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Original Article

Carbapenem resistance profile of *Escherichia coli* and *Klebsiella pneumoniae* in our hospital

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ABSTRACT

Aims: This study aimed to evaluate the resistance rates of *Escherichia coli (E. coli)* and *Klebsiella pneumoniae (K. pneumoniae)* strains isolated from hospitalized patients in our hospital between 2011 and 2014 against carbapenem antibiotics.
Methods: A total of 5266 *E. coli* and 1360 *K. pneumoniae* strains isolated from different clinical samples were included in the study. Identification and antibiotic susceptibility tests were performed using the BD Phoenix 100 (Becton Dickinson, USA) automated system. Carbapenem resistance rates were evaluated according to imipenem, meropenem and ertapenem resistance.
Results: Carbapenem resistance was detected at a higher rate in *K. pneumoniae* strains compared to *E. coli* both bacteria were most frequently isolated from internal medicine ward and urine samples. Ertapenem stood out as the most resistant antibiotic. An increasing trend in carbapenem resistance was noted throughout the study.
Conclusion: The increasing carbapenem resistance observed in *K. pneumoniae* strains necessitates the development of more careful and effective strategies regarding antibiotic use in the management of nosocomial infections.
Keywords: Antibiotic resistance, *Enterobacteriaceae*, Carbapenem

INTRODUCTION

Escherichia coli (E. coli) and *Klebsiella pneumoniae (K. pneumoniae)* are the most common causative agents of urinary tract, respiratory tract and bloodstream infections worldwide. They can spread rapidly among patients in hospital settings and cause hospital outbreaks if appropriate prevention and control measures are not taken.[1] Increasing resistance mechanisms in *Enterobacteriaceae* members and rapid spread of resistant strains pose a problem for clinicians in the treatment of infections caused by these species. Carbapenem group antibiotics are one of the most preferred antibiotic groups in the treatment of these infections.[2] However, today, bacteria have acquired resistance to carbapenems thanks to the carbapenemase enzymes they synthesize, and as a result, this leads to treatment difficulties in infections caused by *Enterobacteriaceae*.[3]

The most important mechanism for gram-negative bacteria to develop resistance to beta-lactam antibiotics is beta-lactamase production.[4] The production of extended-spectrum beta-lactamases (ESBL) in the *Enterobacteriaceae* family, especially in *E. coli* and *K. pneumoniae*, is of great clinical and microbiological importance because they hydrolyze penicillins and broad-spectrum cephalosporins.[5] Globally, nosocomial infections caused by multidrug-resistant *E. coli* and *K. pneumoniae* pathogens are associated with the highest risk of mortality and cause high treatment costs.[6]

The aim of this study was to determine the frequency and antibiotic resistance rates of *E. coli* and *K. pneumoniae* strains isolated from various clinical samples from inpatients in our hospital and to contribute to the correct use of antibiotics by monitoring antibiotic resistance.

METHODS

This study was produced from a master's thesis titled "Carbapenem resistance status in *Escherichia coli* and *Klebsiella pneumoniae* bacteria in our hospital" conducted at Sivas Cumhuriyet University, Institute of Health Sciences. Before starting the study, written permission was obtained from the Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 19.02.2016, Decision No: 2016-02/10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In our study, *E. coli* and *K. pneumoniae* isolates from the cultures of various clinical samples sent to the Microbiology Laboratory of Sivas Cumhuriyet University Medical Faculty Application and Research Hospital during the four-year period between 2011-2014 were retrospectively analyzed. BACTEC (Becton Dickinson, USA) fully automated blood culture systems were used for the study of blood culture samples. For the cultivation of all samples, 5% sheep blood agar and eosin methylene blue (EMB) agar media were used and petri dishes were incubated at 36+1°C for 24-48 hours. Phoenix™100 automated identification system (BD Phoenix System, Beckton Dickinson, USA) was used for species level

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identification of *Enterobacteriaceae* isolates determined by conventional methods such as colony morphology, gram staining, carbohydrate and citrate utilization, urease test. In-vitro antibiotic susceptibilities of bacteria were studied with the Phoenix™100 automated identification system (BD Phoenix System, Beckton Dickinson, USA) used for identification according to Clinical and Laboratory Standards Institute (CLSI) criteria. The first isolate identified from each patient was evaluated.

Statistical Analysis

The data of the study were transferred to the SPSS 22.0 package program in computer environment and data control and analysis were performed in this program. In statistical evaluation, descriptive values were given as mean and (%) percentages.

RESULTS

In our study, 174707 various clinical samples sent to the laboratory from outpatient clinics and clinics of Sivas Cumhuriyet University Hospital between 2011-2014 were cultured.

Antimicrobial resistance tests were performed on 29355 (16.80%) bacteria isolated from these cultures and thought to be possible infection agents.

When the distribution of *E. coli* and *K. pneumoniae* bacteria isolated from the samples delivered from outpatient clinics/clinics was analyzed according to clinical samples, it was observed that the most common bacterial isolation was in urine, followed by wound swab, blood, respiratory secretions, vaginal swabs, abdominal specimens, sterile fluids (pleural, thoracentesis and paracentesis), abscess swabs and other specimens (Table 1).

Table 1. Distribution of *E. coli* and *K. pneumoniae* bacteria isolated from various clinical samples between 2011 and 2014

	Bacteria type		
Sample type	***E. coli* n (%)**	***K. pneumoniae* n (%)**	**Total n (%)**
Urine	3648 (82.6)	766 (18.4)	4414 (66.6)
Wound swab	387 (81.1)	90 (18.9)	477 (7.20)
Blood	326 (69.8)	141 (30.2)	467 (7.1)
Respiratory secretion	200 (52.1)	184 (47.9)	384 (5.8)
Vaginal swab	230 (83.9)	44 (16.1)	274 (4.1)
Abdominal region	89 (92.7)	7 (7.3)	96 (1.5)
Sterile liquids	48 (78.7)	13 (21.3)	61 (0.9)
Abscess swab	44 (91.7)	4 (8.3)	48 (0.7)
Other	294 (72.6)	111 (27.4)	405 (6.1)
Total	5266 (79.5)	1360 (20.5)	6626

E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae

When the distribution of isolated *E. coli* and *K. pneumoniae* bacteria according to the services was examined, it was seen that the most frequently isolated service was internal medicine service, followed by pediatrics+newborn service, urology, obstetrics and gynecology, ICU, general surgery, neurology, infection, emergency department, other (Table 2).

When the resistance and susceptibility of *E. coli* isolates to ertapenem, imipenem and meropenem between 2011-2014 were analyzed, the changes in resistance rates against these antibiotics were found to be significant (Table 3).

Table 2. Distribution of isolated *E. coli* and *K. pneumoniae* bacteria according to wards between 2011-2014

	Bacteria type		
Wards	***E. coli* n (%)**	***K. pneumoniae* n (%)**	**Total n (%)**
Internal medicine	1147 (81.6)	259 (18.4)	1406 (21.2)
Pediatrics+newborn	1002 (76.7)	305 (23.3)	1307 (19.7)
Urology	798 (86.7)	122 (13.3)	920 (13.9)
Obstetrics and gynecology	411 (86.9)	68 (13.1)	479 (7.2)
ICU	283 (66.4)	143 (33.6)	426 (6.4)
General surgery	358 (85.6)	60 (14.4)	418 (6.3)
Neurology	179 (68.6)	82 (31.4)	261 (3.9)
Infection	164 (87.7)	23 (12.3)	187 (2.8)
Emergency department	157 (84.4)	29 (15.6)	186 (2.8)
Other	767 (74.0)	269 (26.0)	1036 (15.6)
Total	5266 (79.5)	1360 (20.5)	6626

E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae, ICU: Intensive care unit

Table 3. Carbapenem resistance status of *E. coli* isolates between 2011-2014

	Years					
Antibiotics	**2011**	**2012**	**2013**	**2014**	**Total**	**p**
Ertapenem	45/1393 (3.23%)	31/1288 (2.40%)	65/1161 (5.59%)	59/1403 (4.20%)	200/5245 (3.81%)	p=0.003*
Imipenem	0/1393 (0.0%)	1/1288 (0.07%)	39/1161 (3.35%)	47/1403 (3.34%)	87/5245 (1.65%)	p=0.001*
Meropenem	0/1393 (0.0%)	0/1288 (0.0%)	4/1161 (0.34%)	32/1403 (2.28%)	36/5245 (0.68%)	p=0.001*

E. coli: Escherichia coli, *p<0.05 important

The changes in resistance against *K. pneumoniae* isolates between 2011 and 2014 were significant for ertapenem and imipenem, whereas the difference for meropenem was not statistically significant (Table 4).

Table 4. Carbapenem resistance status of K. pneumoniae isolates between 2011-2014

	Yıllar					
Antibiyotik	**2011**	**2012**	**2013**	**2014**	**Toplam***	**p**
Ertapenem	60/379 (15.83%)	13/339 (3.83%)	40/291 (13.74%)	32/349 (9.16%)	145/1358 (10.67%)	p=0.001*
Imipenem	16/379 (4.22%)	3/339 (0.88%)	18/291 (6.18%)	26/349 (7.44%)	63/1358 (4.63%)	p=0.001*
Meropenem	17/379 (4.48%)	0/339 (0.0%)	10/291 (3.43%)	19/349 (5.44%)	46/1358 (3.38%)	p=0.233

*p<0.05 important

DISCUSSION

Antimicrobial resistance (AMR) has been reported by the World Health Organization as one of the top 10 global public health threats facing humanity.[7] Antibacterial resistance may develop through different mechanisms. Some microorganisms have the potential to be resistant to multiple drugs by harboring several mechanisms. The emergence of multidrug-resistant gram-negative enteric bacteria poses a major problem in the management of both nosocomial and community-acquired infections.[8] Like *E. coli*, *K. pneumoniae* is a common cause of urinary, respiratory tract and bloodstream infections and can be easily transmitted, leading to the risk of nosocomial outbreaks.[9]

In a study covering four years in Turkiye, it was reported that carbapenem-resistant *K. pneumoniae* isolates were mostly isolated from urine (45.1%), blood (25.8%) and respiratory tract samples (18.5%), while carbapenem-resistant *E. coli* isolates were isolated from urine (71.0%), blood (15.0%) and wound (7.0%) samples.[10] Duran et al.[11] also reported that 56.8% of *E. coli* strains were isolated from urine, 16.7% from endotracheal aspirate (ETA), 16.5% from blood and 6.8% from wound specimens; 37.1% of *K. pneumoniae* strains were isolated from urine, 32.7% from ETA, 19.3% from blood and 5.4% from wound specimens. In accordance with these studies, the most common isolations of both bacteria were isolated from urine, blood, wound site and respiratory specimens.

In a study conducted in our country, the distribution of carbapenem-resistant *K. pneumoniae* strains according to clinics was determined as internal medicine wards (40%), intensive care units (36.0%), surgical wards (15.0%), and pediatric wards (9.0%). In the same study, it was emphasized that there was an increasing resistance (from 0.6% to 14.2%) in *K.pneumoniae* bacteria between years (2012-2020). In the study conducted by Telli,[12] similar results to our study were found and it was observed that the most frequently isolated wards of both bacteria were internal medicine wards and there was an increasing resistance in *K. pneumoniae* bacteria.

Between 2019 and 2023, carbapenem-resistant *K. pneumoniae* showed the largest increase (+2.9%) in the European Union/European Economic Area (EU/EEA) population-weighted average AMR percentage of all bacterial-antibiotic combinations under EARS-Net surveillance.[13]

Referring to isolates obtained in 2021, it was emphasized that resistance to carbapenems reported to AMR surveillance networks was higher in *K. pneumoniae* than in *E. coli*. For *K. pneumoniae*, out of 45 countries in the WHO European region, 14 (31%) reported AMR percentages below 1%, 15 (33%) equal to or above 25% and eight (18%) equal to or above 50% (Belarus, Georgia, Greece, Moldova, Romania, Russia, Serbia and Ukraine). For *E. coli*, percentages were also reported to be generally low in the northern and western parts of the WHO European Region. Eight out of 44 countries (18%) (Belarus, Cyprus, Georgia, Greece, Russia, Serbia, Turkey and Ukraine) reported percentages of 1% or higher in 2021, with the remaining countries reporting <1% (9).

In a multicenter study conducted by Süzük et al.[14] in our country, *K. pneumoniae* resistance rates were reported to be higher than *E. coli*. For *E. coli*, ertapenem, imipenem and meropenem resistance rates were 25.2%, 17.3% and 17.3%, respectively. In the same study, it was reported that ertapenem, imipenem and meropenem resistance rates for *K. pneumoniae* were 58.2%, 48.6% and 51.9%, respectively. In the study by Tümtürk et al.[15] the carbapenem resistance rate among *E. coli* strains was found to be 7.5% in 2017, compared to 4.1% in 2014. While the carbapenem resistance rate among *K. pneumoniae* strains was 32.2% in 2014, this rate increased to 48.9% in 2017. In 2017, it was determined that the resistance rate continued to increase. In a 2021 meta-analysis, it was reported that the carbapenem resistance rate was 16.6% for *E. coli* and 34.9% for *K. pneumoniae*.[16] Consistent with our study, higher resistance rates to carbapenem antibiotics were found in *K. pneumoniae* compared to *E. coli*. At the same time, it is noteworthy that the resistance rates increased as the years progressed.

Carbapenem resistance is usually caused by carbapenemase production and mechanisms such as efflux pump, impermeability, AmpC or ESBL production are reported to be involved in resistance development.[17] ESBL were first reported in Germany in 1983, just after the introduction of broad-spectrum beta-lactam antibiotics against *K. pneumoniae* species.[18] *K. pneumoniae* and *E. coli*, members of *Enterobacterieceae*, have been reported to possess genes encoding the enzyme extended-spectrum beta-lactamase (ESBL).[19] In a study conducted by Orak et al.[20] in 2023, 40.7% OXA-48, 31.5% MBL and 22.3% ESBL were detected in carbapenem resistant *E.coli* and *Klebsiella* spp. isolates. In a study conducted in Turkiye in 2025, it was reported that *E. coli* isolates were resistant to ertapenem, imipenem and meropenem by 1.0%, 1.0% and 10.0%, respectively, and 48% (n=28) of the isolates had ESBL. In the same study, it was reported that 49.0%, 49.0% and 54.0% of *K. pneumoniae* isolates were resistant to ertapenem, imipenem and meropenem, respectively, and ESBL was detected in 80.0% (n=37) of the isolates.[21]

Limitations

This study has several limitations. Firstly, as it is a retrospective design, it is based on tests performed in a specific time interval for complete and accurate data collection. Furthermore, only carbapenem group antibiotics were analyzed and clinical findings and other antibiotic groups were not evaluated. In addition, the data obtained from a specific geographical region in our study may be insufficient to reflect the overall carbapenem resistance.

CONCLUSION

In conclusion, we retrospectively analyzed the resistance data of *E. coli* and *K. pneumoniae* bacteria against carbapenem group antibiotics. These resistance data are regionally important in terms of the start of correct empirical treatment and effective treatment results. In our hospital and current studies, an increasing resistance is observed especially in *K. pneumoniae* bacteria. We believe that determination of beta-lactamase enzymes both retrospectively and by molecular and genotypic methods is extremely important for more accurate antibiotic selection and monitoring of effective treatment methods.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 19.02.2016, Decision No: 2016-02/10).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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