroquinolones (ciprofloxacin: 56.1%, norfloxacin: 59.4%) exceed those reported in similar studies from Nepal (20) and India (2).

The MDR rate of 82.2% in *E. coli* isolates is higher than compared to earlier studies (26). A study by Alghoribi et al. (27) reported 78% MDR rate in *E. coli* isolates from urinary tract infections (UTIs), with notable resistance to ceftriaxone (72%) and ciprofloxacin (65%). Similarly, our findings in Al Jubayhah indicated high resistance rates to these antibiotics, suggesting a regional pattern of antimicrobial resistance. Notably, colistin remained highly effective (94.5% sensitivity). It is speculated that the Jordanian community generally has poor knowledge and awareness toward antibiotics use and antibiotic resistance that is also affected by socio-economic factors (28). In Egypt, a study by Enany et al. (29) found that 85% MDR in *K. pneumoniae* isolates were from intensive care unit (ICU) patients, with resistance to third-generation cephalosporins exceeding 70%. Our study observed comparable resistance levels in ICU settings, highlighting the critical need for stringent infection control measures (30).

Limited data exist on UTI pathogens in Jordanian CKD patients, a study from Al-Karak Governmental Hospital found comparable resistance patterns in general UTIs, with *E. coli* showing 62% resistance to ciprofloxacin (31). This study confirms these trends but extends them to a CKD-specific population, where immunosuppression and frequent hospital vis-

its likely exacerbate resistance. High UTI antibiotic resistance in Jordan is driven by widespread over-the-counter dispensing of antibiotics without prescriptions, high patient self-medication due to long clinic wait time, and low public awareness regarding proper antibiotic use (28).

The high prevalence of MDR uropathogens in our CKD cohort (67.3% of isolates) represents a significant therapeutic challenge, with resistance rates substantially higher than those reported in non-CKD populations. The findings demonstrate particularly alarming MDR rates in Gram-negative pathogens, with *E. coli* and *K. pneumoniae* showing resistance to multiple antibiotic classes, including fluoroquinolones and third-generation cephalosporins. The elevated MDR rates likely reflect several CKD-specific factors, including frequent antibiotic exposure due to recurrent infections, prolonged hospitalization, and immune dysfunction associated with uremia (32). Lack of adherence to recent antibiotic prescription guidelines leads to antibiotic resistance which causes treatment failure and the development of disease complications in patients with urinary tract infection (UTI). A study by Jarab et al. (33), at Jordanian hospital, aimed to evaluate patterns and appropriateness of antibiotic selection among hospitalized patients with UTI. They found that the choice of antibiotics was inappropriate in 32.43% of the studied cases. The most common inappropriate antibiotic choice was prescribing IV ceftriaxone and IV imipenem/cilastatin in cases with uncomplicated pyelonephritis and complicated cystitis and prostatitis. Lack of adherence to antibiotic selection guidelines sheds light on the necessity to improve antibiotics prescription practice and avoid the inappropriate antibiotic selection and hence antibiotic resistance among patients with UTI. In this scenario, our study provides useful insights on prevalence and antibiogram of uropathogens in CKD patients that could be exploited in managing antibiotic resistance in Jordanian hospitals.

Notably, Gram-positive isolates, while less prevalent, demonstrated concerning resistance patterns, including emerging vancomycin resistance in *E. faecalis*. These findings emphasize the critical need for CKD-specific antimicrobial stewardship programs that incorporate regular local resistance surveillance, restrict high-resistance empirical therapies, and promote targeted antibiotic use based on culture results (24). The high efficacy of amikacin and colistin against MDR Gram-negative isolates suggests

these agents should be reserved for complicated cases, while linezolid remains a valuable option for Gram-positive infections. It is recommended to carry out ongoing surveillance to guide empiric therapy and promote appropriate antibiotic use. Tailoring treatment based on patient-specific factors is essential to effectively managing antimicrobial resistance and improving clinical outcomes (33, 34). The high rate of urinary tract infection (UTI) antibiotic resistance in Jordanian hospitals could be rise in Extended-Spectrum Beta-Lactamases (ESBL) producing bacteria. These enzymes biologically degrade and neutralize common broad-spectrum antibiotics, like third-generation cephalosporins (34). In a study from Jordan conducted genetic mapping of uropathogens showed that nearly 98% of ESBL-producing *E. coli* isolates in Jordan carry the *bla*_{CTX-M} gene, with a majority also carrying the *bla*_{OXA} gene. These genes are highly efficient at disabling penicillin and cephalosporin-class drugs (35).

Important clinical variables that may influence the prevalence of urinary tract infections and antimicrobial resistance include CKD stage, duration of dialysis, catheter use, diabetes mellitus, and prior antibiotic exposure. Recently, in a study conducted by Scherberich et al. (36), showed lower estimated glomerular filtration rate (eGFR) and advanced CKD stages impair local urothelial immunity, reduce uropathogen clearance, and create a pro-inflammatory state that elevates UTI prevalence. Renal impairment correlates with higher rates of resistant gram-negative isolates, such as *Escherichia coli* and *Pseudomonas aeruginosa*, which display high rates of beta-lactam resistance. A study by Birlutiu and Birlutiu (37) emphasized the urgent necessity for heightened surveillance of local antimicrobial resistance patterns and underscore the profound vulnerability of hemodialysis patients to severe infectious outcomes. Longer dialysis vintage increases cumulative healthcare exposure, raising the likelihood of acquiring resistant bacterial strains during vascular or peritoneal access. It has been found that indwelling urinary catheters or central venous lines introduce foreign surfaces that promote microbial biofilm formation. Biofilms shield bacteria from host defenses and systemic antibiotics, accelerating the horizontal transfer of antimicrobial resistance genes and predisposing patients to recurrent MDR infections (38). Diabetic nephropathy and chronic hyperglycemia impair neutrophil function, lower leukocyte response, and supply urinary glu-

cose that encourages bacterial proliferation. Diabetes is an established independent predictor for both frequent symptomatic UTIs and rapid progression to severe complications like urosepsis (39). Moreover, it has been observed that recent or repeated courses of broad-spectrum antimicrobials disrupt protective commensal flora and exert selective pressure. This process eradicates susceptible organisms and enriches reservoirs of resistant pathogens, strongly predicting extended-spectrum beta-lactamase (ESBL) production and multidrug resistance (20, 38).

Implementation of enhanced infection control measures, including screening for ESBL carriage in dialysis patients and improved catheter care protocols, may help mitigate the spread of MDR organisms in this vulnerable population (5). Public awareness of the causes and consequences of antibiotic resistance is crucial to mitigate the inappropriate use of antibiotics, particularly in the low- and middle-income countries. There are lesser studies that assessed the awareness, attitude, and knowledge about antibiotic use and antibiotic resistance among the Jordanian public in affluent and deprived areas (28). The findings of our study underscore the urgent need for multidisciplinary approaches to address the growing threat of antimicrobial resistance in CKD-associated UTIs. Forthcoming UTI treatment and prevention strategies could employ novel bactericidal compounds, combinations of new and classic antimicrobials that enhance bacterial killing, medications that prevent bacterial attachment to uroepithelial cells, repurposing drugs, and vaccines to curtail the rising rates of antibiotic resistance in uropathogenic bacteria and improve outcomes in people with UTI (40).

CONCLUSION

Future UTI management practices could be driven by the evolution of antimicrobial stewardship, improved and readily available diagnostics, and an improved understanding of how the microbiome affects UTI. The study emphasizes the predominance of Gram-negative bacteria and the concerning rates of antibiotic resistance among CKD patients with UTIs. These findings highlight the necessity for customized antibiotic therapy and comprehensive antimicrobial stewardship programs to effectively manage UTIs in this high-risk population. However, the study has following limitations:

1. Single-Center Study: The research was conducted at a single hospital (Al-Bashir Hospital, Amman), which may limit the generalizability of the findings to other regions or healthcare settings in Jordan.

2. Sample Size: The study included 150 participants (100 CKD patients and 50 controls), which, while sufficient for preliminary analysis, may not capture the full spectrum of bacterial diversity and resistance patterns in the broader CKD population.

3. Short Study Duration: Data collection spanned only two months (May–June 2025), which might not account for seasonal variations in UTI prevalence and bacterial resistance trends.

4. Lack of Molecular Characterization: The study relied on conventional microbiological methods (Gram staining, biochemical tests) without involving automated identification (VITEK/MALDI-TOF), also without molecular techniques (e.g., PCR, whole-genome sequencing) to detect resistance genes or clonal relationships among isolates.

5. A lack of concurrent processing of reference strains alongside test isolates for antibiotic susceptibility profile. While strict adherence to standardized CLSI testing protocols was maintained, the absence of parallel ATCC control runs should be considered when interpreting the absolute baseline values of marginal zone diameters.

6. No Follow-Up Data: The study did not track long-term outcomes, such as recurrence rates or treatment failures, which are critical for assessing clinical implications.

To improve UTI management in CKD patients, the study recommends other studies in developing local empirical antibiotic guidelines based on current resistance trends, particularly addressing fluoroquinolone resistance and the effectiveness of colistin and amikacin. Empirical use should be limited in favor of culture-guided therapy with renal dose adjustments. Preventive strategies include strict catheter care, screening for asymptomatic bacteriuria, and vaccination. Enhancing diagnostics with rapid molecular tools and ESBL detection is essential.

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