ORIGINAL ARTICLE

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Susceptibility Trends of Enterobacterales Isolated from Blood Culture Samples: A Four-Year Analysis with the Rise of Carbapenem Resistance

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ABSTRACT

Objective: Bloodstream infections (BSIs) caused by Enterobacterales pose a significant challenge in healthcare, especially given the growing threat of antimicrobial resistance. This study aimed to evaluate the distribution and antimicrobial susceptibility patterns of Enterobacterales isolated from blood cultures at Necmettin Erbakan University Meram School of Medicine Hospital in Konya, Türkiye, over a four-year period.

Materials and Methods: A retrospective laboratory-based analysis was conducted using blood culture samples collected between January 2020 and January 2023. Bacterial identification and antimicrobial susceptibility testing were performed using the BD Phoenix system. Results were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (version 15.0). Demographic and clinical data were analyzed using descriptive statistics.

Results: A total of 11,319 blood culture samples were analyzed during the study period. Enterobacterales were isolated from 1513 patients, with *Klebsiella pneumoniae* (52.2%) and *Escherichia coli* (34.9%) being the most prevalent pathogens. High resistance rates were observed for ampicillin (91.7%) and amoxicillin-clavulanic acid (76.7%) in *E. coliand* particularly among *Klebsiella* spp. (98.9% and 85%, respectively). Extended-spectrum β-lactamase (ESBL) production was detected in 81% of Klebsiella spp., and approximately 47% of *E. coli* isolates. Colistin emerged as the most effective antibiotic. Notably, *Klebsiella* spp. also exhibited elevated carbapenem resistance (58.1%), whereas *E. coli* showed low resistance to both colistin (0.6%) and meropenem (1.5%). The rate of ESBL production peaked at 75.5% in 2020, then declined before rising again to 63.7% in 2023. Carbapenem-resistant isolates fluctuated around 33% of total isolates annually; however, in 2023, this rate increased to 36.3%, suggesting a potential upward trend.

Conclusion: The findings indicate a concerning burden of carbapenem-resistant *Klebsiella* spp. among Enterobacterales BSI, with colistin remaining the most consistently effective agent. Continuous surveillance, effective infection control measures, and prudent antibiotic use are essential to limit further resistance.

Keywords: Bloodstream infections, Enterobacterales, ESBL, carbapenem resistance

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Rising Carbapenem Resistance in Bloodstream Enterobacterales: A Four-Year Analysis

Background

This study evaluates Enterobacterales distribution and susceptibility patterns (2020–2023) with a specific focus on rising carbapenem resistance.

Objective

To evaluate the distribution and antimicrobial susceptibility of Enterobacterales in blood cultures over a 4-year period (2020–2023).

Methods

- Retrospective analysis of 11,319 blood cultures.
- Identification and AST: BD Phoenix system (EUCAST guidelines).

Results

Most common isolates: *K. pneumoniae* (52.2%) and *E. coli* (34.9%).

ESBL rates: 81% in *Klebsiella* spp. and 47% in *E. coli*.

Key Finding: Carbapenem resistance in *K. pneumoniae* reached 25.4%.

Conclusion

A significant rise in carbapenem-resistant *Klebsiella* spp., with colistin remaining the only effective agent, highlights the necessity for continuous surveillance, stringent infection measures, and prudent antibiotic use.

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Graphic Abstract

INTRODUCTION

Bloodstream infections (BSIs) occur when microorganisms overcome the host's normal defense mechanisms and spread through the bloodstream. These infections can lead to serious outcomes, such as sepsis, septic shock, and organ dysfunction, significantly increasing mortality and morbidity rates (1,2). In Europe, 1,200,000 episodes of BSIs are estimated to occur annually (3), whereas the incidence ranges between 122 and 220 cases per 100,000 population (4). The Turkish Society of Intensive Care Medicine and Sepsis Study Group conducted a multicenter study in 94 hospitals to assess sepsis in Turkish intensive care units (ICUs). The study reported prevalence rates of 10.9% for sepsis, 17.3% for severe sepsis, and 13.5% for septic shock, with high mortality rates of 55.7% for severe sepsis and 70.4% for septic shock (5).

BSIs can be caused by a variety of microorganisms. The most commonly isolated infectious agents are Gram-positive cocci and Gram-negative bacilli (6). Recent reports indicate a shift in the prevalence of microbial agents causing BSIs, with Gram-negative pathogens increasingly responsible for bacteremia (7). The order Enterobacterales includes various genera that primarily reside in the gut and share similar biochemical and genetic traits. Some members are significant opportunistic human pathogens responsible for various infections. Notable genera include *Klebsiella pneumoniae*, *Escherichia*

HIGHLIGHTS

- *Klebsiella* spp. and *E. coli* were the most common pathogens causing bloodstream infections.
- Older adults and hospitalized patients had the highest infection prevalence.
- High resistance to ampicillin and β-lactam antibiotics was observed, whereas susceptibility to colistin remained high.
- High rates of ESBL-producing and carbapenem-resistant Enterobacterales were identified.

coli, *Proteus* spp., *Citrobacter* spp., and *Enterobacter* spp. (8).

In hospitals, high antibiotic selective pressure contributes to the emergence of multidrug-resistant (MDR) pathogens (9), particularly Enterobacterales (e.g., *E. coli* and *K. pneumoniae*) (7,10). Infections caused by extended-spectrum β-lactamase (ESBL)-producing bacteria are challenging to the physicians (11). Carbapenems are commonly used to treat infections caused by these strains. However, their extensive use has resulted in carbapenem-resistant Enterobacterales (CRE), which are difficult to treat (12). Infections caused by CRE are associated with higher mortality rates, increased healthcare costs, and prolonged hospital stays (13).

Empirical antibiotic therapy is initiated promptly in suspected cases of sepsis, based on clinical and epidemiological data (14). Early intervention is critical, as the risk of mortality increases with each hour of delay (10). A thorough understanding of pathogen susceptibility patterns may assist clinicians in optimizing empirical therapy at an earlier stage (15). This study aimed to retrospectively evaluate the distribution and resistance patterns of Enterobacterales from blood cultures at Necmettin Erbakan University Meram School of Medicine Hospital in Konya, Türkiye, over a four-year period.

MATERIALS AND METHODS

This retrospective, laboratory-based descriptive study was conducted at Necmettin Erbakan University Meram School of Medicine Hospital and was approved by the university's Ethics Committee (Decision no. 2024/5400). Blood culture samples collected between January 2020 and January 2023 were included in the study.

Blood samples were collected in blood culture bottles and then loaded into the BACT/ALERT automated system (BioMérieux, Marcy L'Etoile, France) and incubated for five days. Samples that signaled positive were cultured on 5% sheep blood agar and eosin methylene blue agar and incubated at 37°C for 24–48 hours. Isolated microorganisms were initially identified based on colony morphology and Gram staining characteristics using conventional methods. Species-level identification was performed using the automated BD Phoenix system (Becton Dickinson, Sparks, MD, USA). Antimicrobial susceptibility testing was performed using the same system. Susceptibility to colistin and tigecycline was determined using the microdilution method. The minimum inhibitory concentration (MIC) values were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (version 15.0).

For patients with multiple blood culture samples, only the first isolate of the same bacterium was included in the analysis. For blood samples collected simultaneously from the right and left arms of the same patient, if the same bacterium was isolated from both cultures, the isolate was considered the causative pathogen. Samples considered contaminants were excluded from the study.

Extended-spectrum β-lactamase production was detected using a modified double-disk synergy test (DDST) with cefotaxime, ceftazidime, cefepime, and aztreonam discs placed 20 mm apart around a disc containing amoxicillin-clavulanic acid. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to calculate the frequencies and percentages of age groups, gender, isolated organisms, antimicrobial susceptibility, and resistance rates.

RESULTS

A total of 11,319 blood culture samples were analyzed during the study period. Table 1 presents the demographic and clinical characteristics of 1513 patients with Enterobacterales bloodstream infections identified between 2020 and 2023. Among the study population, 54.8% were male and 45.2% were female. Most patients were older adults (55.3%), followed by adults (29%), infants (11.3%), and children and adolescents (4.4%).

More than half of the isolates (55.5%) were isolated from patients in general wards, whereas 43.6% were recovered from patients in ICUs. Outpatient clinic visits constituted only 0.9% of the total patient population.

The majority of *Klebsiella* spp. isolates (81%) and nearly half of *E. coli* isolates (47%) were identified as ESBL producers, whereas other members of the Enterobacterales order exhibited significantly lower ESBL production rates. Carbapenem resistance was markedly higher in *Klebsiella* spp. (58.1%), compared to only 1.5% of *E. coli* isolates.

Among the identified species, *K. pneumoniae* and *E. coli* were the most dominant, accounting for 52.2% and 34.9% of the isolates, respectively. *K. pneumoniae*, *Serratia marcescens*, and *Providencia stuartii* were more frequently identified in ICU patients, whereas *E. coli* and other Enterobacterales species were primarily detected among patients from general wards and outpatient clinics, as detailed in Table 2.

Table 3 presents the resistance patterns of Enterobacterales species across different patient settings. Almost all isolates demonstrated high resistance to ampicillin and amoxicillin/clavulanic acid. Resistance rates varied among species; *Klebsiella* spp. and *E. coli* demonstrated resistance rates of 20.4% and 0.6% to colistin, respectively. In addition, *E. coli* isolates exhibited low resistance to meropenem (1.5%), amikacin (2.3%), and tigecycline (5.5%). In contrast, other Enterobacterales species showed resistance rates of 19.7% to both meropenem and trimethoprim-sulfamethoxazole. Remarkably, Enterobacterales isolates obtained from ICU patients showed higher resistance rates compared to those from ward patients.

Table 4 shows the resistance profiles of ESBL-producing *Klebsiella* spp., with the lowest resistance rate was observed for colistin (24.6%). Other Enterobacterales species exhibited a resistance rate of 47.6% to trimethoprim-sulfamethoxazole. Moreover, ESBL-producing *E. coli* isolates exhibited notably low resistance to several antibiotics, including colistin (0.8%), meropenem (2.8%), and tigecycline (6.4%).

Carbapenem-resistant Enterobacterales frequently exhibited resistance to antibiotics from multiple classes. Among these isolates, *E. coli* displayed a low colistin resistance rate (12.5%), whereas *Klebsiella* spp. showed higher resistance (30.9%). Other Enterobacterales species showed the highest colistin resistance (76.5%). In this group, the lowest resistance rate was observed for trimethoprim-sulfamethoxazole (23.5%).

Table 1. General characteristics of patients with Enterobacterales bloodstream infections, 2020–2023.

	n (%)
Sex	
Male	829 (54.8)
Female	684 (45.2)
Age groups	
Infancy (0–2 years)	171 (11.3)
Children/Adolescents (3–17 years)	66 (4.4)
Adults (18–60 years)	439 (29)
Elderly (>60 years)	837 (55.3)
Patient location	
Wards	840 (55.5)
Intensive care unit	660 (43.6)
Outpatient clinics	13 (0.9)
Isolated microorganisms	
Klebsiella spp.[1]	812 (53.7)
E. coli	528 (34.9)
Other Enterobacterales[2]	173 (11.4)
ESBL-producing Enterobacterales	
Klebsiella spp.	658 (81)
E. coli	248 (47)
Other Enterobacterales	63 (36.4)
Carbapenem-resistant Enterobacterales	
Klebsiella spp.	472 (58.1)
E. coli	8 (1.5)
Other Enterobacterales	34 (19.7)

[1]*Klebsiella* spp. includes *K. pneumoniae* and *K. oxytoca*.
[2]Organisms with an isolation rate of less than 30% were classified as "Other Enterobacterales."

The Figure 1 illustrates the trends in ESBL-producing Enterobacterales and CRE over four years. Overall, ESBL rates consistently exceeded CRE rates, peaking at 75.5% in 2020 before declining and

Table 2. The distribution of BSIs caused by various members of Enterobacterales in relation to different types of patient care.

	Total Isolates n (%)	Wards n (%)	ICU n (%)	Outpatient Clinics n (%)
Klebsiella pneumoniae	790 (52.2)	279 (33.2)	508 (77)	3 (23.1)
Klebsiella oxytoca	22 (1.5)	17 (2)	3 (0.5)	2 (15.4)
Escherichia coli	528 (34.9)	465 (55.4)	56 (8.5)	7 (53.8)
Serratia marcescens	51 (3.4)	8 (1)	43 (6.5)	0 (0)
Enterobacter spp.	74 (4.9)	47 (5.6)	26 (3.9)	1 (7.7)
Pantoea agglomerans	7 (0.5)	6 (0.7)	1 (0.2)	0 (0)
Salmonella spp.	10 (0.7)	9 (1.1)	1 (0.2)	0 (0)
Proteus (Proteus mirabilis)	10 (0.7)	4 (0.5)	6 (0.9)	0 (0)
Providencia stuartii	16 (1.1)	1 (0.1)	15 (2.3)	0 (0)
Citrobacter freundii	2 (0.1)	2 (0.2)	0 (0)	0 (0)
Morganella morganii	1 (0.1)	1 (0.1)	0 (0)	0 (0)
Hafnia paralvei/ Hafnia alvei	2 (0.1)	1 (0.1)	1 (0.2)	0 (0)

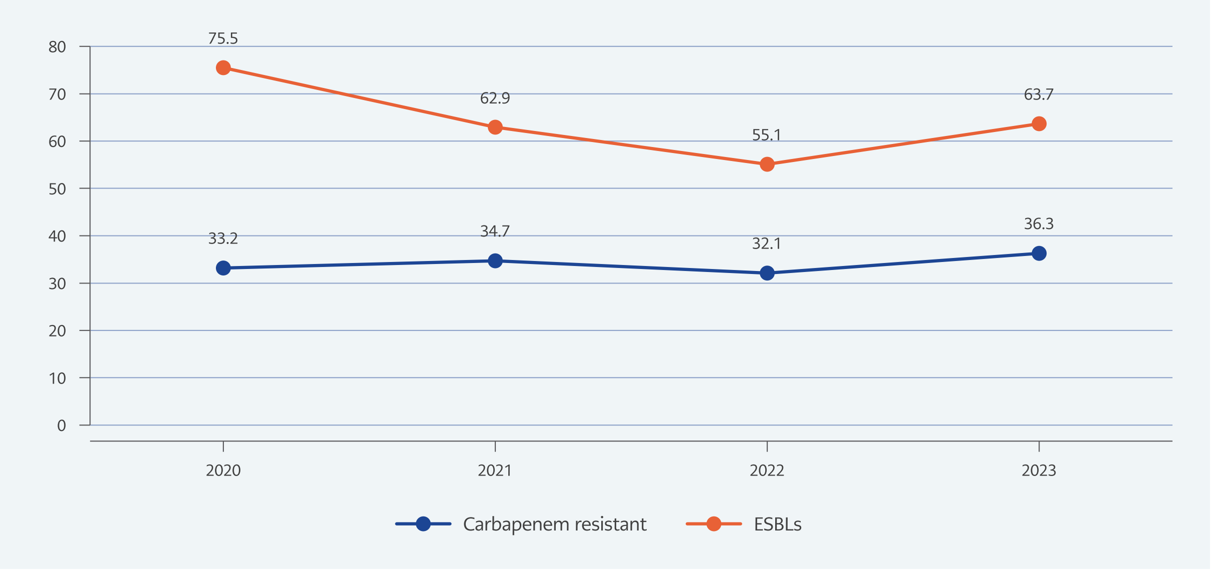

Figure 1. Percentage change in the distribution of ESBLs and carbapenem-resistant Enterobacterales over four years.

rising again to 63.7% in 2023. In contrast, CRE rates remained relatively stable throughout the study period but increased significantly to 36.3% in 2023.

DISCUSSION

Bloodstream infections are prevalent worldwide and have significant direct and indirect social and economic impacts (16). They rank as the second most common condition linked to deaths caused by antimicrobial resistance, following respiratory infections (17). This study aimed to assess the distribution and susceptibility patterns of Enterobacterales responsible for BSIs and to determine the prevalence of ESBL production and carbapenem resistance among these species.

Table 3. Antimicrobial resistance rates of Enterobacterales causing bloodstream infections by patient location.

	All isolates, n (%)			Ward isolates, n (%)			ICU isolates, n (%)			Outpatient clinic isolates, n (%)		
	Klebsiella spp.	*E. coli*	Other Enterobacterales	*Klebsiella* spp.	*E. coli*	Other Enterobacterales	*Klebsiella* spp.	*E. coli*	Other Enterobacterales	*Klebsiella* spp.	*E. coli*	Other Enterobacterales
Amikacin	351 (43.2)	12 (2.3)	36 (20.8)	79 (26.7)	9 (1.9)	5 (6.3)	271 (53)	3 (5.4)	31 (33.3)	1 (20)	0 (0)	0 (0)
Amoxicillin-Clavulanic Acid	690 (85)	322 (61)	149 (86.1)	198 (66.9)	282 (60.6)	58 (73.4)	489 (95.7)	36 (64.3)	90 (96.8)	3 (60)	4 (57.1)	1 (100)
Ampicillin	803 (98.9)	434 (82.2)	150 (86.7)	291 (98.3)	382 (82.2)	62 (78.5)	507 (99.2)	46 (82.1)	87 (93.5)	5 (100)	6 (85.7)	1 (100)
Piperacillin-Tazobactam	630 (77.6)	76 (14.4)	62 (35.8)	149 (50.3)	64 (13.8)	13 (16.5)	478 (93.5)	12 (21.4)	48 (51.6)	3 (60)	0 (0)	1 (100)
Ertapenem	606 (74.6)	36 (6.8)	62 (35.8)	139 (47)	25 (5.4)	11 (13.9)	463 (90.6)	11 (19.6)	50 (53.8)	4 (80)	0 (0)	1 (100)
Meropenem	472 (58.1)	8 (1.5)	34 (19.7)	109 (36.8)	6 (1.3)	4 (5.1)	362 (70.8)	2 (3.6)	30 (32.3)	1 (20)	0 (0)	0 (0)
Ciprofloxacin	569 (70.1)	278 (52.7)	38 (22)	160 (54.1)	244 (52.5)	9 (11.4)	407 (79.6)	31 (55.4)	29 (31.2)	2 (40)	3 (42.9)	0 (0)
Gentamicin	439 (54.1)	141 (26.7)	49 (28.3)	98 (33.1)	128 (27.5)	10 (12.7)	338 (66.1)	13 (23.2)	39 (41.9)	3 (60)	0 (0)	0 (0)
Cefazolin	699 (86.1)	310 (58.7)	144 (83.2)	201 (67.9)	266 (57.2)	57 (72.2)	495 (96.9)	40 (71.4)	86 (92.5)	3 (60)	4 (57.1)	1 (100)
Cefuroxime	684 (84.2)	307 (58.1)	143 (82.7)	189 (63.9)	265 (57)	56 (70.9)	492 (96.3)	38 (67.9)	86 (92.5)	3 (60)	4 (57.1)	1 (100)
Ceftazidime	667 (82.1)	252 (47.7)	64 (37)	179 (60.5)	213 (45.8)	15 (19)	484 (94.7)	36 (64.3)	49 (52.7)	4 (80)	3 (42.9)	0 (0)
Ceftriaxone	667 (82.1)	276 (52.3)	70 (40.5)	175 (59.1)	234 (50.3)	18 (22.8)	488 (95.5)	38 (67.9)	52 (55.9)	4 (80)	4 (57.1)	0 (0)
Cefepime	658 (81)	247 (46.8)	59 (34.1)	171 (57.8)	209 (44.9)	12 (15.2)	483 (94.5)	34 (60.7)	47 (50.5)	4 (80)	4 (57.1)	0 (0)
Tigecycline1	-	29 (5.5)	-	-	25 (5.4)	-	-	4 (7.1)	-	-	0 (0)	-
Colistin	166 (20.4)	3 (0.6)	84 (48.6)	35 (11.8)	2 (0.4)	18 (22.8)	130 (25.4)	1 (1.8)	66 (71)	1 (20)	0 (0)	0 (0)
Trimethoprim-Sulfamethoxazole	512 (63.1)	272 (51.5)	34 (19.7)	149 (50.3)	239 (51.4)	10 (12.7)	361 (70.6)	30 (53.6)	24 (25.8)	2 (40)	3 (42.9)	0 (0)

[1]According to EUCAST Clinical Breakpoint Tables v.15.0, tigecycline susceptibility for Enterobacterales other than *Escherichia coli* is variable; therefore, only *E. coli* isolates were evaluated.

Table 4. Antimicrobial resistance patterns of ESBL-producing and carbapenem-resistant Enterobacterales.

Antibiotic	ESBL-producing Enterobacterales, n (%)			Carbapenem-resistant Enterobacterales, n (%)		
	Klebsiella spp.	*E. coli*	Other Enterobacterales	*Klebsiella* spp.	*E. coli*	Other Enterobacterales
Amikacin	407 (61.8)	22 (12.9)	36 (57.1)	327 (69.3)	1 (12.5)	17 (50)
Amoxicillin-Clavulanic Acid	635 (96.5)	191 (77)	63 (100)	470 (99.6)	6 (75)	34 (100)
Ampicillin	658 (100)	248 (100)	63 (100)	470 (99.6)	7 (87.5)	34 (100)
Piperacillin-Tazobactam	614 (93.3)	63 (25.4)	53 (84.2)	469 (99.4)	6 (75)	33 (97.1)
Ertapenem	592 (90)	29 (11.7)	46 (73)	472 (100)	8 (100)	34 (100)
Meropenem	519 (78.9)	7 (2.8)	32 (50.8)	472 (100)	8 (100)	34 (100)
Ciprofloxacin	570 (86.6)	200 (80.6)	39 (61.9)	454 (96.2)	7 (87.5)	17 (50)
Gentamicin	430 (65.3)	97 (39.1)	41 (65.1)	305 (64.6)	2 (25)	17 (50)
Cefazolin	658 (100)	248 (100)	63 (100)	469 (99.4)	7 (87.5)	34 (100)
Cefuroxime	658 (100)	248 (100)	63 (100)	469 (99.4)	8 (100)	34 (100)
Ceftazidime	658 (100)	248 (100)	63 (100)	467 (98.9)	6 (75)	30 (88.2)
Ceftriaxone	658 (100)	248 (100)	63 (100)	470 (99.6)	6 (75)	17 (50)
Cefepime	652 (99.1)	245 (98.8)	62 (98.4)	471 (99.8)	6 (75)	33 (97.1)
Tigecycline	-	16 (6.4)	-	-	1 (12.5)	-
Colistin	162 (24.6)	2 (0.8)	47 (74.6)	146 (30.9)	1 (12.5)	26 (76.5)
Trimethoprim-Sulfamethoxazole	479 (75.5)	160 (64.5)	30 (47.6)	363 (76.9)	5 (62.5)	8 (23.5)

In our study, the isolation patterns of Enterobacterales from blood cultures showed that *K. pneumoniae* had the highest isolation rate (52.2%), followed by *E. coli* (34.9%). This finding contrasts with most studies conducted by other researchers (18–21), which typically identify *E. coli* as the predominant isolated species among Gram-negative pathogens causing BSIs. However, our results are comparable to those reported by Asena (22) and Mun et al. (23), suggesting that many patients may have developed infections associated with healthcare settings. *Klebsiella* spp. and other Enterobacterales were more frequently detected in ICU settings, while *E. coli* was more commonly isolated from patients in hospital wards. This observation aligns with a study conducted in Izmir (18).

Regarding resistance patterns, nearly all *Klebsiella* spp. demonstrated resistance to ampicillin (98.9%) and amoxicillin-clavulanic acid (85%). Similar findings were reported by Kłos et al. (7), who observed 100% resistance to ampicillin, and by Küçük et al. (6), who reported a resistance rate of 76.7% to amoxicillin-clavulanic acid. High resistance levels to multiple generations of cephalosporins have also been reported. Our findings are consistent with studies conducted in Türkiye (1,5), whereas a report from Poland indicated lower resistance rates for the same group of antibiotics (7). The resistance trend to penicillins and penicillin inhibitors among *Klebsiella* spp. may be attributed to mobile genetic elements carrying resistance genes. On the other hand, colistin exhibited the lowest resistance rate (20.4%), with most *Klebsiella* spp. remaining susceptible to this antibiotic. Our results are close to those reported by Kula et al. (1), who observed a colistin resistance rate of 22.6%. However, Müderris et al. (18) observed a significantly lower resistance rate of 4.5%. The extensive use of colistin for infections caused by MDR bacteria may contribute to the development of resistance.

E. coli isolates exhibited high resistance to ampicillin (82.2%), comparable to the estimates of earlier studies by Kula et al. (1) and Öksüz et al. (20). Colistin and meropenem were the most effective antibiotics against *E. coli in vitro*, with only 0.6% and 1.5% of isolates showing resistance, respectively. Our findings align with previous studies conducted in Türkiye (1,18). *E. coli* strains may remain susceptible to these antibiotics because developing resistance is energetically costly and hinders bacterial growth. Furthermore, resistance genes associated with these antibiotics remain uncommon among *E. coli* isolates.

The results of the present study revealed that the majority of *Klebsiella* spp. isolates were ESBL-producing, accounting for 81% of isolates, while 47% of *E. coli* isolates produced ESBLs. These rates are higher than those reported in Poland, where ESBL prevalence was 66.7% in *Klebsiella* spp. and 25.7% in *E. coli* (7). Moreover, these values exceed those previously reported in Türkiye by Öksüz et al. (20) and Varışlı et al. (21). Until recently, antibiotic prescription and use in Türkiye were not strictly regulated, which may have contributed to misuse and overuse of antibiotics and, subsequently, to the emergence of resistant bacterial strains.

Colistin was the only antibiotic that remained consistently effective against ESBL-producing *Klebsiella* spp., which showed a low resistance rate of 24.6%. In contrast, ESBL-producing *E. coli* isolates demonstrated low resistance not only to colistin (0.8%) but also to meropenem (2.8%) and tigecycline (6.4%). Consistent with many previous studies, carbapenems remain the drugs of choice for treating infections caused by ESBL-producing bacteria (20,21). However, carbapenems were less effective against ESBL-producing *Klebsiella* spp., which frequently exhibited an MDR pattern with low susceptibility even to carbapenems, leaving colistin as a last-resort therapeutic option.

In our study, the carbapenem resistance rate in *Klebsiella* spp. was 58.1%, which aligns closely with the 53.1% reported by Aslan et al. (24). However, our findings were higher than those reported in earlier studies conducted in Türkiye (20,21, 25), where resistance rates ranged from 34.6% to 39.1%. Additionally, carbapenem resistance among *E. coli* isolates was 1.5%. In contrast, other retrospective studies reported rates of 3.6%, 4.7%, and 6.1% (20,21,24). Differences in carbapenem resistance may be related to variations in the study periods and settings. Furthermore, the extensive use of carbapenems to treat infections caused by MDR bacteria may have contributed to the increase in resistance observed in recent years.

Colistin remained the only effective agent against carbapenem-resistant Enterobacterales; however, susceptibility varied significantly among species. The lowest susceptibility was noted in carbapenem-resistant *Klebsiella* spp., with a resistance rate of 30.9%. Although this rate is lower than that reported by Aslan et al. (24), it remains concerning.

Analysis of ESBL and CRE trends over the four-year study period showed that ESBL rates consistently exceeded CRE rates. Notably, the highest ESBL rate was recorded in 2020 (75.5%). According to a report by the World Health Organization (WHO), approximately 75% of hospitalized patients with COVID-19 received antibiotics during the pandemic, with cephalosporins being among the most frequently prescribed agents (26). This situation may partially explain the increased prevalence of ESBL-producing Enterobacterales observed during that period. In contrast, the proportion of CRE remained relatively stable throughout the study period but increased markedly in 2023 to 36.3%. This value falls within the range reported by the European Centre for Disease Prevention and Control (ECDC), which varies between 0% and 58.3% (13). According to ECDC reports, carbapenem resistance among Enterobacterales has increased considerably since 2019.

CONCLUSION

This four-year analysis underscores significant shifts in the epidemiology and resistance patterns of Enterobacterales causing bloodstream infections. *K. pneumoniae* has emerged as the leading isolate, surpassing *E. coli*. Alarmingly high resistance rates to β-lactam antibiotics among *Klebsiella* spp. have limited therapeutic options, leaving colistin as the last reliable therapeutic alternative. Although colistin and carbapenems remain effective against *E. coli*, the increasing reliance on colistin for *Klebsiella* infections raises concerns regarding the potential emergence of further resistance. Additionally, the surge in ESBL-producing isolates during the COVID-19 pandemic and the sharp increase in carbapenem resistance observed in 2023 highlight the consequences of excessive antibiotic use. Since part of the study period coincided with the pandemic, the findings may not be fully comparable to the non-pandemic periods. Continuous surveillance, strengthened infection control measures, improved antimicrobial stewardship programs, and the development of novel therapeutic strategies are essential to combat the mounting burden of MDR Enterobacterales in BSIs.

Ethical Approval: This study was approved by the Ethics Committee of Necmettin Erbakan University on December 20, 2024, with the decision no. 2024/5400.

Informed Consent: N.A.

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