NORTHWESTERN MEDICAL JOURNAL

Northwestern Med J. 2024;4(2):64-69
DOI: 10.54307/NWMJ.2024.108

RESEARCH ARTICLE

Antibiotic resistance rates of *Klebsiella pneumoniae* strains isolated from urine cultures

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Cite as: Aytaç Ö. Antibiotic resistance rates of *Klebsiella pneumoniae* strains isolated from urine cultures. Northwestern Med J. 2024;4(2):64-69.

ABSTRACT

Aim: Our study aimed to determine the antibiotic resistance rates of *K. pneumoniae* by retrospectively examining the results of urine culture samples studied in our laboratory.

Methods: Urine samples with *K. pneumoniae* growth, sent to our laboratory from various wards, outpatient clinics, and intensive care units between July 1, 2018 and December 31, 2022 were included in the study and retrospectively examined.

Results: The antibiotic to which *K. pneumoniae* was most resistant was cefixime (53.3%), and the antibiotic to which it was least resistant was imipenem (12.1%). While the lowest resistance rates were observed in the samples of outpatients, the highest resistance rates were observed in the samples of ward patients and to cefixime (81%), amoxicillin clavulanic acid (AMC) (80%), trimethoprim-sulfamethoxazole (TMT/SXT) (74.8%), and ciprofloxacin (72.1%). Ertapenem (48.9%), meropenem (50.2%) and piperacillin-tazobactam (PRP) (57.3%) resistance was found to be higher in intensive care patients.

Conclusion: Although fluctuations in resistance rates have been observed over the years, resistance rates have generally been found to be high for antibiotics frequently used in the empirical treatment of urinary tract infections. Re-adjusting treatment according to culture results and keeping resistance rates in mind for empirical treatment will be important for treatment success.

Keywords: antibiotic resistance, *Klebsiella Pneumoniae*, urine cultures

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Received: 15.09.2023 **Accepted:** 14.12.2023 **Published:** 30.04.2024

INTRODUCTION

Klebsiella pneumoniae (*K. pneumoniae*) is an important Gram-negative bacterium causing hospital-acquired infections associated with septicemia, pneumonia, and urinary tract infections (1). The Centers for Disease Control and Prevention (CDC) reported in 2019 that the multi-resistance seen in *Acinetobacter baumannii* (43.6%), *K. pneumoniae* (15.6%), *Escherichia coli* (*E. coli*) (7.3%), and *Pseudomonas aeruginosa* (3.9%) was concerning (2). Today, the increase in multi-resistance in bacteria has become an important public health problem, especially in hospital environments, as resistant strains are increasingly spreading in our globalized world (3). According to data from a study published in the Lancet in 2022, based on predictive statistical modeling, *K. pneumoniae* ranks third in deaths associated with antimicrobial resistance. *K. pneumoniae* ranks second in deaths attributed to antimicrobial resistance, and according to this study, the rate of carbapenem-resistant *K. pneumoniae* in Türkiye was reported to be 20–30% (4).

Urinary tract infections (UTI) are currently the most common bacterial infections across all age groups, both within and outside hospital settings (5). Although many bacterial species and fungi cause urinary tract infections, *E. coli* and *Klebsiella* spp. are reported to cause approximately 90% of these infections (6). According to the European Association of Urology Guidelines on Urological Infections, antibiotics with resistance above certain rates are not suitable for use in empirical treatment (7). Therefore, to determine the appropriate antibiotic to be used in empirical treatment, the change over the years and the status of the antibiotic resistance rates of *K. pneumoniae*, which is found to be the most common causative agent of urinary tract infections after *E.coli*, in our region, must be well known. This study aimed to determine the antibiotic resistance rates of *K. pneumoniae* by retrospectively analyzing the results of urine culture samples from patients admitted to our hospital.

METHODS

Urine samples with *K. pneumoniae* growth sent to our laboratory from various wards, outpatient clinics, and intensive care units between July 1, 2018 and December 31, 2022 were included in the study and examined retrospectively. Urine samples were plated on blood agar and eosin methylene blue (EMB) agar (Oxoid, Basingstoke, United Kingdom) media with a quantitative method using loops capable of holding 0.01 ml of urine and incubated at 37 C in an aerobic environment for 18-24 hours. Identification and antibiotic susceptibility tests were performed on samples with bacterial growth of 100,000 cfu/ml and above and on samples with lower numbers of microorganisms thought to be the causative agent by taking into account characteristics such as the number of colonies grown, the number of species, the presence of leukocytes in the urine sample, and the clinical condition of the patient. Identification of microorganisms and antibiotic susceptibility tests were performed using the VITEK 2 Compact system (bioMérieux-France). Antibiotic susceptibility tests were evaluated according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (8). Extended-spectrum beta-lactamase (ESBL) confirmation tests could not be conducted, which is a limitation of our study; consequently, potential rates were reported based on the results obtained from the automated identification system.

Approval for this study was obtained from Fırat University Faculty of Medicine Non-Interventional Clinical Ethics Committee (Decision No: 04-18 Date: 17.03.2022). The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

In our study, significant growth was detected in 20.1% (5,877) of a total of 29218 patients who were admitted to the outpatient clinic and were requested a urine culture. *K. pneumoniae* was detected in 14.1% (830) of the patients whose samples showed growth (Table 1). Among the patients with *K. pneumoniae*, 60% (498) were female and 40 % (332) were male. The mean age of outpatients with *K. pneumoniae* was 27.00±27.57 years.

In our study, a total of 10,093 urine culture samples were sent to our laboratory from the wards. Growth was detected in 11.9% (1200) of these samples.

Table 1. *K. pneumoniae*-detected sample distribution by ward and time period N (%).

	2018 (last six months)	2019	2020	2021	2022	Total
Ward	18 (16.5)	99 (21.1)	39 (14.0)	64 (17.2)	85 (16.3)	305(17.4)
Intensive Care	24 (22.0)	152 (32.5)	136 (48.7)	113 (30.4)	188 (36.2)	613(35.1)
Outpatient Clinic	67 (61.5)	217 (46.4)	104 (37.3)	195 (52.4)	247 (47.5)	830(47.5)
Total	109	468	279	372	520	1748

K. pneumoniae was detected in 25.4% (305) of the patients whose samples showed growth (Table 1). Of the patients with *K. pneumoniae*, 54.1% (165) were female and 45.9% (140) were male. The mean age of the ward patients with *K. pneumoniae* was 61.74±27.16 years.

In our study, a total of 9564 urine culture samples were sent to our laboratory from intensive care units. Growth was detected in 22.3% (2128) of these samples, and *K. pneumoniae* was detected in 28.8% (613) of these samples (Table 1). Of the patients with *K. pneumoniae*, 62.8% (385) were female and 37.2 % (228) were male. The mean age of intensive care unit patients with *K. pneumoniae* was 69.34±31.18 years.

The antibiotic to which *K. pneumoniae* was most resistant was cefixime (53.3%), and the antibiotic to which it was least resistant was imipenem (12.1%). When the resistance rates by year were analyzed, it was found that even though the highest resistance rates for the majority of antibiotics were detected in 2020, resistance rates fluctuated over time (Figure 1).

When the resistance rates were evaluated by clinics, it was found that while the resistance rates were the lowest in the samples of outpatients, the highest resistance to antibiotics was in ward patients and to cefixime (81%), amoxicillin clavulanic acid (AMC) (80%), trimethoprim-sulfamethoxazole (TMT/SXT) (74.8%), and ciprofloxacin (72.1%). Ertapenem (48.9%), meropenem (50.2%), and piperacillin-tazobactam (PRP) (57.3%) resistance were higher in intensive care unit patients (Figure 2).

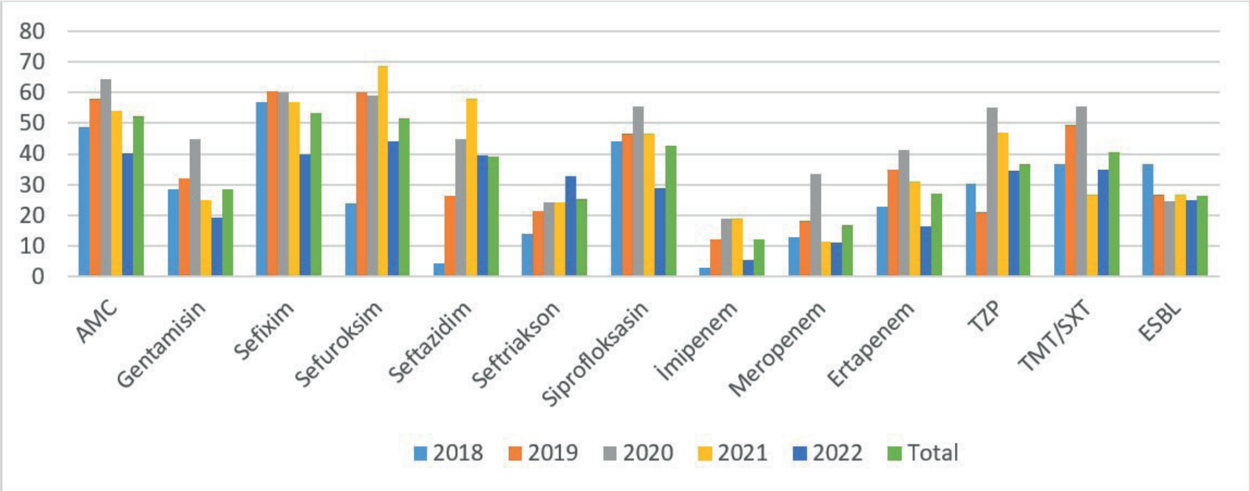

Figure 1. Resistance profile of Klebsiella spp. isolates from urine cultures to different antibiotics by year (%).

AMC: Amoxicillin-clavulanate; TZP: Piperacillin-tazobactam; TMP-SXT: Trimethoprim-sulfamethoxazole; ESBL: extended-spectrum beta lactamase.

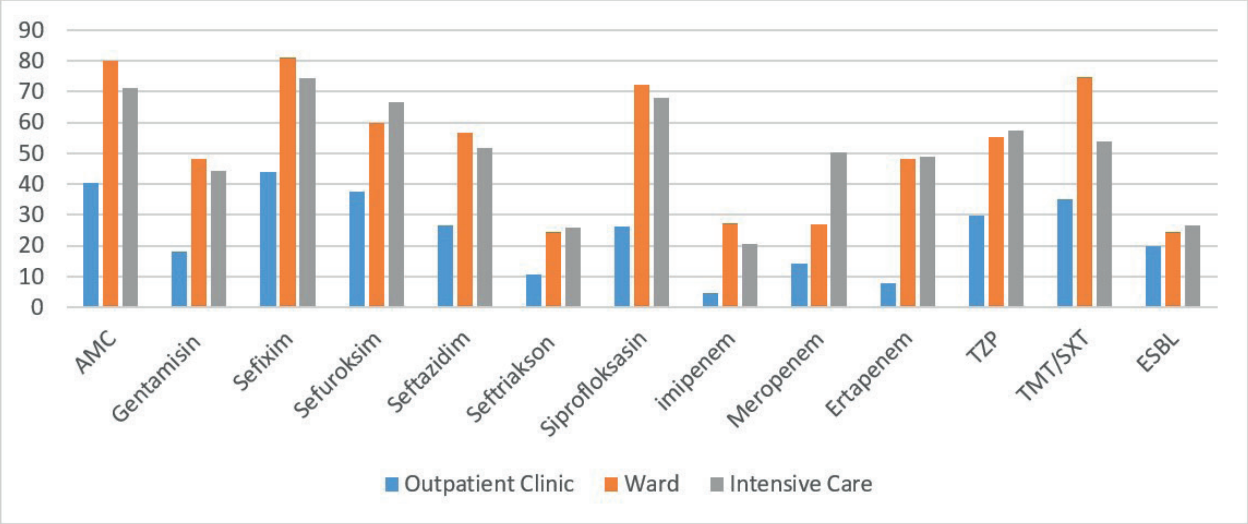

Figure 2. Resistance profile of *Klebsiella* spp. strains isolated from urine culture to various antibiotics by clinics (%).

AMC: Amoxicillin-clavulanate; TZP: Piperacillin-tazobactam; TMP-SXT: Trimethoprim-sulfamethoxazole; ESBL: extended-spectrum beta lactamase.

DISCUSSION

UTIs, which affect 150 million people worldwide every year, are among the most common infectious diseases (9). The distribution of infectious agents and profiles of antibiotic resistance may vary regionally. Additionally, resistance rates in the same region may also change over time. Having a good command of local epidemiologic data and knowing antibiotic resistance rates are important for rational antibiotic use (10). It would therefore be beneficial for centers to conduct research on infectious agents and antibiotic resistance rates in their regions.

K. pneumoniae isolates are emerging as community- and hospital-acquired infectious agents with various antibiotic resistance mechanisms. Antibiotic treatment poses a significant problem as *K. pneumoniae* isolates become fully resistant by producing ESBL, high-level AmpC beta-lactamase, carbapenemase, and oxacillinase due to multi-resistant strains, which are especially prevalent in intensive care patients (11).

According to the results of our study, *K. pneumoniae* strains exhibited the lowest level of resistance to carbapenems. Ertapenem was the carbapenem with the highest resistance throughout all years. Meropenem (50.2%) was the most resistant carbapenem among intensive care unit patients when analyzed by ward. According to World Health Organization data for 2021, the percentage of invasive *K. pneumoniae* isolates resistant to carbapenems (imipenem/meropenem) was between 10% and 25% in Türkiye (12). According to National Antimicrobial Resistance Surveillance System (NAMDSS) 2014 data, the level of carbapenem resistance in invasive *K. pneumoniae* strains is 15% (13). In our study, although carbapenem resistance varied over time, ertapenem (41.2%) and meropenem (33.3%) resistance rates were the highest in 2020. Although carbapenem group antibiotics generally exhibited the lowest resistance rates, the fact that carbapenem resistance was significantly higher in 2020 than in other years may be attributable to the increased use of carbapenems, particularly in wards and intensive care units, as a result of the COVID-19 pandemic.

The Infectious Diseases Society of America recommends quinolones, fosfomycin, trometamol, or nitrofurantoin as first-line treatment for UTI if the regional resistance rate is above 20% and trimethoprim-sulfamethoxazole if it is below 20% (14,15). The resistance rates to ciprofloxacin, trimethoprim sulfamethoxazole, and AMC, which are frequently preferred in the treatment of community-acquired UTIs, were 26.1%, 35.1%, and 40.4%, respectively, in outpatient, and 72.1%, 74.8%, and 80%, respectively, in ward patients. Similar rates were found in other studies conducted for ciprofloxacin, trimethoprim sulfamethoxazole, and AMC in outpatients (16-18). It would be beneficial to avoid these antibiotics in empirical treatment due to high resistance rates.

While antibiotic resistance has been an important problem for hospital-acquired infections, it has also become an important problem for community-acquired agents (19). With their resistance mechanisms, gram-negative ESBL-positive bacteria develop resistance to several antibiotic groups. Studies have shown an increase in ESBL rates over the years. According to the results of a review of 101 articles published in Türkiye, the ESBL rate was reported to be 8.09% in 1996–2001, 10.61% in 2002–2007, and 28.17% in 2007–2012 (20,21). In a study conducted in Türkiye between 2018 and 2019, the ESBL type resistance rate was reported to be 40-47% in *Klebsiella* spp and E. coli strains isolated from community-acquired UTIs (6). In another study conducted between 2020 and 2021, 84.63% of the 423 *K. pneumoniae* isolates examined were ESBL-positive (22). In our hospital, there were no significant changes in ESBL rates, and the average rate was determined to be 26.4%. However, as a limitation of our study, extended-spectrum beta-lactamase (ESBL) confirmation tests could not be performed, and potential rates were reported according to the results obtained from the automated identification system.

CONCLUSION

In conclusion, this study emphasizes that the rational use of antibiotics is very important, that local epidemiological data should be closely monitored, and that necessary precautions should be taken. Moreover, it should be kept in mind that reassessing each treatment according to the antimicrobial susceptibility profile plays a crucial role in both increasing treatment success and decreasing resistance rates due to the high resistance rates of antibiotics frequently used in the empirical treatment of UTIs.

Ethical approval

This study has been approved by the Fırat University Non-invasive Research Ethics Committee (approval date 17/03/2022, number 2022/04-18). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: ÖA; Concept: ÖA; Design: ÖA; Data Collection or Processing: ÖA; Analysis or Interpretation: ÖA; Literature Search: ÖA; Writing: ÖA. The author reviewed the results and approved the final version of the article.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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