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Analysis of the Multiple Drug Resistance (MDR) Pattern Among Uropathogenic *Klebsiella Pneumoniae* Isolates from Immunocompromised Patients

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Abstract

Background: Multidrug-resistant (MDR) *Klebsiella pneumoniae* is a major causative agent of urinary tract infections (UTIs) and represents a growing therapeutic challenge, particularly in immunocompromised patients. The purpose of this study was to determine the prevalence of MDR in *K. pneumoniae* isolates from immunocompromised patients with UTIs. **Methods:** Urine samples were collected from 597 immunocompromised patients with UTIs. *K. pneumoniae* was isolated and identified, and the isolates were subjected to susceptibility testing against 25 antibiotics. **Results:** Fifty-two (12.2%) *K. pneumoniae* isolates were isolated from 427 positive urine samples. The results showed a high prevalence of MDR (73.1%) with specific resistance patterns associated with certain antibiotic classes. The relationship between MDR and patient demographic and clinical variables was also analyzed, and statistically significant associations were found between the presence of the pattern and length of hospital stay ($P=0.0238$), prolonged infection duration ($P=0.0026$), use of indwelling urinary catheter ($P=0.0014$), and history of antibiotic treatment ($P=0.0019$). **Conclusion:** The prevalence of MDR *K. pneumoniae* was higher in immunocompromised patients, and its occurrence was associated with a longer length of stay, prolonged infection, catheter use, and a history of antibiotic treatment.

Highlights:

- 73.1% of *K. pneumoniae* isolates were multidrug-resistant.
- MDR linked to longer hospital stays, catheter use, and prior antibiotics.
- Serious concern for treating UTIs in vulnerable patients.

Keywords: Multidrug Resistance, *Klebsiella Pneumoniae*, Urinary Tract Infection, Immunocompromised Patients, Antibiotic Resistance

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Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, affecting millions of people annually. Their severity is particularly high in immunocompromised patients, which increases the risk of complications [1] [2]. Among these pathogens, *K. pneumoniae* stands out as a major pathogen, particularly in hospital settings, where it has an increasing capacity to resist antibiotics [3]

Multidrug resistance (MDR) is a growing challenge in the treatment of *K. pneumoniae* infections. An increase in isolates producing extended-spectrum beta-lactamases and carbapenemases has been observed, limiting treatment options and increasing morbidity and mortality rates [4] [5]. This problem can be exacerbated in immunocompromised patients, such as organ transplant recipients, cancer patients, and diabetics [6] [7] [8]

The prevalence of multidrug-resistant *K. pneumoniae* varies globally, with reports of increased carbapenem resistance in different regions, raising concerns about the future treatment of these infections [9]. In Iraq, some studies indicate high rates of antibiotic resistance among bacteria isolated from urinary tract infections, including *K. pneumoniae*. However, the prevalence of multidrug resistance (MDR) in *K. pneumoniae* isolates in immunocompromised patients with UTIs remains a matter of comprehensive study.

In light of this, this study aims to determine the prevalence of multidrug resistance (MDR) in *K. pneumoniae* isolates in immunocompromised patients with UTIs. By identifying the prevalence of MDR and its most important associated factors, this study can contribute to providing baseline data to guide infection control strategies and optimal treatment selection for this at-risk patient population in both local and global contexts.

Method

A. Study Design, Isolation, and Identification of Bacteria

This cross-sectional study included 597 immunocompromised patients with urinary tract infections (UTIs) from different regions of Iraq. Midstream urine samples were collected in the laboratory during the study period (from late November 2023 to May 2024); all clinical data were collected during the collection of patient samples using a pre-prepared form. Samples were cultured on appropriate media (such as MacConkey agar, blood agar, and chromogenic agar). *Klebsiella pneumoniae* was identified using standard biochemical tests (such as IMViC tests and saccharide fermentation).

B. Antibiotic Susceptibility Testing

Antibiotic susceptibility testing was performed using the Kirby-Bauer disk method according to CLSI (Clinical and Laboratory Standards Institute) 202 guidelines. The isolates were tested against a panel of 25 antibiotics representing various classes commonly used to treat urinary tract infections, including: Ampicillin, Piperacillin, Amoxicillin-clavulanic acid, Ampicillin-Salbactam, Piperacillin-Tazobactam, Cefazolin, Cefuroxime, Ceftriaxone, Cefepime, Ceftazidime, Cefotetan, Aztreonam, Imipenem, Meropenem, Gentamicin, Amikacin, Tetracycline, Doxycycline, Ciprofloxacin, Levofloxacin, Trimethoprim/sulfamethoxazole, Fosfomycin, Nitrofurantion, Colistin, and Polymyxin B. Results were interpreted as susceptible, intermediate, or resistant based on CLSI (2021) guidelines, and isolates were considered MDR based on the definition [10]

C. Statistical Analysis

Data were analyzed using Excel and GraphPad Prism 8. Descriptive statistics were used to display frequencies and percentages. The Chi-square test was used to analyze the association between MDR patterns and demographic and clinical variables. A P value of ≤ 0.05 was considered statistically significant.

Results and Discussion

A. Result

In a study of 597 urine samples collected from immunocompromised patients, 427 samples (71.5%) showed positive bacterial growth. *K. pneumoniae* was isolated in 52 (12.2%) of these positive samples, as shown in Figure 1.

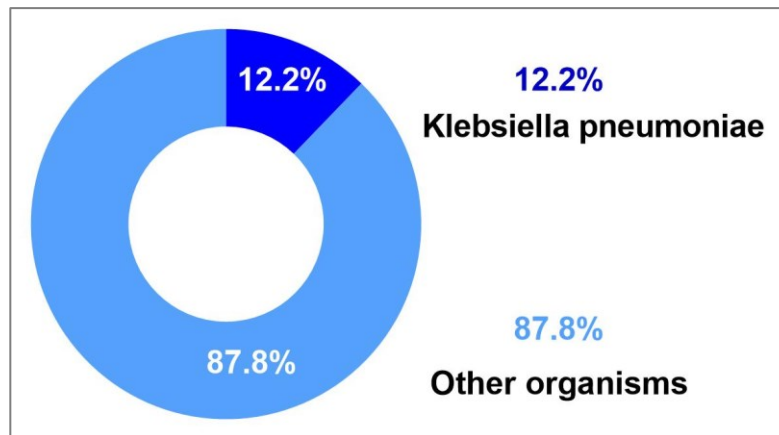


Figure 1. Prevalence of *K. pneumoniae* isolates in urine samples from immunocompromised patients

The study showed that the prevalence of *K. pneumoniae* isolates was higher among males than females (61.5% and 38.5%, respectively). Analyzing the distribution of these isolates across different disease conditions within the immunocompromised patient group, the highest prevalence was observed in diabetic patients (44.2%), followed by cancer patients (30.8%), and then renal failure patients (25%). In addition, the results indicated that most patients with UTIs caused by *K. pneumoniae* isolates acquired the infection in the community compared to hospital-acquired infections (67.3% and 32.7%, respectively), Table 1.

Variables	No.	Percent %
Gender		
Male	32	61.5%
Female	20	38.5%
Disease conditions		
Diabetes	23	44.2%
Renal failure	13	25.0%
Cancer	16	30.8%
Acquired infections		
Community	35	67.3%
Hospital	17	32.7%

Table 1. Distribution characteristics of *K. pneumoniae* isolates isolated from the urine of immunocompromised patients.

Klebsiella pneumoniae isolates exhibited diverse resistance patterns to the tested antibiotics. Exceptionally high resistance was observed to beta-lactam antibiotics, with resistance rates reaching 86.5% to ampicillin and 67.3% to piperacillin, as shown in Table 2.

For cephalosporins, resistance rates ranged from moderate (44.2-59.6%), and similarly, aztreonam showed a resistance rate of 44.2%. As for aminoglycosides, their resistance rates varied, reaching 57.7% for gentamicin and 23.1% for amikacin.

The antibiotics tetracycline, doxycycline, ciprofloxacin, levofloxacin, and Fosfomycin have shown moderate resistance rates of 40.4% to 50%.

In contrast, antibiotics containing beta-lactamase inhibitors (Amoxicillin-clavulanic acid, Ampicillin-Salbactam, and Piperacillin-Tazobactam), carbapenems (Imipenem and Meropenem),

trimethoprim/sulfamethoxazole (SXT), nitrofurantoin, and polymyxins (Colistin and Polymyxin B) showed high efficacy, as the levels of resistance of the isolates to these antibiotics were relatively low.

Antibiotics	Resistance		Intermediate		Sensitive	
	No	Percent (%)	No	Percent (%)	No	Percent (%)
Ampicillin	45	86.5%	1	1.9%	6	11.5%
Piperacillin	35	67.3%	14	26.9%	3	5.8%
Amoxicillin-clavulanic acid	16	30.8%	13	25.0%	23	44.2%
Ampicillin-Salbactam	11	21.2%	15	28.8%	26	50.0%
Pipracillin-Tazobactam	14	26.9%	7	13.5%	31	59.6%
Cefazolin (1)	29	55.8%	9	17.3%	14	26.9%
Cefuroxime (2)	28	53.8%	8	15.4%	16	30.8%
ceftriaxone (3)	28	53.8%	4	7.7%	20	38.5%
Cefepime (4)	26	50.0%	7	13.5%	19	36.5%
Ceftazidime (4)	23	44.2%	5	9.6%	24	46.2%
Cefotetan	31	59.6%	2	3.8%	19	36.5%
Aztreonam	23	44.2%	0	0.0%	29	55.8%
Imipenem	11	21.2%	2	3.8%	39	75.0%
Meropenem	15	28.8%	0	0.0%	37	71.2%
Gentamicin	30	57.7%	2	3.8%	20	38.5%
Amikacin	12	23.1%	2	3.8%	38	73.1%
Tetracycline	26	50.0%	3	5.8%	23	44.2%
Doxycycline	26	50.0%	4	7.7%	22	42.3%
Ciprofloxacin	21	40.4%	5	9.6%	26	50.0%
Levofloxacin	22	42.3%	6	11.5%	24	46.2%
STX	12	23.1%	6	11.5%	34	65.4%
Fosfomycin	23	44.2%	2	3.8%	27	51.9%
Nitrofurantion	14	26.9%	1	1.9%	37	71.2%
Colistin	3	5.8%	0	0.0%	49	94.2%
Polymyxin B	2	3.8%	1	1.9%	49	94.2%

Table 2. Rates of resistance of *Klebsiella pneumoniae* to different antibiotics.

The prevalence of multidrug resistance (MDR) in *K. pneumoniae* isolates was 73.1% (38/52). The prevalence of this pattern among these patients was statistically significant ($P < 0.0001$), Figure 2.

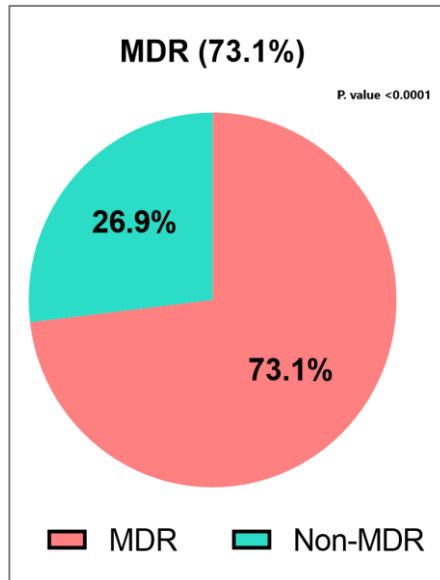


Figure 2. Prevalence of multidrug resistance (MDR) in *Klebsiella pneumoniae* isolates.

The results of the current study (shown in Table 3) showed no statistically significant association between patient gender, immunocompromised group, general source of infection (hospital-acquired or community-acquired), recurrence, and the occurrence of multidrug-resistant (MDR) patterns among *K. pneumoniae* isolates causing urinary tract infections.

In contrast, statistically significant associations were observed between other factors and the occurrence of MDR: length of hospital stay was statistically associated with the occurrence of MDR in hospital-acquired isolates ($P = 0.0238$), with patients with longer hospital stays more likely to be infected with MDR isolates. The duration of infection also showed a strong statistical significance in the occurrence of MDR, with isolates from patients with infection for more than 21 days being more likely to be MDR (89.5%).

The use of indwelling catheters was strongly and statistically significantly associated with MDR, as all isolates from these patients exhibited this resistance spectrum (100%, P value = 0.0014). Patients who had received antibiotic treatment within the past one to three months were more likely to develop multidrug-resistant isolates, with the emergence of this pattern being associated with the duration of treatment (P value = 0.0019).

Variables	MDR		Non-MDR		Total	Chi-square	P value
	No.	%	No.	%			
Gender							
Male	22	68.8%	10	31.3%	32	0.7917	0.3736
Female	16	80.0%	4	20.0%	20		
Disease							
Diabetics	17	73.9%	6	26.1%	23	0.136	0.9343
Renal	9	69.2%	4	30.8%	13		
Cancer	12	75.0%	4	25.0%	16		
Hospital							

In	13	76.5%	4	23.5%	17	0.1478	0.7006
Out	25	71.4%	10	28.6%	35		
Hospital Stay Duration							
3 days	3	42.9%	4	57.1%	7	7.473	0.0238
1 week	3	100%	0	0%	3		
> week	7	100%	0	0%	7		
Infection period							
1-6 days	4	40.0%	6	60.0%	10	14.25	0.0026
7-13 days	0	0.0%	2	100.0%	2		
14-21 days	17	81.0%	4	19.0%	21		
>21 day	17	89.5%	2	10.5%	19		
Recurrent infection							
Month	0	0.0%	1	100.0%	1	6.386	0.0943
3 months	2	66.7%	1	33.3%	3		
6 months	9	100.0%	0	0.0%	9		
1 year	27	69.2%	12	30.8%	39		
Catheter							
Used	18	100.0%	0	0.0%	18	10.14	0.0014
Not used	20	58.8%	14	41.2%	34		
Use of antibiotics							
Do not use	3	33.3%	6	66.7%	9	17.08	0.0019
72 hours	3	60.0%	2	40.0%	5		
1 week	2	40.0%	3	60.0%	5		
1 month	16	100.0%	0	0.0%	16		
3 months	14	82.4%	3	17.6%	17		

Table 3. Prevalence of MDR according to selected clinical variables.

B. Discussion

This study demonstrated a high prevalence of MDR (73.1%) in *K. pneumoniae* isolates from immunocompromised patients with UTIs in different regions of Iraq. This is consistent with the increasing reports of antibiotic resistance in *K. pneumoniae* globally and locally. A study conducted by [11] at a

teaching hospital in Sulaymaniyah Governorate reported a prevalence of 76.9% in *K. pneumoniae* isolates isolated from immunocompromised patients. This similarity suggests that the problem of multidrug resistance may be widespread in the region. A study conducted in Iran also reported a similar rate (79.1%), confirming the trend of *Klebsiella* isolates developing increased antibiotic resistance [12]

In contrast to the study conducted by [13] in Morocco, which showed a statistically significant association between patient gender and MDR prevalence, with prevalence being higher in males, we did not find a similar association in our study. This difference may reflect unique local factors influencing antibiotic use or exposure patterns between the sexes in our population.

For immunocompromised patient groups, we did not observe a significant difference in the prevalence of MDR among patients with diabetes, cancer, or renal failure. Unfortunately, to our knowledge, no previous study has quantified the prevalence of this spectrum among *K. pneumoniae* isolates in these patients in such a comparative context. Therefore, the lack of a significant difference in the prevalence of MDR among different immunocompromised patient groups may be surprising, as each disease condition is expected to have different risk factors. However, this may indicate that immunocompromise itself is a major risk factor for MDR, regardless of the specific cause of immunocompromise.

Interestingly, we found no significant difference in the prevalence of MDR between community-acquired and hospital-acquired isolates when considering all immunocompromised patients in general. This finding is consistent with the study by [14], which indicated a higher prevalence of MDR strains in the community, potentially reducing the difference between community and hospital-acquired infections.

The lack of a relationship between recurrent infection and the presence of an MDR phenotype may indicate that other factors (such as the type of antibiotic used in previous treatment or other risk factors) may be more important in determining the development of resistance than the number of infections. The findings of this study contrast significantly with those of [15] [16], which indicated a significant association between recurrent infection and the presence of this phenotype. On the other hand, the study by [13] reported a similar result, indicating no relationship between recurrent infection and infection with isolates with the MDR spectrum.

The association of longer hospital stays with an increased risk of MDR in hospital-acquired isolates is consistent with a study by [17], which documented a gradual increase in antibiotic resistance rates with longer hospital stays in Saudi Arabia. This reinforces known findings that the hospital environment represents a selective environment for the spread of resistant strains.

The association of a long infection period (>21 days) with an increased risk of MDR is consistent with a study by [15], which indicated that a six-month infection period with a urinary tract infection increases the risk of drug-resistant bacteria by approximately twofold. A study [18] also indicated that patients with chronic or recurrent urinary tract infections often receive repeated courses of antibiotics, which may contribute to the development of resistance.

The strong and statistically significant association between indwelling urinary catheter use and MDR phenotype is consistent with studies by [19] [20], which found that the majority of *K. pneumoniae* isolates from patients with long-term catheter use were MDR. Both studies also reported a statistically significant association between the presence of this phenotype and catheter use ($P = 0.05$). This finding supports the known role of catheters in biofilm formation and increased risk of resistant bacteria. On the other hand, [15] reported that the association between phenotype presence and catheter use was not statistically significant ($P > 0.05$).

Finally, the association of receiving antibiotic treatment within the past 1-3 months with an increased risk of MDR suggests the ongoing influence of antibiotic selective pressure, which is consistent with studies by [15] [13] [21] that showed that a history of antibiotic use was a significant risk factor for MDR infection.

Conclusion

This study demonstrated a high prevalence of multidrug resistance (MDR) in *Klebsiella pneumoniae* isolates isolated from immunocompromised patients with urinary tract infections, with significant associations with length of hospital stay (for hospital-acquired isolates), prolonged duration of infection, use of indwelling urinary catheters, and a history of antibiotic treatment. These findings underscore the

need for continuous monitoring of antibiotic resistance patterns and the implementation of effective strategies to manage antibiotic use and control infections in our healthcare institutions.

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