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Antimicrobial Susceptibility Profile of Enterobacterales Isolated from Blood Cultures Between 2016-2021

2016-2021 Yılları Arasında Kan Kültürlerinden İzole Edilen Enterobacterales Türlerinin Antimikrobiyal Duyarlılık Profili

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Abstract

Aim Blood culture is the gold standard in the diagnosis of bacteraemia and sepsis. When antimicrobial treatment is delayed, severe infections may occur, which may cause high morbidity and mortality. We aimed to determine the distribution of Enterobacterales isolates and their antimicrobial susceptibility profile from blood culture samples sent to the laboratory between 2016 and 2021.

Materials and Methods Enterobacterales isolated from blood culture samples sent to Ondokuz Mayis University Medical Microbiology laboratory between January 2016 and December 2021 was enrolled in the study. Vitek MS (BioMérieux, France) was used for identification of bacterial species and Vitek2 (BioMérieux, France) Compact automated system were used for determination of antibiotic susceptibility of bacteria. EUCAST criteria were used for the evaluation of antibiotic susceptibility of the isolates.

Results The most three isolated bacteria were Escherichia coli, Klebsiella spp. and Enterobacter spp. respectively. The resistance rates were 9.06% for meropenem, 8.89% for imipenem and 15.67% for ertapenem, 7.57% and 6.28% for amikacin and tigecycline, respectively.

Conclusions Since the antibiotic resistance rates of the agents causing bloodstream infections show regional differences, it is thought that screening epidemiological data and reporting the results will increase the correct treatment rate and decrease the mortality rate.

Keywords Antibiotic Resistance, Blood culture, Enterobacterales

Öz

Amaç *Kan kültürü, bakteriyemi ve sepsis tanısında altın standarttır. Antimikrobiyal tedavi geciktiğinde, yüksek morbidite ve mortaliteye neden olabilecek ciddi enfeksiyonlar ortaya çıkabilir. Bu çalışmada, 2016-2021 yılları arasında laboratuvara gönderilen kan kültürü örneklerinden izole edilen Enterobacterales izolatlarının dağılımının belirlenmesi ve antibiyotik direnci değişim oranlarının tespit edilmesi amaçlanmıştır.*

Gereç ve Yöntem *Ocak 2016 - Aralık 2021 tarihleri arasında Ondokuz Mayıs Üniversitesi Tıbbi Mikrobiyoloji laboratuvarına gönderilen kan kültürü örneklerinden Enterobacterales üyelerinin dağılımı değerlendirildi. Bakteri türlerinin tanımlanmasında Vitek MS (BioMérieux, Fransa) ve bakterilerin antibiyotik duyarlılıklarının belirlenmesinde Vitek2 (BioMérieux, Fransa) Compact otomatize sistemleri kullanılmıştır. İzolatların antibiyotik duyarlılığının değerlendirilmesinde EUCAST kriterleri kullanılmıştır.*

Bulgular *2016-2021 yılları arasında 2034 Enterobacterales üyesi çalışmaya dahil edilmiştir. Bu izolatların yıldan yıla dağılımı sırasıyla 2019, 2020, 2021, 2016, 2018, 2017 olarak belirlenmiştir. En çok izole edilen ilk üç bakteri sırasıyla Escherichia coli, Klebsiella spp. ve Enterobacter spp. olmuştur. Direnç oranları meropenem için %9,06, imipenem için %8,89 ve ertapenem için %15,67 iken, amikasin ve tigesiklin için sırasıyla %7,57 ve %6,28'dir.*

Sonuç *Kan dolaşımı enfeksiyonlarına neden olan etkenlerin antibiyotik direnç oranlarının bölgesel farklılıklar göstermesi nedeniyle epidemiyolojik verilerin taranması ve sonuçların raporlanmasının doğru tedavi oranını artıracağı ve mortalite oranını azaltacağı düşünülmektedir.*

Anahtar Kelimeler *Antibiyotik Direnci, Enterobacterales, Kan Kültürü*

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INTRODUCTION

Enterobacterales species have continued to pose a global challenge due to the increasing antimicrobial resistance observed in recent years.[1] Changes in antimicrobial resistance patterns, pathogen distribution, demographics, and healthcare delivery may influence the epidemiology of bloodstream infections. Therefore, it is essential to continuously monitor trends in the microbiology of bloodstream infection pathogens on a global scale.[2] A wide range of microorganisms can cause bloodstream infections, but bacteria are responsible for over 90% of these infections.[3,4] Infections caused by carbapenem-resistant Enterobacterales (CRE) are associated with high mortality rates.[5]

This study aimed to assess the antimicrobial susceptibilities of Enterobacterales isolates recovered from blood cultures.

MATERIALS and METHODS

Enterobacterales isolates grown in blood culture samples from patients admitted to the Medical Microbiology Laboratory of Ondokuz Mayis University between January 2016 and December 2021 were included in the study. For patients with multiple positive cultures, only the first isolate was included.

Blood culture samples were incubated in the BacT/Alert system (BioMérieux, France). When a positive growth signal was detected, Gram staining was performed, and subcultures were made on blood agar and eosin methylene blue (EMB) agar, followed by incubation at 37°C for 18-24 hours. Bacterial species identification was performed using the Vitek MS (BioMérieux, France) system, and antibiotic susceptibility testing was carried out using the Vitek2 Compact (BioMérieux, France) automated system. Results were interpreted according to the criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[6] Data related to the included isolates were obtained from the hospital information system and retrospectively analyzed.

This study was approved by the Clinical Research Ethics Committee of Ondokuz Mayis University (Date: 24.08.2022, Decision No: OMÜ KAEK 2022/393).

RESULTS

When evaluating the 2304 blood culture samples (male: 1201; female: 1103) included in the study, the most frequently isolated bacteria were found to be *E. coli* (44.61%, n=1028), Klebsiella spp. (36.02%, n=830), *Enterobacter spp.* (10.28%, n=237), and Serratia spp. (4.03%, n=93). The resistance distribution of the strains is presented in Table 1. The top three clinical departments from which the isolates were obtained were internal medicine (35%, n=807), emergency (20%, n=466), and intensive care units (ICU) (17%, n=388), as shown in Figure 1. The highest isolation rate by year was observed in 2019 (18.79%, n=433), with the distribution for other years provided in Table 2. The annual distribution of the most frequently isolated organisms, including *E. coli, Klebsiella spp*., and *Enterobacter spp.*, is also provided in Table 2. The resistance rates of the strains included in the study were as follows: meropenem 9.06%, imipenem 8.89%, ertapenem 15.67%, amikacin 7.57%, and tigecycline 6.28%.

Table 1. Antimicrobial Resistance Distribution of Microorganisms According to Antibiotics

Microorganism (n)	AMP n(%)	AMC n(%)	TZP n(%)	CAZ n(%)	FEP n(%)	MEM n(%)	AMK n(%)	GEN n(%)	CIP n(%)	SXT n(%)
***E. coli* (1028)**	755 (73.44)	531 (51.65)	218 (21.20)	466 (45.33)	433 (42.12)	10 (97)	22 (2.14)	197 (19.16)	466 (45.33)	492 (47.85)
***Citrobacter spp.* (22)**	21 (95.45)	18 (81.81)	4 (18.18)	6 (27.27)	3 (13.63)	-	-	2 (9.09)	-	3 (13.63)
E*dwarsiella tarda* (2)	-	-	-	-	-	-	-	-	-	-
***Enterobacter spp.* (237)**	237 (100)	236 (99.57)	49 (20.67)	74 (31.22)	50 (21.09)	14 (5.90)	13 (5.48)	27 (11.39)	19 (8.01)	27 (11.39)
***Hafnia alvei* (1)**	1 (100)	1 (100)	1 (100)	1 (100)	-	-	-	-	-	-
***Klebsiella spp.* (830)**	830 (100)	502 (60.48)	392 (47.22)	508 (61.20)	487 (58.67)	169 (20.36)	137 (16.50)	291 (35.06)	344 (41.44)	419 (50.48)
***Morganella morganii* (17)**	17 (100)	17 (100)	2 (11.76)	4 (23.52)	-	-	-	4 (23.52)	8 (47.05)	8 (47.05)
***Pantoea spp.* (27)**	17 (62.96)	1 (3.70)	-	1 (3.70)	-	-	-	-	-	-
***Proteus mirabilis* (26)**	11 (42.30)	4 (15.38)	1 (3.84)	4 (15.38)	5 (19.23)	-	1 (3.84)	6 (23.07)	7 (26.92)	12 (46.15)
***Proteus vulgaris* (2)**	2 (100)	-	-	-	-	-	-	-	-	1 (50)
***Providencia rettgeri* (1)**	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	-	-	1 (100)	-
***Providencia stuartii* (1)**	1 (100)	1 (100)	-	-	-	-	-	1 (100)	-	-
***Raoultella ornitholytica* (4)**	4 (100)	2 (50)	-	1 (25)	1 (25)	-	-	1 (25)	1 (25)	1 (25)
***Raoultella planticola* (3)**	3 (100)	-	-	-	-	-	-	-	-	-
***Salmonella enteritidis* (8)**	1 (12.5)	1 (12.5)	-	-	-	-	-	-	1 (12.5)	-
***Serratia spp.* (93)**	92 (98.92)	91 (97.84)	13 (13.97)	12 (12.90)	10 (10.75)	3 (3.22)	-	4 (4.30)	5 (5.37)	3 (3.22)
Total resistant ®	1994	1406	681	1078	990	197	173	533	852	966

Table 2. Distribution Rates of E. coli, Klebsiella spp., Enterobacter spp. Isolates According to Years

	2016 n (%)	2017 n(%)	2018 n(%)	2019 n(%)	2020 n(%)	2021 n(%)
Escherichia coli	175 (47.04)	162 (44.87)	169 (46.17)	180 (41.66)	179 (44.97)	163 (43.69)
Klebsiella spp.	113 (30.37)	125 (34.62)	120 (32.78)	176 (40.74)	143 (35.92)	153 (41.01)
Enterobacter spp.	46 (12.36)	37 (10.24)	43 (11.74)	45 (10.41)	43 (10.80)	23 (6.16)

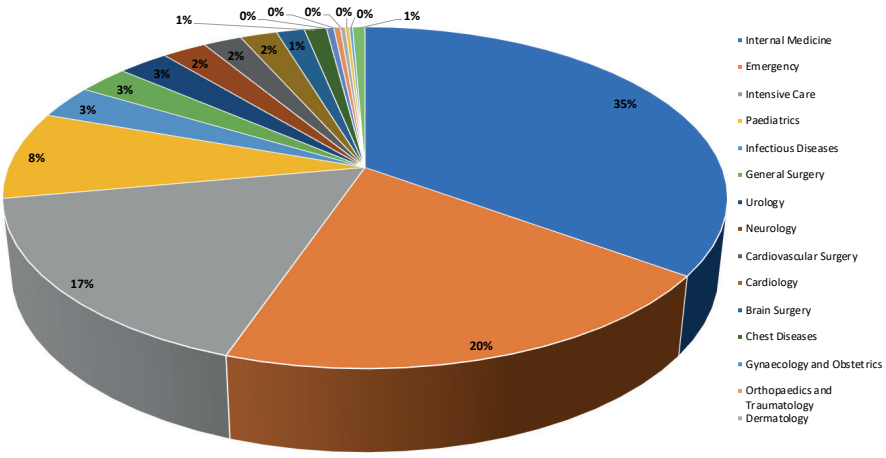

Figure 1. Clinical distribution of the isolates.

DISCUSSION

In cases of septicemia, the delay in administering appropriate antimicrobial treatment can result in severe infections with high morbidity and mortality rates.[7] The widespread use of broad-spectrum antibiotics has led to a significant rise in multidrug-resistant bacteria in recent years, becoming an urgent global issue. Sepsis infections have been recognized as a global health priority by the World Health Organization (WHO).[8,9] In cases of sepsis, which require immediate diagnosis and treatment, each hour of delay in management increases the mortality rate by 10-20%.[10]

Between 1997 and 2016, a study conducted on 264,901 bloodstream infection isolates collected consecutively from more than 200 medical centers across 45 different countries identified *S. aureus, E. coli, K. pneumoniae, P. aeruginosa*, and *Enterococcus faecalis* as the most common pathogens, respectively. *S. aureus* and *E. coli* together accounted for over 40% of bloodstream infections. During the period from 1997 to 2004, *S. aureus* was the most frequently isolated pathogen, followed by *E. coli*. However, between 2005 and 2016, the proportion of *E. coli* isolates from blood surpassed that of *S. aureus*. Nevertheless, when averaging the data across the entire study period, the two leading pathogens were *S. aureus* (20.7%) and *E. coli* (20.5%). The prevalence of multidrug-resistant (MDR) Enterobacterales increased from 6.2% in 1997-2000 to 15.8% in 2013-2016. The rate of bacteremia due to MDR Enterobacterales more than doubled between 1997 and 2016, rising from 6.3% to 15.8%.[2]

In a study conducted by Tabah et al. in 2012 across 24 countries and 162 intensive care units, the most commonly isolated bloodstream infection pathogens were identified as *Acinetobacter spp*. (12.2%), *Klebsiella spp*. (11.9%), and *Pseudomonas spp*. (11.4%).[11]

In a study conducted in Canada, *E. coli* was found to be the most frequently isolated Gram-negative bacterium in patients with bacteremia in the intensive care unit, accounting for 21% of cases.[12]

In a study with Enterobacterales isolates (n=717), *E. coli* was the most commonly isolated bacterium (59.97%, n=430), followed by *K. pneumoniae* (29.28%, n=210). Additionally, 4.8% (n=35) of Enterobacterales isolates were found to be resistant to carbapenems.[13]

In the hematology department of the hospital, a total of 72 bacterial isolates were obtained from febrile neutropenic patients between 2005 and 2007. Of these, 69% were Gram-negative bacilli, with *E. coli* being the most

frequently isolated bacterium in 43% (n=31) of the blood cultures.[14] Çekin et al. (2023) analyzed the distribution of 1,723 Gram-negative bacteria isolated from blood cultures between 2018 and 2021. The results showed that *E. coli* accounted for 32.32%, *K. pneumoniae* for 29.77%, *Acinetobacter spp*. for 20.25%, *Pseudomonas spp*. for 12.24%, and *Enterobacter spp*. for 5.39% of the isolates. Most of the patient samples were from intensive care units (44.93%), internal medicine wards (42.3%), and surgical wards (12.75%).[8]

Among 1,976 patients with positive blood cultures between January 2018 and December 2022, 48.5% (n=1,570) of the isolates were Gram-negative bacteria. The most frequently isolated Gram-negative bacteria were *K. pneumoniae* (29.5%, n=461), *Acinetobacter baumannii* (26.5%, n=415), and E. coli (14%, n=219).[15]

In the 2020 WHO CAESAR (Central Asian and Eastern European Surveillance of Antimicrobial Resistance) report, which included data from 120 laboratories across various geographical regions of Turkey, over 90% of the isolates were from blood samples. The most frequently isolated bacteria were reported as *E. coli, K. pneumoniae, A. baumannii,* and *P. aeruginosa*. The antibiotic resistance rates for *E. coli* were found to be 70.6% for ampicillin, 50% for ciprofloxacin, 44.4% for ceftazidime, 27.3% for gentamicin, 11% for piperacillin-tazobactam, and 2% for amikacin.[16] The findings of Çekin et al. (2023) were similar to the WHO CAESAR 2020 report on antibiotic resistance rates in Turkey, with resistance rates of 79% for ampicillin, 52% for ciprofloxacin, 47% for ceftazidime, 26% for gentamicin, 22% for piperacillin-tazobactam, and 2% for amikacin.[8] In our study, the antibiotic resistance rates of E. coli were 73.44% for ampicillin, 45.33% for ciprofloxacin, 45.33% for ceftazidime, 19.16% for gentamicin, 21.20% for piperacillin-tazobactam, and 2.14% for amikacin.

In addition to the literature data, the results of our study identified the most frequently isolated microorganisms as E. coli (44.61%), *Klebsiella spp*. (36.02%), and *Enterobacter spp*. (10.28%). It was observed that the clinical service where the isolates were most frequently identified was internal medicine, accounting for 35.02%.

The Enterobacterales family, which contains many bacterial genera and species, is of significant medical importance. Infections caused by these strains, particularly those isolated from the bloodstream, are associated with high mortality and morbidity. The variation in the isolation distribution of these pathogens over the years may indicate that bloodstream infections could be related to hospital outbreaks. Therefore, increasing infection control measures and improving sanitation practices are essential to reduce resistance rates and bacterial isolation frequency. Furthermore, monitoring resistance rates epidemiologically is crucial in guiding empirical treatment options and informing antibiotic stewardship policies.

Ethics Approval

This study was approved by the Clinical Research Ethics Committee of Ondokuz Mayis University (Date: 24.08.2022, Decision No: OMÜ KAEK 2022/393).

Peer-review

Externally and internally peer-reviewed.

Authorship Contributions

Concept: Y.T.Ç., Design: Y.T.Ç., Data Collection or Processing: İ.B., C.Ç., M.Y., Analysis or Interpretation: İ.B., C.Ç., M.Y., Y.T.Ç., Literature Search: İ.B., C.Ç., M.Y., Writing: İ.B., C.Ç., Y.T.Ç.

Conflict of Interest

No conflict of interest was declared by the authors.

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