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Emerging Antibiotic Resistance in *Klebsiella pneumoniae* Among Diabetic Patients With Urinary Tract Infections: A Regional Study From Khorramabad City, Iran

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ABSTRACT

Background: Diabetic patients are at a heightened risk of urinary tract infections (UTIs) caused by antibiotic-resistant bacteria. This study aimed to determine the antimicrobial resistance patterns of *Klebsiella pneumoniae* isolated from diabetic patients with UTIs in Khorramabad City, Iran.

Materials and Methods: In this cross-sectional study (May 2020 to March 2021), 500 *K. pneumoniae* isolates were obtained from 3130 diabetic patients with culture-confirmed UTIs. Identification was performed using standard microbiological methods. Antimicrobial susceptibility testing against nine antibiotics was conducted via the Kirby-Bauer disk diffusion method, interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: The highest resistance rates were observed for gentamicin (66%) and ampicillin (58%). The lowest resistance was observed for cefazolin (17%), nitrofurantoin (21%), and ceftazidime (22%). Multidrug resistance (MDR) was identified in 17% of isolates. The patient distribution was 57% female, 39% male, and 4% pediatric.

Conclusion: High resistance to empiric antibiotics, such as gentamicin and ampicillin, was found, underscoring the need for revised treatment guidelines and robust antimicrobial stewardship in the management of diabetic UTI in this region.

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Introduction

Diabetes mellitus is a major global health challenge that impairs host defense mechanisms and increases susceptibility to infections, such as urinary tract infections (UTIs) [1, 2]. UTIs in diabetic patients are not only more frequent but also more severe and challenging to treat due to the rising prevalence of antibiotic-resistant uropathogens [3, 4].

Klebsiella pneumoniae is a leading cause of healthcare-associated and community-acquired UTIs, renowned for its capacity to develop multidrug resistance (MDR), including to extended-spectrum beta-lactams and aminoglycosides [5]. Inappropriate empirical antibiotic therapy, often driven by outdated resistance data, can lead to treatment failure, prolonged illness, and increased healthcare costs [6].

Regional surveillance of antimicrobial resistance patterns is critical for guiding effective empirical therapy. However, comprehensive data on the resistance profiles of *K. pneumoniae* from diabetic patients with UTIs in Khorramabad, Iran, are lacking. This study was conducted to investigate the antimicrobial resistance patterns and MDR prevalence of *K. pneumoniae* isolates from diabetic patients with UTIs in this region, to inform local clinical practice and stewardship efforts.

Materials and Methods

Study design and sample collection

A cross-sectional study was conducted from May 2020 to March 2021. Clean-catch mid-stream urine samples were collected from diabetic patients (type 1 and type 2) presenting with UTI symptoms at healthcare centers in Khorramabad City, Iran. Patients who had received antibiotics within 72 hours prior to sampling were excluded.

Bacterial isolation and identification

Samples were cultured on eosin methylene blue and blood agar plates (Condalab, Spain) and incubated at 37°C for 24 hours. Significant growth was defined as $\geq 10^5$ CFU/mL. *K. pneumoniae* was identified using standard methods: Gram-negative rods, positive for catalase, citrate, urease, and Voges-Proskauer tests, and negative for oxidase, indole, and motility [1].

Antimicrobial susceptibility testing

Susceptibility testing was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, following the Clinical and Laboratory Standards Institute (CLSI) guidelines [2]. The antibiotic disks used (Paatanteb, Iran) were ampicillin (10 µg), gentamicin (10 µg), sulfamethoxazole/trimethoprim (1.25/23.75 µg), amikacin (30 µg), cefazolin (30 µg), nitrofurantoin (300 µg), ceftazidime (30 µg), cefotaxime (30 µg), and tetracycline (30 µg). *Escherichia coli* ATCC 25922 was used for quality control. MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories [3].

Results

From 3,130 diabetic patients, *K. pneumoniae* was isolated from 500(15.97%). The cohort comprised 285 females (57%), 195 males (39%), and 20 pediatric patients (4%).

More complete information on gender and drug resistance patterns is presented graphically (Figures 1, 2, and 3).

Discussion

This study provides critical insights into the alarming antibiotic resistance patterns of *K. pneumoniae*, a major uropathogen isolated from patients with diabetic UTI in Khorramabad City. The high prevalence of *K. pneumoniae* (15.97% of culture-positive cases) aligns with its established role in causing complicated UTIs, particularly in hosts with compromised immunity, such as diabetic individuals [5, 7]. The most striking finding is the exceptionally high resistance to gentamicin (66%) and ampicillin (58%). Gentamicin resistance in our setting surpasses rates reported from other regions in Iran (e.g. ~40-50% in some studies) and many international reports, likely reflecting its historical and potentially indiscriminate use in both hospital and community settings for various infections [8, 9]. This severely limits its utility as an empiric option for severe UTIs or pyelonephritis in our region. The high ampicillin resistance is expected, as most *Klebsiella* spp. produce intrinsic sulfhydryl variable1 beta-lactamase, rendering them resistant to aminopenicillins [10]. However, its persistence underscores the inappropriateness of ampicillin/amoxicillin as empirical therapy for suspected gram-negative infections. In contrast, the relatively preserved susceptibility to cefazolin (83% sensitive) and nitrofurantoin (79% sensitive) is encouraging and offers valuable clinical guidance. Nitro-

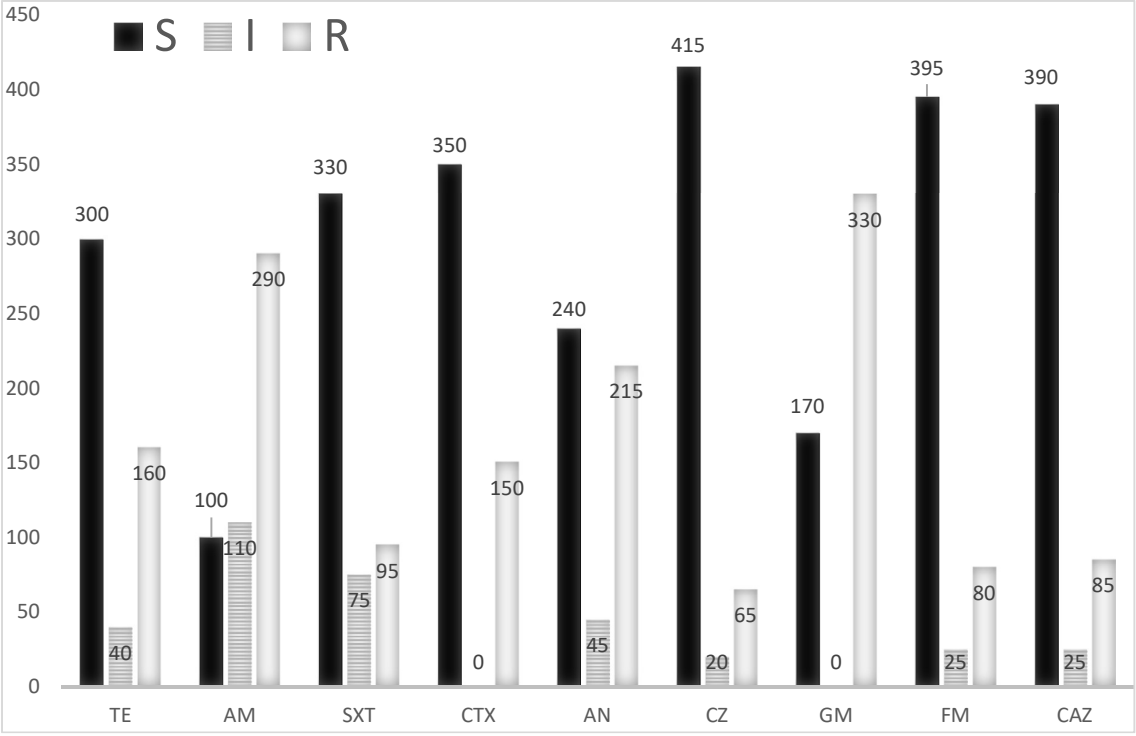

Figure 1. Frequency of phenotypic sensitivity and resistance in 500 *K. pneumoniae* isolates obtained from urinary tract infections in Khorramabad City, Iran

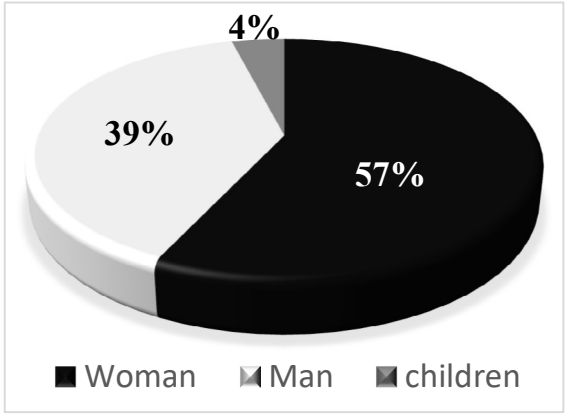

Figure 2. Patient gender

furantoin, due to its high urinary concentration, minimal impact on gut flora, and low resistance selection pressure, remains a strongly recommended first-line oral agent for uncomplicated cystitis, even in diabetic populations [11, 12]. Our data support its continued use for lower UTIs in this cohort. The low resistance to ceftazidime (22%) is also notable, though it necessitates vigilance for emerging extended-spectrum beta-lactamase (ESBL) producers, as indicated by the higher resistance to cefotaxime (41%). This discrepancy might suggest the presence of specific ESBL enzymes with higher affinity for cefotaxime. The identification of MDR in 17% of isolates represents a serious public health concern. This rate is comparable to reports from other developing regions but highlights a significant and growing challenge [7, 13]. The convergence of diabetes—a condition that increases infection frequency and severity—with MDR pathogens creates a perfect storm, leading to longer hospital stays,

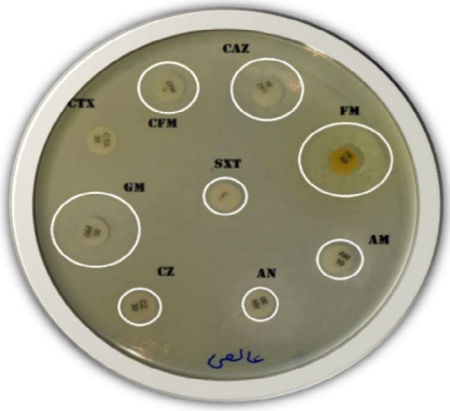

Figure 3. Picture of an example of an antibiogram test

higher treatment costs, increased use of last-resort antibiotics, and greater mortality [6]. The MDR phenotype often limits treatment options to broader-spectrum agents like carbapenems, further driving the resistance cycle.

Clinical implications and recommendations

Our results strongly argue against the empirical use of ampicillin or gentamicin for UTIs in diabetic patients in Khorramabad City. Local antibiograms should guide empirical therapy and may favor:

• Nitrofurantoin for uncomplicated lower UTIs in patients with preserved renal function.

• Cefazolin or ceftazidime as potential parenteral options for more serious infections requiring hospitalization, pending culture results.

The substantial MDR prevalence underscores the non-negotiable need for culture and susceptibility testing before initiating or adjusting therapy in this high-risk group. Furthermore, these findings underscore the critical urgency of implementing robust antimicrobial stewardship programs (ASPs) in all healthcare settings. ASPs can optimize antibiotic use, reduce selection pressure, and preserve the efficacy of remaining effective antibiotics, such as nitrofurantoin and certain cephalosporins.

Study limitations

This study has several limitations. Its single-center, cross-sectional design may limit the generalizability of the findings to the entire country. Furthermore, the lack of molecular characterization of resistance genes (e.g. for ESBLs, carbapenemases, aminoglycoside-modifying enzymes) means we cannot elucidate the precise genetic mechanisms driving the observed resistance patterns. Future studies should incorporate molecular epidemiology to track resistant clones and understand their transmission dynamics.

Conclusion

In conclusion, this study reveals a high burden of antibiotic resistance, including a significant MDR rate, among *K. pneumoniae* isolates from patients with diabetic UTI in Khorramabad. The particularly high resistance to commonly used empiric agents, such as gentamicin and ampicillin, is alarming. These findings highlight a critical concern for clinicians, microbiologists, and healthcare authorities in the region. Revising empirical treatment protocols based on this local surveillance data is imperative. Equally important is the enforcement of strict antimicrobial stewardship and infection control practices to mitigate this threat. A concerted effort towards culture-guided therapy, rational antibiotic use, and continuous surveillance is essential to improve patient outcomes and curb the rising tide of antimicrobial resistance in this vulnerable diabetic population.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Lorestan University of Medical Sciences, Lorestan, Iran (Code: IR.LUMS.REC.1401.098).

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Authors contribution's

All authors contributed equally to the conception and design of the study, data collection and analysis, interception of the results and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflict of interests.

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