

Original Article

## *Klebsiella pneumoniae* Antibiotic Resistance Pattern Towards Antimicrobial Agents in Urinary Tract Infection Patients in Zawia City / Libya

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### ABSTRACT

Urinary Tract Infections (UTIs) represent a significant public health concern, contributing to serious health issues, extensive antibiotic use globally, and ranking as the second most common reason for clinical consultations in community settings. Various bacteria, particularly from the Enterobacteriaceae family, including *Klebsiella* spp., are implicated in the etiology of UTIs. This study focused on assessing the prevalence and antibiotic resistance patterns of uropathogenic *K. pneumoniae* across different age groups and genders. A total of 819 urine samples were collected from patients visiting Zawia hospitals and clinics between September 2022 and February 2023. Identification of *K. pneumoniae* was performed through colony morphology, Gram staining, and biochemical assays, followed by antibiotic susceptibility testing. Out of all samples, 271 (33.07%) exhibited significant bacterial growth. The incidence of UTIs was notably higher in females (40.15%) compared to males (20.6%). The age group of 1-9 years showed the highest susceptibility to UTIs at 35.4%. *K. pneumoniae* accounted for 23.9% of all UTI cases, with a higher prevalence in males (31.14%) than in females (21.9%). The 1-9 year age group was identified as the most vulnerable to *K. pneumoniae* infections, with a prevalence of 29.2%. *K. pneumoniae* demonstrated a high susceptibility rate of 86.2% to Meropenem, while showing significant resistance to Tetracycline at 70.8%. The findings indicate a high prevalence of UTIs in the 1-9 year age group, with females at greater risk. Males exhibited a higher susceptibility to *K. pneumoniae*, particularly in the younger age group. The bacterium showed strong sensitivity to Meropenem and considerable resistance to Tetracycline. Increased awareness and regular monitoring of antimicrobial usage in healthcare settings are essential to mitigate resistance rates and combat this pathogen.

**Keywords:** Urinary tract infections (UTIs), *K. pneumoniae*, Antibiotic resistance, Meropenem, Tetracycline,

**Citation:** Abougrara G., alkhboli A., twair F., Shaglabow S. Incidence and Antibiotic Susceptibility of *Klebsiella pneumoniae* Isolated from Urinary Tract Infection Patients in Zawia City. <https://orcid.org/10.54361/ljmr18-1.06> Received:03 /02/24; accepted: 12 /02/24; published:15 /02/24 Copyright ©Libyan Journal of Medical Research (LJMR) 2021. Open Access. Some rights reserved. This work is available under the CC BY license <https://creativecommons.org/licenses/by-nc-sa/3.0/igo> <https://orcid.org/0009-0003-0125-0853>

## INTRODUCTION

Urinary tract infections (UTIs) caused by bacterial pathogens represent a significant public health concern, impacting millions of individuals in both community and hospital environments globally each year [1]. UTIs rank as the second most prevalent type of infection within the human body [2]. While the mortality associated with UTIs is relatively low, they impose a considerable economic strain on healthcare systems due to escalating treatment expenses [3].

In recent years, the management and treatment of UTIs have become increasingly challenging due to the rising antimicrobial resistance observed in uropathogens, particularly within the *Enterobacteriaceae* family [4-5]

*Klebsiella pneumoniae* is a rod-shaped Gram-negative bacterium, it is the most important clinical member of the *Klebsiella* genus of *Enterobacteriaceae*. It is an important pathogen in community- and hospital-acquired infections, is linked to a range of infections, with UTIs being the most frequently encountered worldwide. Additionally, *K. pneumoniae* is associated with more severe conditions such as bacteremia, meningitis, pneumonia, liver abscesses, and upper respiratory tract infections, *K. pneumoniae* is one of the most prevalent bacteria that causes nosocomial infections particularly when they infect hospitalized or immunocompromised individuals [6]. The heightened virulence and dissemination of *K. pneumoniae* contribute to a growing vulnerability to infections among the population [7]. Numerous studies have identified *Escherichia coli* and *Klebsiella* species as the predominant organisms responsible for UTIs [8,9]. A comprehensive understanding of the risk factors associated with UTIs in humans can aid healthcare providers in developing targeted prophylactic strategies [10]. Recently, *K. pneumoniae* has become clinically significant owing to its increased antibiotic resistance, which is achieved through multiple

mechanisms that enhance antimicrobial resistance [11].

Prompt treatment of UTIs is crucial in mitigating the severity of the infection, typically involving empirically prescribed antibiotics [12]. To ensure effective therapeutic interventions, it is vital to accurately identify the primary bacterial agents implicated in urinary tract infections and their respective antibiotic resistance profiles [13].

Investigating the most significant uropathogenic organisms, such as *K. pneumoniae*, and their susceptibility patterns is essential for improving clinical outcomes

The aim of this study was to isolate and determine the resistance profile to common antibiotics of *K. pneumoniae* isolated from urine samples over a 6-month period in (2022 - 2023) in Zawia City, Libya.

## METHODS

### ***Specimen collection Isolation, identification, and antibiotic sensitivity test***

The cross-sectional study was performed from September 2022 to February 2023 in Zawia City, Libya.

Clean midstream urine samples were collected in sterile tubes from 819 patients (296 males and 523 females) who attended Zawia hospitals or clinics with clinical symptoms of UTI. Information related to these patients, such as sex, and age, was obtained.

The patients were instructed how to collect the urine sample to avoid contamination.

Urine samples were transported in ice to the laboratory. Then the samples were inoculated aseptically on MacConkey Agar plates and incubated for overnight at 37°C. Urine samples showing a colony count of more than 10,000 Cfu/ml were considered to be significant for urinary tract infections [14], In the

next step, the isolated bacteria were identified by colony characteristics, Gram staining of bacterial colonies, and biochemical tests, based on standard procedures and international guidelines. These tests include; oxidase, urease, catalase, and IMViC tests and Simon's Citrate test) [15]. Susceptibility to a range of antibiotics which were available and used, was performed on Mueller-Hinton agar using the disk diffusion technique. According to the guidelines of Clinical and Laboratory Standards Institute (CLSI) 2015 [16].

### Ethics Statement

The patients were informed and consented to their data being used in this research.

### Data Analysis

Statistical analysis of all data was done by SPSS 16 software.

## RESULTS

This study was performed between September 2022 until February 2023, showed that overall, of the total 819 patients, only 271 (33.07%) samples were positive for bacterial growth in both genders.

The total prevalence of UTIs among the female's population was 40.15% (210/523) while among males was 20.6% (61/296). UTIs were more frequent in females than in males. The highest risk age group for UTIs, irrespective of gender, was found to be in the age range 1-9 years (35.4%) followed by age range 10-19 years (17.7%), and then >60 years (14%), while the lowest risk age group of UTIs was in the 50-59 years (4.7%).

Among the total patients, the *K. pneumoniae* represented 23.9% (65/271) of all the urinary bacteria

isolates. The percentage of *K. pneumoniae* isolates of females over the six months, were 21.9% (46/210), while among male patients the rate of *K. pneumoniae* was 31.14% (19/61) (Table 1). So, in males the UTIs caused by *K. pneumoniae* were more frequent than in females.

**Table 1: Distribution of uropathogenic *K. pneumoniae* according to gender during September 2022 until February 2023**

Gender	September 2022 until February 2023 N (%)
Male	31.14% (19/61)
Female	21.9% (46/210)
Total	23.9% (65/271)

The age group 1-9 years showed the highest percentage of *K. pneumoniae* isolates (29.2%) followed by age range 30-39 years (26.2%), and then between 40-49 years (15.4%), while the lowest risk age group for UTIs was in the 20-29 years (3.08%) (Table 2).

**Table 2: Distribution of uropathogenic *K. pneumoniae* according to age groups during September 2022 until February 2023**

Age group (Years)	September 2022 until February 2023 No (%)
1-9	19/65 (29.2%)
10-19	5/65 (7.7%)
20-29	2/65 (3.07%)
30-39	17/65 (26.2%)
40-49	10/65 (15.4%)
50-59	3/65 (4.62%)
≥60	9/65 (13.8%)
Total	65

In this study all the 65 *K. pneumoniae* isolates were assessed for antimicrobial resistance toward different types of antibiotics. The sensitivity of *K. pneumoniae* was 86.2% toward Meropenem, 73.8% to Levofloxacin, 69.2% to Nitrofurantoin, 67.7% to Norfloxacin and Ceftriaxone, 61.5% to Erythromycin, 60% to Amikacin and Ciprofloxacin, and 50.8% to Amoxicillin + Clavulanic acid. The other tested antibiotics showed less than 50% susceptibility. On the other hand, the *K. pneumoniae* isolates showed high resistance against Tetracycline (70.8%), Trimethoprim-Sulfamethoxazole (69.2%), Cefixime (66.2%), Nalidixic acid (61.5%), Gentamicin, Cefotaxime (60%), azithromycin (55.4%).

**Table 3: Susceptibility of the *K. pneumoniae* isolates against different antibiotics during September 2022 - February 2023.**

Antibiotic agents (Disk content)	Resistant No. (%)	Sensitive No. (%)
(AMC) (20/10 µg)	32 (49.2%)	33 (50.8%)
(CFM) (5 µg)	43 (66.2%)	22 (33.8%)
(CRO) (30 µg)	21 (32.3%)	44 (67.7%)
(CTX) (30 µg)	39 (60%)	26 (40%)
(TE) (30 µg)	46 (70.8%)	19 (29.2%)
(NIT) (300 µg)	20 (30.8%)	45 (69.2%)
(NA) (30 µg)	40 (61.5%)	25 (38.5%)
(CIP) (5 µg)	26 (40%)	39 (60%)
(NOR) (10 µg)	21 (32.3%)	44 (67.7%)
(LEV) (5 µg)	17 (26.2%)	48 (73.8%)
(MEM) (10 µg)	9 (13.8%)	56 (86.2%)
(AZM) (15 µg)	36 (55.4%)	29 (44.6%)
ERY (15 µg)	25 (38.5%)	40 (61.5%)

(AK) (30 µg)	26 (40%)	39 (60%)
(CN) (10 µg)	39 (60%)	26 (40%)
(SXT) (1.25/ 23.75 µg)	45 (69.2%)	20 (30.8%)

## DISCUSSION

Urinary Tract Infections are one of the major causes of serious health problems. In this study, 33.07% of the urine samples were positive for bacterial growth. Females had a significant high rate of UTIs (40.15%) compared to males (20.6%). Several studies showed similar results [17, 18]. Females were more affected by the infection than males. The reason is due to female anatomy, particularly with regards, the female urethra is much shorter in length than men, which allow bacterial quick access to the bladder [19]. One another reason is the fact of that female urethra is located closer to the rectum, which carries waste and bacteria such as *E. coli*, and increase the rate of UTIs [20]. In this study the highest rate of UTIs was observed among individual with age group 1-9 years (35.4%) and 10-19 years (17.7%).

In this study, *K. pneumoniae* comes after *E. coli* as the main cause of UTIs, the *K. pneumoniae* rate among UTIs was found to be 23.9%. Similar studies revealed varied rates for *K. pneumoniae* such as (7.39%) (10.25%) in Subrata, Algmel Cities in Libya [21], 8.8% in Italy [22], 17.1% in Egypt [23], 23.5% in Saudi Arabia [24]. 14.3 in Peshawar, Pakistan [25]. *K. pneumoniae* was found with high pathogenicity and virulence. mediated by several virulence factors essential for the the bacteria to allow it to evade host innate immune defense, these factors include the lipopolysaccharide, adhesins, biofilm formation and

polysaccharide capsules that give bacteria the ability to invade the host and prevent bacterial phagocytosis [26].

This study revealed that *K. pneumoniae* was prevalent among 31.14% of men and 21.9% among women. These results come in accordance to a study done by Varughese and Beniwal [27], in India, who found that uropathogenic *K. pneumoniae* in males (31.6%) was more prevalent than females (7.3%). It was also reported by Sattar *et al.*, [28], in Pakistan that men were more susceptible to uropathogenic *K. pneumoniae*. However, other studies reported that females were more susceptible to be infected with uropathogenic *Klebsiella spp* than males [19,29].

In his study the age range of 1-9 years was the highest prevalence rate of *K. pneumoniae* infection (29.2%), followed by 30-39 years (26.2%), and 40-49 years (15.4%), while the lowest rate was the age 20-29 years (3.08%). This result disagrees with a study by Nirwati *et al.*, [30] and Yang and Zhang [31] which revealed that most *K. pneumoniae* were abundant in people within the age group of 18-65 and 40-65 years old respectively. Yang and Zhang [31] found that the highest rate of this pathogen was at the age group above 70 years. While, Magliano *et al.*, [19] revealed no significant differences in rates within the age groups. Age-related differences in people could be due to their immune system response.

The rapid emergence of resistant bacteria is occurring worldwide, had endangering the efficacy of antibiotics [32-33]. A great interest to *K. pneumoniae* is due to the rise in the UTI infections and increase their resistance to antibiotics. [34].

Empirical antibiotic therapy selection is based upon an integration of most likely pathogens and local antimicrobial susceptibility patterns. [35, 36].

In this study, the pattern of antibiotic sensitivity of *K. pneumoniae* revealed that all isolates were multidrug-resistant to at least some commonly prescribed antibiotics. The *K. pneumoniae* susceptibility was 86.2% (56/65) to Meropenem which belonged to Carbapenem group of antibiotics making them optimal options for the empiric treatment of UTIs. However, the overuse of these drugs will inevitably lead to selection pressure [37]. For Levofloxacin was 73.8% (48 /65), For the Nitrofurantoin group, Nitrofurantoin also found to be effective against *K. pneumoniae* isolates with the efficacy of 69.2% (45/65). On the other hand, the *K. pneumoniae* isolates showed high resistance against Tetracycline 70.8% (46/65), Trimethoprim-Sulfamethoxazole 69.2% (45/65), Cefixime 66.2% (43/65), Nalidixic acid 61.5% (40/65). Gentamicin, Cefotaxime 60% (39/65), Azithromycin 55.4% (36\65). A comparable result was shown in number of other studies in terms of resistance trends of *Klebsiella* species in urinary isolates.

## CONCLUSION

In conclusion in this study we observed the prevalence of UTIs was 33.07%. Females were significantly more susceptible to UTIs than males. The age group of 1-9-year were more prevalent to UTIs. *K. pneumoniae* represented 23.9% of the isolated urinary bacteria. Males were more susceptible to uropathogenic *K. pneumoniae* than females. A high prevalence of *K. pneumoniae* was observed in the age group of 1-9 years. The study revealed Meropenem as the most effective antibiotic for the treatment of UTI. Finally, this study emphasizes the increasing issue of antibiotic

resistance in *K. pneumoniae*, with notable resistance toward the most commonly used antibiotics. So, we must diffuse awareness about the causes of UTI, and more accurate testing is required to improve antibiotic usage and decrease the incorrect therapy.

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