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Original Study

Examination of Blood and Tracheal Aspirate Culture Results in Intensive Care Patients: 5-year analysis

Yoğun Bakım Hastalarında Kan ve Trakeal Aspirat Kültürü Sonuçlarının İncelenmesi: 5 Yıllık Analiz

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Ethics Committee Approval: This study was approved by the Istanbul Medeniyet University Goztepe Training and Research Hospital Ethic Committee for Clinical Studies (12 March 2019, 2016/0067).
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ABSTRACT

Objective: *Majority of nosocomial infections are seen in intensive care units (ICUs) and they course with higher rates of mortality, and morbidity rates. In this study, we aimed to investigate the distribution of microorganisms isolated from the tracheal aspirate and blood cultures of ICU hospitalized patients, and their antibiotic resistance profiles.*
Method: *Tracheal aspirate and blood cultures sent from ICU patients were evaluated retrospectively between 2014-2018. Antimicrobial susceptibility tests were performed on microorganism cultures that were identified by conventional methods and using an automated system.*
Results: *A total of 23.275 samples were accepted during the study period. The microorganisms isolated from tracheal aspirate cultures were Gram-negative (89.7%), Gram-positive (9.3%) and yeasts (1%). The most common Gram (-) microorganisms were A.baumannii (%25.7). The rates of meropenem resistance were documented as 98.3% for A.baumannii in 2014, 95.7% in 2018, 69.2% for P.aeruginosa. in 2014, and 35.6% in 2018, 45.55 for K.pneumoniae in 2014, and 5.8% in 2018 and 8% for E.coli in 2014, and 2% in 2018. The rates of methicillin resistance in S.aureus were documented as 28.0% in 2018, and 67.7% in 2015. The rates of penicillin resistance for S. pneumonia was documented as 76.8% in 2018, and 13.4% in 2015. The microorganisms isolated from blood culture were Gram (-) (31.4%), Gram (+) (57.9%) and yeasts (10.6%). The most frequently isolated Gram (-) bacteria were K.pneumonia (9.3%) and A.baumannii (8.8%). The rates of meropenem resistance were documented as 97.3% for A.baumannii. in 2014 and 79.2% in 2018, as 76.9% for K.pneumoniae in 2014 and 37.3% in 2018 and 79.2% for P.aeruginosa in 2014 and 26.1% in 2018. The artes of methicillin resistance were documented as 89.2% in 2018, and 78.5% for CNS in 2015, and 42.6% in 2018 while it was 92.4% for S. aureus in 2015*
Conclusions: *Our study showcased a drop throughout the year in rates of carbapenem resistance against Gram (-) microorganisms and methicillin resistance in S.aureus. However, the persistently high carbapanem resistance in A.baumannii isolates demonstrates the crucial need to continue with infection control measures.*

Keywords: *Intensive care units, culture, drug resistance*

ÖZ

Amaç: *Nozokomiyal enfeksiyonların büyük bir kısmı yoğun bakım ünitelerinde (YBÜ) görülmekte ve yüksek mortalite ve morbidite ile seyretmektedir. Çalışmamızda hastanemiz yoğun bakım ünitesindeki hastaların kan ve trakeal aspirat kültürlerinden izole edilen mikroorganizmaları ve antibiyotik direnç profillerini araştırmayı amaçladık.*
Yöntem: *Yoğun bakım ünitemizden 2014-2018 yılları arasında gönderilen kan ve trakealaspirat kültürleri retrospektif olarak değerlendirildi. Kültürleri yapıldıktan sonra üreyen mikroorganizmalar konvansiyonel metodlar ve otomatize sistemler ile tanımlandı ve antimikrobiyal duyarlılık testleri yapıldı.*
Bulgular: *Çalışma sırasında 23.275 örnek kabul edildi. Trakeal aspirat kültürlerinde Gram-negatif bakteri üreme oranı %89,7, Gram-pozitif bakteri üreme oranı %9,3 ve maya üreme oranı %1 olarak bulundu. A. baumannii (%25,7) en yaygın Gram-negatif mikroorganizma idi. Meropenem direnci; A.baumannii' de 2014 yılında % 98,3, 2018 yılında % 95,7, P.aeruginosa 2014 yılında %69,2, 2018 yılında %36,5 ve E. coli de 2014 de %8, 2018 yılında %2, K.pneumoniae. de 2014'de %45,5, 2018'de %45,8 olarak belirlendi. S.aureus'da metisilin direnci 2015 yılında %67,7 iken 2018 yılında %28 olarak saptandı. S. pneumonia da penisilin direnci 2015'de %13,4 iken 2018'de %76,8 olarak bulundu. Kan kültürlerinde üreyen mikroorganizmalrın %31.4'ü Gram-negatif bakteri,%57,9'u Gram-pozitif bakteri ve %10,6 maya olarak belirlendi. En sık izole edilen Gram-negatif bakteriler Klebsiella pneumonia (%9,3) ve Acinetobacter baumannii (%8,8) idi. Meropenem direnci; Acinetobacter spp.'de 2014 yılında %97.3 2018 yılında %79,2, Klebsiella spp.'de 2014'de %76,9 2018 de %37,3, Pseudomonas spp'de 2014 yılında %79,2, 2018 yılında %26,1 olarak bulundu. KNS bakterilerde Metisilin direnci 2015'de %78,5 iken 2018'de %89,2, S.aureus'da 2015'de %92,4 iken 2018'de % 42,6, Enterokok cinsi bakterilerde ampisilin direnci 2014 yılında %23, 2018'de %11,7 olarak bulundu.*
Sonuç: *Çalışmamızda Gram-negatif mikroorganizmalarda karbapenem direnç oranlarında ve Staphylococcus aureus'da metisilin direnç oranlarında yıllar içinde düşme izlenmiştir. Ancak A. baumannii izolatlarında karbapenem direncinin hâlâ yüksek olması enfeksiyon kontrol önlemlerinin ısrarla devam etmesi gerektiğini göstermektedir.*

Anahtar kelimeler: *Yoğun bakım, kültür, antibiyotik direnci*

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INTRODUCTION

Nosocomial infections are defined as infections that occur more than 48 hours after hospital admission which was not present or incubating at the time of admission[1]. The majority of hospital infections are seen in intensive care units. Bacteremia during hospital infections causes serious health problems. Bacteremia is associated with high morbidity and mortality and is a major risk factor for patients hospitalized in high-risk areas, such as intensive care units. Despite advances in medicine, nosocomial infections are important health problems for the whole world[2].

The intensive care unit (ICU) is within the hospital unit, where patients often receive intensive drug therapy due to multiple organ dysfunctions which require many invasive procedures along with mechanical ventilation (MV). Among common hospital-acquired infections, the ICU is a unit where broad-spectrum antibiotics are being used due to the presence of resistant pathogens[3].

Important reasons for the emergence of infections that are difficult to treat due to resistant pathogens in the ICU include invasive procedures, such as mechanical ventilation, tracheostomy, catheter application in addition to the use of broad-spectrum antibiotics, and duration of stay in intensive care[3].

Pneumonia is one of the most common hospital infections. Clinical and radiological findings have lower diagnostic sensitivity and specificity in the diagnosis of pneumonia. Gram staining and culture of lower respiratory tract samples, such as endotracheal aspirate (ETA), bronchoalveolar lavage (BAL), and protected specimen brush sample guide diagnosis and treatment[4]. It is important to correctly determine the etiologic factor and to start antimicrobial treatment earlier. It has been shown that a delay of treatment for 4-8 h increases mortality. Therefore, empirical antibiotic treatment is typically initiated by the clinician without waiting for laboratory results[4,5].

Bloodstream infections (BSI) are one of the most important causes of morbidity and mortality worldwide. The first and most sensitive method for diagnosis is blood culture. Early detection and identification of the causative microorganism from blood cultures and determination of antibiotic susceptibility are important in terms of providing appropriate treatment to the patient and reducing mortality. Automated blood culture systems, with increasing microorganism detection rate and speed, are currently the most preferred method for culturing blood samples[6,7]. Differences in the distribution of antibiotherapy requiring microorganisms and antibiotic resistance rates in ICUs can be observed amongst various hospitals, as well as in the same unit over time. Factors and antibiotic susceptibilities detected in these units should be known and monitored at regular intervals. Treatment protocols should be updated according to these follow-up results.

This study aimed to investigate the distribution of pathogenic microorganisms isolated from tracheal aspirates and blood cultures of the patients, and their antibiotic resistance profiles in the ICU.

MATERIAL and METHOD

Our study was a retrospective research , and ethics approval was obtained from the Medeniyet University Goztepe Training and Research Hospital Ethics Committee (decision number 2019/0090). The tracheal aspirate and blood cultures sent to Istanbul Medeniyet University Goztepe Training and Research Hospital Medical Microbiology Laboratory between January 2014 and December 2018 were evaluated retrospectively.

Incubation and evaluation

Tracheal aspirate samples were obtained under sterile conditions using special catheters designed for sampling and aspiration of saline from the endotracheal tube. The samples were incubated with 5% sheep blood agar, chocolate agar, and Eosin Methylene Blue (EMB) agar quantitatively

and incubated at 37°C under aerobic conditions. Plates where growth of ≥100,000 cfu/ml microorganisms were seen in pure culture were included in the study. Only the first tracheal aspirate isolate from each patient was included in the analysis and subsequent isolates from the same patient were excluded. Isolates that were confirmed as causative infectious agents were included in the analyses.

Blood culture samples were incubated in an automated blood culture system BacT/ALERT 3D (BioMérieux, Marcy-'Etoile, France). Blood samples obtained from patients with pneumonia were cultured on 5% sheep blood agar and EMB agar media and incubated at 37°C under aerobic conditions. All bacteria were examined according to their macroscopic appearance, colony-forming, and Gram-staining characteristics.

Only the first blood culture isolate from each patient was included in the analyses, subsequent isolates from the same patient were excluded. Also, only one of the blood cultures taken simultaneously was considered to be contaminated when a microorganism of the skin flora was produced. When a single blood culture was sent, its evaluation was made based on the clinical status of the patient. Strains considered as contaminated were not evaluated.

Antimicrobial susceptibility

Antimicrobial susceptibility tests of microorganisms were done by conventional methods and also using an automated system (VITEK-2, bioMérieux, Marcy-l'Etoile, France). The antimicrobials used in susceptibility testing were selected in accordance with the recommendations of the Working Group on Standardization of Antimicrobial Susceptibility Tests of the Turkish Society of Microbiology (TMC-ADTS)[7,8]. Antibiotic susceptibility tests were performed according to CLSI (Clinical and Laboratory Standards Institute) criteria published in 2014-2016 and EUCAST (The European Committee on Antimicrobial Susceptibility Testing) criteria released in 2017 and 2018[9-12].

Statistical analysis

The data are presented as numerical values and percentages.

RESULTS

During the study period, 5201 tracheal aspirate cultures and 18,074 blood culture samples sent from ICUs were accepted by our laboratory. Most (52.4%) of the tracheal aspirate samples, while 29.2% of the blood culture samples had demonstrated bacterial growth.

In tracheal aspirate cultures, 89.7% of the microorganisms were Gram-negative, 9.3%, and 1% of them Gram-positive and yeasts, respectively. The most common Gram-negative microorganism was A. baumannii (25.7%), followed by P. aeruginosa (25.1%) and K. pneumoniae (21.6%). The most effective antimicrobial agents against A. baumannii were colistin (98.6%), tigecycline (65%), amikacin (44.4%), and gentamicin (38.1%) (Table 1). It has been observed within 5 years that the rates of meropenem resistance ranged between 36.5% to 69.2% in P. aeruginosa, and between 2% to 8% in E. coli, 45.55% in K. pneumoniae isolates in 2014, and 45.8% in 2018 (Table 1). The rates of methicillin resistance in S. aureus were documented as 28.9% in 2018, and as 67.7% in 2015. The rates of penicillin resistance in isolates of S. pneumoniae were documented as 76.9% in 2018, and as 13.4% in 2015 (Table 2).

In blood culture, 31.4% of cultured microrganisms were Gram-negative, and 57.9% of them were Gram-positive bacteria, while 10.6% of them were yeasts. It was determined that Gram-positive bacteria consisted of coagulase-negative staphylococci (CNS) (78.9%), Enterococcus spp. (10.6%) and S. aureus (10.4%). The rates of methicillin resistance were documented as 89.2% in 2018, and 78.5% in 2015 for CNS bacteria, and as 42.6% in 2018, and 92.4% in 2015 for S. aureus

Tablo 1. Percentage antimicrobial resistance of Gram (-) microorganisms grown in from tracheal aspirate cultures (%).

	Year	AN	CAZ	IMP	MEM	CN	CIP	TZP	SXT	TGC	AMC	ERT	CRO	CZ	C	n
A.baumannii.	2014	60.7	98.4	98.3	98.3	82.0	97.7	100.0	93.8	32.4	-	-	-	-	0	60
	2015	34.2	95.6	94.3	93.7	62.7	93.7	94.7	84.2	18.4	-	-	-	-	0	158
	2016	34.0	95.8	96.4	95.8	38.9	95.8	97.2	64.6	30.6	-	-	-	-	0	144
	2017	69.2	94.1	94.7	97.1	53.4	93.3	96.0	82.6	44.2	-	-	-	-	2.2	138
	2018	83.6	96.0	92.5	95.7	83.4	94.1	96.1	85.1	46.9	-	-	-	-	4.8	140
	Total	55.6	95.7	95.0	93.2	61.9	94.5	96.2	80.9	35.0	-	-	-	-	1.4	580
P.aeurigonasa	2014	25.0	56.1	55.6	69.2	50.0	48.6	58.6	-	-	-	-	-	-	5.8	39
	2015	42.7	62.9	0.0	69.7	49.4	52.8	76.4	-	-	-	-	-	-	4.5	89
	2016	19.2	54.4	71.4	59.6	23.3	38.6	78.8	-	-	-	-	-	-	1.7	171
	2017	18.7	36.3	52.0	51.7	20.3	37.5	51.2	-	-	-	-	-	-	2.4	172
	2018	19.4	29.6	39.8	36.5	21.2	33.1	49.1	-	-	-	-	-	-	4.1	170
	Total	22.7	44.4	54.0	53.4	27.2	39.4	58.2	-	-	-	-	-	-	3.7	641
K.pneumoniae	2014	39.4	70.3	30.4	45.5	70.0	66.7	42.9	64.3	8.3	90.9	50.0	75.0	92.9	5.5	22.0
	2015	65.9	87.9	73.5	70.3	83.5	78.0	87.9	74.7	12.9	93.2	70.0	88.5	87.9	4.5	91.0
	2016	43.8	81.3	63.2	50.0	70.0	60.0	71.3	55.0	8.9	83.8	49.0	83.8	83.8	18.7	80.0
	2017	49.0	70.6	60.0	43.3	47.3	70.0	70.5	52.7	54.5	49.3	53.4	73.4	99.2	14.6	150
	2018	47.6	74.5	57.1	45.8	51.3	79.4	72.2	62.4	43.9	54.7	47.3	77.2	100.0	17.1	190
	Total	50.4	73.7	66.7	49.9	59.2	73.2	75.4	60.6	36.4	57.8	53.5	79.1	94.8	12.1	533.0
S.maltophilia	2014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2015	-	33.3	-	-	-	-	-	18.0	-	-	-	-	-	-	-
	2016	-	64.7	-	-	-	-	-	14.0	-	-	-	-	-	-	-
	2017	-	83.3	-	-	-	-	-	9.8	-	-	-	-	-	-	-
	2018	-	96.2	-	-	-	-	-	8.9	-	-	-	-	-	-	-
	Total	-	79.5	-	-	-	-	-	13.3	-	-	-	-	-	-	-
E.coli	2014	16.0	60.0	8.0	8.0	33.3	33.3	27.3	50.0	11.1	75.0	0.0	100.0	66.7	0.0	25.0
	2015	37.5	61.1	0.0	0.0	27.8	50.0	27.8	72.2	0.0	61.1	0.0	61.1	61.5	0.0	18.0
	2016	29.6	70.4	0.0	3.7	29.6	48.1	51.9	33.3	0.0	66.7	4.0	70.4	72.0	4.0	27.0
	2017	30.3	67.6	0.0	3.0	21.2	45.5	45.5	48.5	3.2	45.3	3.0	74.2	100.0	0.0	33.0
	2018	26.0	68.8	0.0	2.0	16.0	60.0	29.4	52.0	4.1	43.8	4.0	69.4	100.0	0.0	50.0
	Total	27.2	66.2	3.4	3.3	46.7	50.7	37.1	50.0	3.7	53.2	3.0	70.5	85.0	0.8	153.0

AN: Amikacin, CAZ: Ceftazidim, IMP: Imipenem, CN: Gentamicin, CIP:Ciprofloxacin, TZP: Piperacilin-tazobactam, SXT: Trimethoprim sulfamethoxazole, TGC: Tigecycline, SAM: Ampicillin sulbactam, AMC: Amoxicillin clavulanate, ERT: Ertapenem, CRO: Seftriakson, CZ: Sefazolin, C: Colistin, n: Bacteria count.

Table 2. Percentage antimicrobial resistance of Gram (+) microorganisms grown in tracheal aspirate (%).

		P	FOX	E	DA	SXT	CIP	LEV	TE	CN	n
S. aureus	2014	-	-	-	-	-	-	-	-	-	
	2015	-	67.7	83.9	51.6	6.5	40.0	38.7	64.5	19.4	31.0
	2016	-	39.5	92.1	26.3	7.9	31.6	15.8	28.9	13.2	38.0
	2017	-	25.2	23.1	16.4	9.6	11.2	12.8	16.0	10.4	107.0
	2018	-	28.9	17.8	18.8	7.4	11.1	13.4	17.0	11.1	114.0
	Total	-	28.8	20.4	18.8	8.4	13.8	13.5	18.1	11.1	287.0
S. pneumoniae	2014	-	-	-	-	-	-	-	-	-	
	2015	13.4	-	50.0	57.1	28.6	-	0.0	57.1	-	7.0
	2016	25.0	-	66.7	57.1	13.3	-	26.7	66.7	-	12.0
	2017	64.3	-	61.5	50.0	42.9	-	14.3	35.7	-	14.0
	2018	76.9	-	66.7	46.2	46.2	-	7.7	46.2	-	13.0
	Total	50.0	-	63.0	52.1	23.2	-	15.2	51.0	-	46.0

P: Penicillin. FOX: Cefoxitin. E: Erythromycin. DA: Clindamycin. SXT: Trimethoprim sulfamethoxazole. CIP: Ciprofloxacin. LEV: Levofloxacin. TE: Tetracycline. CN: Gentamicin. n: bacteria count.

(Table 3). The rates of ampicillin resistance were documented as 23% in 2014, and 11.7% in 2018 for Enterococcus spp. The most common Gram-negative microorganisms were K. pneumoniae (9.3%), followed by A. baumannii (8.8%), and P. aeruginosa (4.1%). A. baumannii was mostly sus-

Table 3. Percentages antimicrobial resistance of Staphylococcus spp. grown in blood culture (%).

		FOX	E	DA	SXT	CIP	LEV	TE	CN	n
S. aureus	2014	92.4	82.3	48.5	63.6	80.0	58.3	14.3	66.7	79
	2015	95.8	80.9	51.1	6.5	32.1	42.6	44.7	31.9	24
	2016	29.4	75.9	22.2	13.0	25.9	11.1	29.6	11.1	54
	2017	30.4	56.3	21.1	8.3	30.8	18.9	37.5	9.7	46
	2018	42.6	55.6	20.9	7.3	26.7	19.0	34.0	10.5	51
	Total	58.3	69.4	34.3	25.1	43.2	28.7	34.7	29.1	254
KNS	2014	78.5	86.9	49.8	37.5	69.6	72.3	72.8	58.7	289
	2015	90.4	91.3	61.9	30.4	43.5	75.4	75.3	62.4	450
	2016	69.2	89.7	61.9	33.2	69.8	68.7	68.2	59.3	632
	2017	65.6	78.3	51.2	29.5	60.8	38.6	54.6	15.7	360
	2018	89.2	77.5	55.5	30.6	64.5	36.3	56.1	15.8	347
	Total	80.6	86.0	57.4	32.1	62.2	59.7	66.1	43.9	2078

FOX: Cefoxitin. E: Erythromycin. DA: Clindamycin. SXT: Trimethoprim sulfamethoxazole. CIP: Ciprofloxacin. LEV: Levofloxacin. TE: Tetracycline. CN: Gentamicin. n: Bacteria count.

Table 4. Percentages antimicrobial resistance of Gram (-) microorganisms grown in blood cultures (%).

	Year	AN	CAZ	IMP	MEM	CN	CIP	TZP	SXT	TGC	AMC	ERT	CRO	CZ	C	n
A.baumannii	2014	50.4	99.3	97.4	97.3	64.0	96.5	93.8	75.2	36.6	-	-	-	-	0	148
	2015	50.4	94.7	93.8	94.7	52.2	94.7	92.5	76.1	25.7	-	-	-	-	4.4	113
	2016	39.2	97.6	97.5	97.6	33.6	96.8	100.0	63.2	20.0	-	-	-	-	0	125
	2017	48.6	84.6	82.4	82.6	55.9	86.7	93.1	45.7	31.8	-	-	-	-	4.1	23
	2018	51.2	86.7	88.2	79.2	51.2	93.3	96.8	46.3	33.3	-	-	-	-	6.8	24
	Total	47.2	96.6	95.5	94.9	51.2	95.6	96.4	66.7	28.0	-	-	-	-	3.06	433
K.pneumoniae	2014	33.8	73.8	48.1	76.9	46.2	54.5	68.1	63.5	50.0	73.7	53.0	74.6	100.0	4.4	39
	2015	61.5	88.0	63.8	65.5	79.5	75.2	84.6	59.0	12.7	89.7	71.3	87.8	91.8	13.6	116
	2016	63.9	86.7	78.6	61.4	65.2	63.3	80.4	68.4	6.3	93.6	64.3	88.5	91.7	80	158
	2017	60.6	69.6	43.8	36.7	44.0	52.4	68.2	43.6	14.6	50.0	37.2	60.9	100.0	19.5	49
	2018	61.8	73.9	41.2	37.3	43.4	52.2	68.7	43.9	17.0	50.8	42.2	57.1	100.0	16.2	51
	Total	57.3	82.8	58.8	58.0	60.7	63.9	76.3	59.2	11.4	94.1	60.1	79.7	93.0	14.6	413
P.aeruginosa.	2014	15.8	80.4	81.1	79.2	10.9	68.4	85.7	-	-	-	-	-	-	1.9	53
	2015	44.4	61.1	69.7	66.7	41.7	55.6	77.8	-	-	-	-	-	-	11.1	36
	2016	26.0	58.9	59.4	58.3	32.9	47.9	79.5	-	-	-	-	-	-	4.1	72
	2017	13.0	40.0	25.0	25.0	5.3	17.6	50.0	-	-	-	-	-	-	0	20
	2018	16.0	47.1	26.1	26.1	13.6	16.7	52.2	-	-	-	-	-	-	5	23
	Total	22.8	58.4	64.6	58.3	23.9	49.8	75.0	-	-	-	-	-	-	4.4	204
E. coli	2014	6.9	41.9	3.2	3.2	32.3	51.9	34.6	62.1	0.0	53.3	0.0	45.5	85.7	0	31
	2015	16.0	63.6	0.0	12.5	28.0	32.0	62.5	62.5	7.1	88.0	17.4	54.2	76.9	0	24
	2016	20.8	29.2	0.0	8.3	16.7	41.7	29.2	33.3	4.5	45.8	4.2	37.5	40.9	0	24
	2017	37.5	60.8	17.2	17.1	27.7	61.2	45.3	58.8	0.0	46.3	11.8	57.5	63.2	11.5	35
	2018	40.0	60.4	20.0	20.0	25.0	60.4	47.2	59.6	3.3	47.3	12.1	60.0	65.0	14.8	35
	Total	23.6	53.6	10.0	11.9	26.3	50.0	44.4	56.7	3.0	53.2	9.6	52.7	61.7	5.2	149

AN: Amikacin. CAZ: Ceftazidim. IMP: Imipenem. CN: Gentamicin. CIP: Ciprofloxacin. TZP: Piperacilin-tazobactam. SXT: Trimethoprim sulfamethoxazole. TGC: Tigecycline. AMC: Amoxicillin clavulanate. ERT: Ertapenem. CRO: Ceftriaxon. CZ: Cefazolin. C: Colistin. n: bacteria count.

ceptible to antimicrobial colistin (97%), followed by tigecycline (72%), amikacin (52.8%), and gentamicin (47.8%).

The rates of meropenem resistance were documented for Acinetobacter spp. as 97.3% in 2014 and 79.2% in 2018, as 76.9% for K. pneumoniae in 2014 and 37.3% in 2018 and as 79.2% for P. aeruginosa in 2014 and 26.1% in 2018 (Table 4).

DISCUSSION

Our study showcased a drop throughout the year in carbapenem resistance across Gram-negative

microorganisms and methicillin resistance in S. aureus. The decline in resistance is tied to the prudent antibiotic usage practices in our hospital.

Lower respiratory tract infections are the most common infections among hospital infections seen in the ICU[13]. Gram-negative, non-fermentative bacteria, such as P. aeruginosa and A. baumannii are among the causative agents of these infections, with high mortality and morbidity rates[14]. The Gram-negative microorganisms frequently isolated from ICUs in the SENTRY program (2009-2011, 65 centers from USA and 36 from Europe) were E. coli, K. pneumoniae, P. aeruginosa, Enterobacter spp., Serratia spp., Haemophilus influenzae, A. baumannii and Proteus mirabilis[15]. Also, in two studies that investigated the growth of microorganisms in tracheal aspirate cultures in ICUs in Turkey, the most common causative agents were A. baumannii and P. aeruginosa[14,16]. The data obtained from our study were also consistent with the results of these studies.

Within the scope of the SENTRY program conducted between 2000 and 2006 and among studies of carbapenem resistance in A. baumannii isolates grown in samples sent from Turkey, imipenem and meropenem susceptibility rates in year 2000 were 80.4% and 71.7%, respectively. By 2006 this was reported to be 40% for both antimicrobial agents. This study showcased genes encoding oxacillinases showing carbapenemase activity (OXA-23, -24 and -58 clusters) which were detected in all carbapenem-resistant A. baumannii isolates[17]. Ozünel et al.[18] found that imipenem resistance was 86. % in Acinetobacter strains grown in ETA cultures between 2012 and 2013. In the study of Aydemir et al.[19] rate of imipenem resistance was found to be 93.3% in Acinetobacter strains grown in ETA cultures in 2015 and 2016. In our study, we concluded that imipenem resistance in ETA culture isolates of A.baumanni declined throughout the years and remained around at 95% in line with the studies mentioned above. The reasons for the high rates of resistance of microorganisms grown in ETA cultures of inpatients in our ICUs include intense invasive treatment of patients, long hospitalization periods, and the administration of broad-spectrum antibiotics to patients rather than the application of restrictive antibiotic program. Therefore, antibiotic management programs should be established and implemented in our country, region, and hospital as soon as possible to better curb the resistance development rates.

In the SENTRY Antimicrobial Survey Program (1997-2008), S. aureus consisted of 28% of nosocomial and ventilator-associated pneumonia (VAP) agents[20]. In a study by Kollef et al.[21] evaluating the bacterial growth of deep tracheal aspirate cultures in patients with pneumonia, MRSA was found in 14.8% of the cases. In a review of Asian countries by Chawla et al.[22] A. baumannii was the major VAP agent in ICUs, while MRSA was not as major of a problem as in Western countries. In our study, S. aureus consisted of 6% of isolated microorganisms, followed by Gram-negative agents. Gram-positive bacteria coagulase-negative staphylococci were most common bacteria in blood cultures.

In a study conducted in China, it was found that the rates of methicillin resistance in S. aureus strains that cause blood-borne infection increased from 8.4% to 63% in 20 years[23]. Aydemir et al.[19] found methicillin resistance in 30% of S. aureus strains. In our study, methicillin resistance in S. aureus strains decreased over the years. The rate of methicillin-resistant S. aureus, which was 67.7% in 2015, decreased to 28.9% in 2018. In a study conducted in India in 2019, the rate of methicillin resistance was 30% in S. aureus strains[22]. In our study, resistance to the primarily preferred glycopeptide agents was not detected in MRSA strains.

Bloodstream infections (BSI) are invasive infections with high morbidity and mortality. Rapid and accurate identification of bacteremia or fungemia agents in blood cultures contributes to the management of treatment, timely infection

control measures, and improved mortality. There have been some changes in the epidemiology of bloodstream infections over time. Gram-negative bacteria were more frequently isolated from BSI in the 1970s, and Gram-positive cocci began to come to the fore in the 1980s[24]. In a multicenter study conducted in Canada, the rates of Gram-positive and Gram-negative bacteria isolated from BSI in ICUs were reported to be 58.6% and 21.2%, respectively[25]. In our study, this rate was 31.5% for Gram-negative and 57.9% for Gram-positive bacteria. The type and capacity of ICUs, different antibiotic treatment protocols applied, hospital or community-based bacteremia, and the number and characteristics of patients included in the study can be cited as the reasons for the differences between centers.

The most common Gram-negative bacteria isolated from blood cultures are E. coli, Klebsiella, Enterobacter, Proteus, Pseudomonas, and Acinetobacter species[2,24]. In studies involving intensive care units, E. coli, Klebsiella, Pseudomonas, and Acinetobacter species were detected more frequently[24,26]. In our study, the most frequently isolated bacteria were A. baumannii, K. pneumonia and P. aeruginosa. Multiple antibiotic resistance in A. baumannii strains is a serious problem in treatment. The increase in carbapenemase production seen in these bacterial species in recent years brings with it increased resistance to the carbapenem group antibiotics.

Uzun et al.[26] reported 86% carbapenem resistance rate in the A. baumannii strains isolated from blood cultures and Sirin et al.[24] reported this resistance rate as 90.4%. In our study, this rate was 95.5%, which is consistent with previous studies. In our study, tigecycline resistance in Gram-negative agents ranged from 3 to 28%. Tigecycline is recommended for the treatment of complicated intraabdominal and complicated skin and soft tissue infections and community-acquired pneumonia, but there are also studies on its use in high doses in clinically critical patients[27]. The fact that carbapenems are frequently preferred and prioritized antibiotics in cases where empirical treatment should first be initiated in ICU infections in our hospital, can be considered as one of the reasons for the high rates of carbapenem resistance in our hospital.

Coagulase-negative Staphylococci and S.aureus account for the majority of Gram-positive bacteria isolated from blood culture samples. Durmaz et al.[7] reported isolation rates of 24.4% and 12.6%, respectively. Şirin et al.[24] reported these values as 25.3% and 4.9%, respectively. In our study, the isolation rates were found to be 42% and 5.2%, respectively. Another important problem among isolates of staphylococci is methicillin resistance. According to the results of EARSS, which is a surveillance study covering European countries, MRSA rates vary between 5 and 100%, and in some countries, it has been reported to decrease gradually over the years[28]. Sirin et al.[24] reported that the rates of methicillin resistance in S. aureus and CNS strains were 79.5% and 12.2%, respectively. In our study, these rates were 58.3% and 80.6%, respectively.

In addition to phenotypic methods, identification of resistance mechanisms at the genotypic level (by molecular methods) is important in terms of limiting the spread of resistance and conducting epidemiological analyzes in infections caused by such multiple resistant bacteria. The most important limitation of our study is the lack of research on the detection of resistance genes at the molecular level.

In conclusion, it should be kept in mind that infections in patients followed up in ICUs are frequently caused by multiple resistant microorganisms. Antimicrobial resistance patterns of agents detected in ICUs should be monitored regularly, and treatment protocols should be updated accordingly. Each center should determine the antimicrobial resistance of the active microorganisms by cumulative antibiogram studies.

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