

Evaluation of carbapenem resistance genes in carbapenem-resistant Enterobacteriaceae isolates with GeneXpert® Carba-R panel

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Abstract

Introduction: Early detection of increases in carbapenem resistance among Enterobacteriaceae infections due to the widespread use of antibiotics is crucial. This study aimed to identify carbapenemase resistance genes in carbapenem-resistant Enterobacteriaceae isolates using the GeneXpert Carba-R Panel (Cepheid, Sunnyvale, USA).

Methodology: A total of 120 carbapenem-resistant Enterobacteriaceae isolates collected between January and June 2022 at the Microbiology Laboratory of Erzincan Mengücek Gazi Training and Research Hospital were included. The samples were cultured, and then incubated at 37 °C for 24–48 hours. Species-level identification and carbapenem resistance were determined using the VITEK MS and VITEK 2 automated systems (bioMérieux, Marcy l'Étoile, France). Carbapenemase gene detection was performed using the GeneXpert Carba-R assay, and antibiotic susceptibility testing was conducted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (version 12.0, 2022) using the VITEK 2 system.

Results: The most common carbapenemase genes detected were *bla_{OXA-48}* (65.0%), *bla_{KPC}* (14.2%), *bla_{NDM}* (4.2%), and *bla_{VIM}* (1.7%). Additionally, combinations of resistance genes were observed in 3.3% (*bla_{VIM}* + *bla_{OXA-48}* + *bla_{KPC}*), 2.5% (*bla_{OXA-48}* + *bla_{KPC}*), and 0.8% (*bla_{VIM}* + *bla_{KPC}*) of isolates. *Klebsiella pneumoniae* was the most frequently isolated species (116). All the isolates were resistant to ertapenem. The most effective antibiotics were colistin, imipenem, amikacin, and trimethoprim-sulfamethoxazole, in descending order of effectiveness.

Conclusions: The findings provide essential insights into alternative treatment options and surveillance of resistance to carbapenem-resistant Enterobacteriaceae. The results may also serve as a reference for future comparative studies and aid in developing effective infection control strategies.

Key words: carbapenem; carbapenemase; Enterobacteriaceae; resistance.

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Introduction

Inappropriate and widespread use of antibiotics leads to an increase in antimicrobial resistance, which in turn elevates mortality and morbidity rates and imposes a significant burden on healthcare systems [1]. This problem becomes even more critical in infections caused by resistant bacteria such as Enterobacteriaceae, where treatment options are limited [1].

Carbapenems are considered last-resort antibiotics in the treatment of Enterobacteriaceae-related infections; however, they are gradually losing their effectiveness due to the increasing prevalence of carbapenemase-producing bacteria [2]. Carbapenemases are classified according to the Ambler classification into class A (*bla_{KPC}*), class B metallo-β-lactamases (*bla_{NDM}*, *bla_{VIM}*, *bla_{IMP}*), and class D enzymes (*bla_{OXA-48-like}*) [3,4]. Differences in the molecular and clinical characteristics of these enzymes can influence both treatment strategies and diagnostic method performance. Considering these differences,

carbapenem-resistant Enterobacteriaceae (CRE) are categorized as carbapenemase-producing (CPE) and non-carbapenemase-producing strains, with CPE strains representing a greater clinical threat due to their ability to spread via horizontal gene transfer [5].

From a clinical perspective, delayed administration of appropriate antimicrobial therapy in critically ill patients is directly associated with increased mortality, and each hour of delay has been reported to increase the risk of death by approximately 20% [6]. Therefore, rapid and accurate detection of carbapenemase-producing bacteria is crucial for effective clinical management.

The commonly used phenotypic methods for detecting carbapenemases in clinical microbiology laboratories include the modified Hodge test (MHT), the carbapenem inactivation method (CIM/mCIM), and the Carba NP test. A study by Kuchibiro *et al.* showed that the diagnostic performance of MHT varies depending on the type of carbapenemase [7], while a

meta-analysis by Zhong *et al.* demonstrated that MHT has lower sensitivity for Ambler class B carbapenemases (*bla*_{NDM}, *bla*_{VIM}, *bla*_{IMP}) and higher performance for class A carbapenemases (*bla*_{KPC}) [8]. The carbapenem inactivation method (CIM), similar to MHT, generally requires overnight incubation and has been reported to be insufficient in detecting *bla*_{OXA-48} and *bla*_{NDM}-producing isolates [9,10]. Moreover, the commonly used phenotypic carbapenemase confirmation tests (e.g., CIM, MHT) are limited by their relatively long turnaround times [11]. The Carba NP test is considered advantageous for its approximately 2-hour turnaround time, compared with the other phenotypic methods. However, its sensitivity has been reported to range from 73% to 100% [12,13], and it has reduced sensitivity to *bla*_{OXA-48-like} carbapenemases, which are endemic in Türkiye. It is also costlier due to reagent requirements [14,15].

Genotypic methods for detecting carbapenemase genes are considered the gold standard due to their high accuracy. However, their widespread use is limited by high costs, the need for specialized personnel, and the need for advanced laboratory infrastructure [16]. To overcome these limitations, newly developed multiplex polymerase chain reaction (PCR)-based molecular assays offer significant advantages, including shorter turnaround times and the ability to be performed directly on clinical specimens (e.g., rectal swabs and other clinical samples) without the need for prior culture, enabling earlier initiation of infection control measures and targeted therapy [17]. A meta-analysis conducted by Bai *et al.* found that the Xpert Carba-R (Cepheid, Sunnyvale, CA, USA) assay demonstrated high sensitivity, specificity, and overall diagnostic accuracy in detecting carbapenemase-producing organisms in both clinical isolates and rectal swab samples [17]. These findings were supported by a multicenter study by Jin *et al.*, which reported positive and negative percent agreement rates of 99.7% and 98.0%, respectively, along with high reproducibility [18]. Additionally, Li *et al.* reported that the Xpert Carba-R assay achieved very high accuracy in detecting major carbapenemase genes (*bla*_{KPC}, *bla*_{NDM}, *bla*_{VIM}, *bla*_{IMP}, and *bla*_{OXA-48}) [19]. Furthermore, the ability of this assay to provide results within approximately 1 hour represents a significant advantage over conventional phenotypic methods.

In this context, the aim of this study was to detect carbapenemase genes in CRE isolates using the Xpert Carba-R assay, and to evaluate their antibiotic susceptibility profiles.

Methodology

Ethical approval

This study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (Date: 30.12.2021, Decision No: 2021/50).

Sample collection, identification of microorganisms, and antibiotic susceptibility testing

A total of 120 CRE isolates obtained from various clinical samples submitted to the Erzincan Mengücek Gazi Training and Research Hospital Microbiology Laboratory between January and June 2022 were included in the study, and the analysis was limited to these isolates selected based on carbapenem resistance during the study period. Clinical samples were inoculated onto 5% sheep blood agar (bioMérieux, Marcy l'Étoile, France) and EMB agar (bioMérieux, France) and incubated at 37 °C for 24–48 hours. Suspensions in growth media were prepared from pure colonies using sterile physiological serum to a 0.5 McFarland standard, ensuring a count of 1.5×10^8 bacteria per milliliter, and were used for species-level identification of isolates and antibiotic susceptibility testing. Identification of isolates to the species level and antibiotic susceptibility testing were performed using the VITEK MS (bioMérieux, Marcy l'Étoile, France) and VITEK 2 compact automated systems (bioMérieux, Marcy l'Étoile, France), with VITEK 2 AST 420 cards (bioMérieux, Marcy l'Étoile, France) suitable for Gram-negative enteric bacteria. Antibiotic susceptibility test results were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (version 12.0, 2022). Isolates were categorized as susceptible (S), susceptible with increased exposure (I), or resistant (R) [20].

GeneXpert® Carba-R panel

The GeneXpert® system (Cepheid, Sunnyvale, CA, USA) is a real-time PCR-based diagnostic platform that automatically performs sample preparation, nucleic acid extraction, amplification, and detection of target genes. The system uses closed-cartridge technology, reducing the risk of cross-contamination. The Xpert Carba-R panel can detect carbapenemase-associated genes *bla*_{KPC}, *bla*_{NDM}, *bla*_{VIM}, *bla*_{OXA-48}, and *bla*_{IMP}.

Suspension preparation and testing for the GeneXpert® Carba-R panel

A loopful of colonies from a medium containing carbapenem-resistant isolates was transferred to the Xpert sample buffer suspension. The suspension was

vortexed for 10 seconds and prepared according to a 0.5 McFarland turbidity standard. The prepared suspension was transferred to the sample well of the Carba-R cartridge using a disposable pipette. The cartridge was inserted into the GeneXpert® instrument according to the manufacturer's instructions, and results were obtained in approximately 45 minutes.

Results

A total of 120 CRE isolates were included in the study, all selected for carbapenem resistance during the study period (100%). The isolates consisted of 116 *Klebsiella pneumoniae*, 2 *Klebsiella oxytoca*, 1 *Enterobacter cloacae*, and 1 *Escherichia coli*.

Of the patients, 53 were female (44.2%), and 67 were male (55.8%). The overall mean age was 67.95 years, with 69.85 years for females and 66.43 years for males.

Regarding clinical specimen types, most isolates were obtained from urine cultures (46, 38.3%), followed by tracheal aspirates (45, 37.5%) and blood cultures (20, 16.7%). A smaller proportion of isolates was obtained from wound cultures (4, 3.3%) and sputum cultures (2, 1.7%); while pleural fluid, cerebrospinal fluid, and tissue samples each accounted for 1 (0.8%) (Table 1).

Among the 116 *Klebsiella pneumoniae* isolates, carbapenem resistance genes were detected in 110. *bla*_{OXA-48} was detected in 78 (65.0%), *bla*_{KPC} in 17 (14.7%), *bla*_{NDM} in 4 (3.4%), and *bla*_{VIM} in 2 (1.7%). Multiple gene combinations were also observed, including *bla*_{KPC} + *bla*_{OXA-48} + *bla*_{VIM} in 4 (3.4%), *bla*_{KPC} + *bla*_{OXA-48} in 3 (2.6%), *bla*_{NDM} + *bla*_{OXA-48} in 1 (0.8%), and *bla*_{KPC} + *bla*_{VIM} in 1 (0.8%). The carbapenem

Table 1. Distribution of clinical specimen types.

Culture	n	%
Tracheal aspirate	45	37.5
Urine culture	46	38.3
Blood culture	20	16.7
Wound culture	4	3.3
Pleural fluid culture	1	0.8
Sputum culture	2	1.7
Cerebrospinal fluid culture	1	0.8
Tissue culture	1	0.8
Total	120	100.0

resistance genes could not be evaluated in 5 *K. pneumoniae* isolates due to device-related technical errors; and no carbapenem resistance gene was detected in 1 *K. pneumoniae* isolate. In addition, *bla*_{OXA-48} was detected in the *E. coli* isolate and *bla*_{NDM} in the *E. cloacae* isolate, whereas no carbapenem resistance gene was detected in the *K. oxytoca* isolates (Table 2).

Regarding gene distribution by specimen type, *bla*_{OXA-48} was the most frequently detected gene and was identified predominantly in tracheal aspirate cultures (30), urine cultures (26), and blood cultures (16). Isolates carrying *bla*_{KPC} were detected in urine cultures (8), blood cultures (3), and tracheal aspirate cultures (5). Isolates harboring *bla*_{OXA-48} + *bla*_{KPC} + *bla*_{VIM} were obtained from urine cultures (3) and tracheal aspirate cultures (1). Overall, gene-positive isolates were most frequently obtained from urine and tracheal aspirate cultures (Table 3).

Regarding distribution across clinical units, *bla*_{OXA-48} positive isolates were most frequently detected in intensive care units (40 isolates), followed by internal medicine services (30 isolates) and outpatient clinics (8 isolates). Among *bla*_{KPC}-positive isolates, 11 were obtained from intensive care units, 4 from internal

Table 2. Distribution of carbapenem resistance genes according to bacterial species.

Bacterial strain	KPC	KPC, OXA-48	NDM	NDM, OXA-48	NEGATIVE	OXA-48	OXA48, KPC	VIM	VIM KPC	VIM, KPC, OXA-48	Device Error	Total
<i>Klebsiella pneumoniae</i>	17	2	4	1	1	78	1	2	1	4	5	116
<i>Enterobacter cloacae</i>	0	0	1	0	0	0	0	0	0	0	0	1
<i>Klebsiella oxytoca</i>	0	0	0	0	2	0	0	0	0	0	0	2
<i>Escherichia coli</i>	0	0	0	0	0	1	0	0	0	0	0	1
Total	17	2	5	1	4	78	1	2	1	4	5	120

Table 3. Distribution of carbapenemase genes in clinical specimens.

Clinical Specimen	KPC	KPC + OXA-48	NDM	NDM + OXA-48	OXA-48	VIM	VIM + KPC	VIM + KPC + OXA-48	Device error	Negative
Tracheal aspirate	5	2	3	0	30	2	0	1	2	0
Urine culture	8	0	1	1	26	0	0	3	3	4
Blood culture	3	0	0	0	16	0	1	0	0	0
Wound culture	0	0	1	0	3	0	0	0	0	0
Pleural fluid culture	0	0	0	0	1	0	0	0	0	0
Sputum culture	0	1	0	0	1	0	0	0	0	0
Cerebrospinal fluid culture	1	0	0	0	0	0	0	0	0	0
Tissue culture	0	0	0	0	1	0	0	0	0	0

Table 4. Distribution of resistance genes according to clinical units.

Resistance gene	internal medicine services	outpatient clinics	intensive care units	Total
Device Error	2	1	2	5
<i>bla</i> _{KPC}	4	2	11	17
<i>bla</i> _{KPC} , <i>bla</i> _{OXA-48}	1	0	1	2
<i>bla</i> _{NDM}	3	0	2	5
<i>bla</i> _{NDM} , <i>bla</i> _{OXA-48}	1	0	0	1
Negative	0	4	0	4
<i>bla</i> _{OXA-48}	30	8	40	78
<i>bla</i> _{OXA-48} , <i>bla</i> _{KPC}	0	0	1	1
<i>bla</i> _{VIM}	0	0	2	2
<i>bla</i> _{VIM} <i>bla</i> _{KPC}	0	0	1	1
VIM, <i>bla</i> _{KPC} , <i>bla</i> _{OXA-48}	3	0	1	4
Total	44	15	61	120

medicine services, and 2 from outpatient clinics. Similarly, *bla*_{NDM}-positive isolates were detected in internal medicine services (3 isolates) and in intensive care units (2 isolates), whereas *bla*_{VIM}-positive isolates were identified only in intensive care units (2 isolates). Multiple gene combinations were observed in a limited number of isolates and were detected mainly in intensive care and internal medicine units (Table 4).

According to the antibiotic susceptibility tests, resistance was detected in 117 (97.5%) isolates to meropenem, 120 (100%) isolates to ertapenem, and 80 (66.6%) isolates to imipenem; while the highest susceptibility rate was detected in colistin (50 isolates, 41.7%), followed by imipenem (40 isolates, 33.3%), amikacin (30 isolates, 25.0%), and trimethoprim-sulfamethoxazole (26 isolates, 21.7%) (Table 5).

Discussion

Antibiotic resistance remains a growing public health problem worldwide. The rise in antimicrobial resistance complicates the treatment of hospital-acquired infections, leading to increased mortality, morbidity, and healthcare costs. Among the most frequently isolated bacteria in nosocomial infections, Gram-negative enteric bacilli have developed resistance to many antibiotics over time. The most common mechanisms of resistance development are mutations and plasmid-mediated gene transfer.

Carbapenem antibiotics, which have long been recognized as effective in combating resistance, are now becoming less effective due to the production of carbapenemases. In particular, the ability of multidrug-resistant *K. pneumoniae* strains to transfer carbapenemase genes via plasmids to other Gram-negative bacteria facilitates the spread of resistance and contributes to difficult-to-control outbreaks [21].

CRE strains are among the microorganisms identified as "urgent priority threats" by the Centers for Disease Control and Prevention (CDC) [22]. It has been reported that carbapenem resistance genes are most frequently observed in *K. pneumoniae* and *E. coli* [23]. For example, a study conducted by Gupta *et al.* in 2006–2007 found resistance rates of 10.6% in *K. pneumoniae* and 4.0% in *E. coli* [24]. In a similar study, this rate was found to be 5.4% for *K. pneumoniae* [25]. The geographic distribution of carbapenemase genes varies. The *bla*_{KPC} enzyme is reported to be endemic in the USA, Italy, and Greece; the *bla*_{NDM} gene in India, Pakistan, and China; and the *bla*_{OXA-48} in Turkey [26]. The *bla*_{VIM} gene is common in Japan and Taiwan, while the *bla*_{VIM} gene is found in Greece [27,28].

*bla*_{VIM-1} was first described in Italy in 1997. Shortly afterwards, its variant *bla*_{VIM-2} was reported in a *Pseudomonas aeruginosa* isolate in France. In a study by Girlich *et al.* in France, the *bla*_{VIM} gene was identified in 14.2% of cases [29]. *bla*_{VIM-2} is currently

Table 5. Distribution of antibiotic susceptibility and resistance.

Antibiotics	S (susceptible)		I (increased dose susceptible)		R (resistant)	
	n	%	n	%	n	%
Piperacillin-tazobactam (TZP)	2	1.67	0	0	118	98.33
Amikacin (AMK)	30	25.00	0	0	90	75.00
Gentamicin (GEN)	16	13.33	0	0	104	86.67
Ciprofloxacin (CIP)	5	4.17	0	0	115	95.83
Ceftazidime (CAZ)	0	0.00	0	0	120	100.00
Meropenem (MEM)	0	0.00	3	2.50	117	97.50
Imipenem (IPM)	20	16.66	20	16.66	80	66.66
Ertapenem (ETP)	0	0.00	0	0	120	100.00
Colistin (CST)	50	41.7	0	0	10	16.66
Cefepime (FEP)	0	0.00	0	0	120	100.00
Trimethoprim-Sulfamethoxazole (SXT)	26	21.67	0	0	94	78.33
Ampicillin	0	0.00	0	0	120	100.00
Aztreonam	5	4.17	0	0	115	95.83

the most frequently reported metallo- β -lactamase worldwide and is particularly prevalent in Southern Europe and Southeast Asia [30]. In Türkiye, *bla*_{VIM}-type carbapenemases were first identified in *E. cloacae* isolates in 2005. A limited number of bacterial isolates carrying the *bla*_{VIM} gene were reported in subsequent studies [31]. The *bla*_{VIM} gene was reported in Türkiye in 2007 with a rate of 5.8% [32]. In 2015, Demir *et al.* reported its presence in 3.5% of *K. pneumoniae* strains [33]. In 2022, Zarakolu *et al.* detected the *bla*_{VIM} gene in 5 of 82 *K. pneumoniae* strains and in 1 of 30 *E. coli* strains [34]. Taşkın Kafa *et al.* and Süzük Yıldız *et al.* reported a 0.5% prevalence of the *bla*_{VIM} gene in *K. pneumoniae* strains [35,36]. The rates of *bla*_{VIM} gene carriage in Türkiye vary. In this study, the *bla*_{VIM} gene was detected in 2 *K. pneumoniae* strains at a rate of 1.7%, consistent with rates reported in Türkiye.

*bla*_{NDM-1} was first isolated in 2008 from a patient who had previously been hospitalized in New Delhi, India, and subsequently traveled to Sweden. While it is frequently observed in the United Kingdom, India, and Pakistan, various studies have reported that *bla*_{NDM-1} has also been detected in many regions worldwide [2]. *bla*_{NDM} was first identified in Turkey in 2011 in a *K. pneumoniae* isolate isolated from the blood culture of a young patient [37]. The *bla*_{NDM-1} gene, reported by Alp *et al.* in 2012, has also been identified in individuals with no history of foreign travel [38]. Subsequent studies have shown that the *bla*_{NDM} gene has become the second most frequently isolated carbapenemase gene in Türkiye [39–41]. In this study, the *bla*_{NDM} gene was detected at a rate of 4.2%, making it the third most frequently isolated carbapenemase gene. While the rate in this study is generally consistent with the data in literature, it is lower.

*bla*_{KPC} was first identified in a *K. pneumoniae* isolate in the United States in 1996 [42]. Although it was initially reported as endemic in northeastern United States, the *bla*_{KPC} carbapenemase gene was detected within a few years in countries such as Greece, Israel, and China; many studies have reported outbreaks associated with isolates carrying the *bla*_{KPC} gene [2,43]. The presence of the *bla*_{KPC} gene in Türkiye was first reported in 2012 in a *K. pneumoniae* strain isolated from an endotracheal aspirate collected from a female patient who came from Romania [44]. In the following period, studies conducted by Poriel *et al.* in 2013 and Kuşkuçcu *et al.* in 2016 evaluated 22 carbapenem-resistant *Enterobacteriales* isolates, revealing the presence of the *bla*_{KPC} gene in two *K. pneumoniae* strains [45,46].

The *bla*_{KPC} gene was detected in 2 of 24 carbapenem-

resistant *E. coli* isolates obtained from various clinical samples at Istanbul University Cerrahpaşa Faculty of Medicine Hospital between March 2011 and May 2012 [46]. In a 2019 study, Okan *et al.* detected the *bla*_{KPC} gene in 7 of 48 *Enterobacteriaceae* isolates (6 from *K. pneumoniae*, 1 from an *E. coli* strain) [47]. However, some studies have also reported that the *bla*_{KPC} carbapenemase gene was not detected [40]. For example, in a 2014 survey conducted at 18 centers, the *bla*_{KPC} gene was not detected in any of the carbapenem-resistant *E. coli* and *K. pneumoniae* isolates [48]. In contrast, a 2019 multicenter study reported that 16% of carbapenem-resistant isolates contained only the *bla*_{KPC} gene, and 2.8% contained both the *bla*_{NDM} and *bla*_{KPC} genes [36]. In the present study, the *bla*_{KPC} gene was detected in 14.2% of the samples and was the second most frequently isolated carbapenemase gene among 120 samples. This rate is broadly consistent with the results of the 2019 multicenter study and indicates that the *bla*_{KPC} gene continues to spread in Türkiye [36].

The *bla*_{OXA-48} enzyme was first identified in a carbapenem-resistant *K. pneumoniae* isolate from a patient in Istanbul in 2001 [26]. The *bla*_{OXA-48}-like β -lactamases have subsequently spread to all inhabited areas of the world [48,49]. In Türkiye, the distribution of carbapenemase gene types in *E. coli* and *K. pneumoniae* isolates collected from different regions was investigated in the European survey on carbapenemase-producing *Enterobacteriaceae* (EuSCAPE) project, which included isolates from 2013. In this study, at least 1 carbapenemase gene was detected by genotyping 136 isolates. The proportions of isolates carrying a single carbapenemase type were reported as *bla*_{OXA-48} (84.6%), *bla*_{NDM-1} (6.3%), *bla*_{VIM} (2.8%), and *bla*_{IMP} (1.4%). In addition, it was determined that 7 isolates carried 2 distinct carbapenemase genes: *bla*_{OXA-48} + *bla*_{NDM-1} (2.1%), *bla*_{OXA-48} + *bla*_{VIM} (2.1%), and *bla*_{VIM} + *bla*_{NDM-1} (0.7%) [37]. Süzük Yıldız *et al.* conducted a study with isolates collected from 26 different provinces and determined the carbapenemase types as *bla*_{OXA-48} (52.2%), *bla*_{KPC} (16.1%), *bla*_{NDM-1} (15%), *bla*_{OXA-48}+*bla*_{NDM-1} (12.6%), *bla*_{KPC} + *bla*_{NDM-1} (2.8%), and *bla*_{VIM} (0.5%) and *bla*_{OXA-48}+*bla*_{VIM} (0.5%) in 1 isolate each [36]. In the study conducted by Demir *et al.* in 2012, the *bla*_{OXA-48} gene was detected in 49 (86%) of 95 *Enterobacteriaceae* isolates [33].

The most common carbapenemase gene identified in the present study was *bla*_{OXA-48} (65.0%), a finding consistent with the resistance patterns commonly observed in Türkiye. In addition, the *bla*_{KPC} gene was identified at a rate of 14.2%, *bla*_{NDM} at 4.2%, and *bla*_{VIM}

at 1.7%. The detection of multiple gene associations with *bla*_{OXA-48} indicates that spread occurs via plasmids. Previous studies have reported that infections caused by CRE occur mainly in patients hospitalized in intensive care units. In a study conducted by Mermutluoğlu *et al.* in 2023, 663 (64.9%) of 1,022 *K. pneumoniae* isolates were obtained from intensive care patients, 207 (20.2%) from ward patients, and 152 (14.9%) from outpatient clinic patients [50]. Similarly, Zakai *et al.* reported a high prevalence of carbapenem-resistant *Enterobacteriaceae* in intensive care units [51]. In the present study, the distribution of patients among clinical units showed that carbapenem-resistant isolates were most frequently detected in intensive care units (50.8%). This may be associated with increased antibiotic exposure, invasive procedures, and prolonged hospital stays in these units. Significant resistance rates were also observed in internal medicine wards, particularly in palliative care units. In this study, the highest resistance rate among carbapenems was observed for ertapenem (100%), meropenem (97.5%), and imipenem (66.6%). Lunha *et al.* demonstrated that outer membrane porin alterations, together with additional resistance mechanisms, contribute to increased minimum inhibitory concentration (MIC) levels and high-level carbapenem resistance [52]. Similarly, Evans *et al.* reported that *bla*_{OXA-48}-type carbapenemases exhibit lower hydrolytic activity against imipenem and meropenem than against ertapenem [53]. In addition, Wang *et al.* described broad resistance patterns among *bla*_{OXA-48}-producing isolates [54].

Consistent with these findings, resistance to ertapenem was detected in all isolates in the present study, whereas relatively lower resistance rates were observed for imipenem. The high prevalence of *bla*_{OXA-48} may have contributed to the elevated resistance to ertapenem. This finding suggests that, additional mechanisms such as porin alterations, beyond the presence of *bla*_{OXA-48}, may contribute to the observed resistance profile. Furthermore, the relatively limited use of imipenem in the hospital may also have contributed to this difference.

In the present study, colistin demonstrated the highest susceptibility rate (41.7%), followed by imipenem (33.4%), amikacin (25.0%), and trimethoprim–sulfamethoxazole (SXT; 21.7%). In a multicenter study by Süzük Yıldız *et al.*, the resistance rates were 49.7% for ertapenem, 43.0% for meropenem, and 40.6% for imipenem [36]. Similarly, Kazar *et al.* evaluated 185 carbapenem-resistant Enterobacterales isolates and found resistance rates of 94.6% to

ertapenem, 38.2% to imipenem, 33.7% to meropenem, and 80.5% to amikacin [55]. In another study by Mermutluoğlu *et al.*, the most effective antibiotics against *K. pneumoniae* isolates were reported as ceftazidime-avibactam (57%), gentamicin (51%), and amikacin (40%) [50]. Overall, the variability in susceptibility rates across studies may be attributed to regional differences in antibiotic usage patterns and the local dynamics of antimicrobial resistance development.

The limitation of this study is the lack of validation of the Xpert Carba-R results using other standard reference methods.

Conclusions

In this study, *K. pneumoniae* was the most frequently identified pathogen among CRE isolates, and *bla*_{OXA-48} was the predominant carbapenemase gene. All the isolates exhibited 100% resistance to ertapenem; colistin was the most effective antibiotic; and imipenem, amikacin, and trimethoprim–sulfamethoxazole showing relatively low susceptibility rates. The GeneXpert Carba-R panel proved to be a rapid and reliable method for detecting carbapenemase genes.

These findings emphasize the critical role of local antimicrobial resistance data in guiding appropriate empirical therapy for carbapenem-resistant infections. Such data are essential for identifying regional resistance patterns, supporting national surveillance systems, and strengthening infection control strategies. Further large-scale, multicenter studies are warranted to improve our understanding and to contribute to global efforts to combat antimicrobial resistance.

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Authors' contributions

CDY, BG, HY: study design, data collection; CDY, BG: literature review, manuscript—first draft; BG, CDY: manuscript—review and finalization. All authors approved the final version for publication.

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Conflict of interest

No conflict of interest is declared.

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