RESEARCH ARTICLE

Distribution of Microorganisms and Antibiotic Resistance Rates Isolated From Blood Cultures: 5-Year Evaluation in a University Hospital in Northern Cyprus

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ABSTRACT

Objective: Bloodstream infections (BSI) are considered to be the most important cause of morbidity and mortality. The main purpose of this study is to examine the distribution of microorganisms in blood cultures and the rates of antimicrobial resistance.

Methods: Microorganisms isolated from 7.866 blood cultures which were sent to our laboratory between January 2016-December 2020 were retrospectively evaluated. Blood culture bottles were incubated in BACTEC 9120 system. Blood samples were taken from the bottles with a sterile syringe and cultured on Eosin-Methylene Blue (EMB) and 5% sheep blood agars if there was a positive signal. The cultivated cultures were left to incubate at 35°C for 24-48 hours. VITEK 2 compact automated system was used for identification and antibiotic susceptibility tests (AST).

Results: Growth was detected in 691 (8.8%) of blood cultures. There were 56.7% gram-negative, 42.7% gram-positive bacteria and 0.6% *Candida* species. The most common bacteria isolated are; coagulase negative staphylococci (CNS) (21.1%), *Escherichia coli* (15.2%), *Klebsiella pneumoniae* (11.9%) and *Staphylococcus aureus* (11.4%). The rate of ESBL-*Escherichia coli* increased in 2020, but this was not statistically significant. ESBL-*Klebsiella pneumoniae* species showed a significant increase over the years and reached the highest level (69.6%) in 2019. MDR (multi drug resistance) rate for *Pseudomonas aeruginosa* was determined as 13%. MDR rate for *Acinetobacter baumannii* was determined as 97%. The rate of methicillin resistant *Staphylococcus aureus* among patients is 30.4%.

Conclusions: It is critical to determine microorganisms and their antibiotic susceptibilities as soon as possible in BSI. Active surveillance systems help manage the BSI.

Keywords: Blood Culture, Infection, Antimictobial Susceptibility, Resistant, Northern Cyprus.

Kan Kültürlerinden İzole Edilen Mikroorganizmaların Dağılımı ve Antibiyotik Direnç Oranları: Kuzey Kıbrıs'ta Bir Üniversite Hastanesindeki 5 Yıllık Değerlendirme

ÖZET

Amaç: Kan dolaşımı enfeksiyoları (KDE), morbidite ve mortalitenin en önemli nedeni sayılmaktadır. Bu çalışmada, kan kültürlerinde üreyen mikroorganizmaların dağılımını ve antimikrobiyal direnç oranlarını incelemek amaçlanmıştır.

Gereç ve Yöntem: Yakın Doğu Üniversitesi (YDÜ) Hastanesi, Mikrobiyoloji Laboratuvarı'na Ocak 2016-Aralık 2020 tarihleri arasında gönderilen 7.866 kan kültüründen izole edilen mikroorganizmalar retrospektif olarak değerlendirmeye alınmıştır. Kan kültür şişeleri BACTEC 9120 otomatize sisteminde inkübe edilmiştir. İnkübasyon sırasında pozitif sinyal elde edilmesi halinde, steril enjektörle kan kültür şişelerinin içerisinden örnek alınarak Eosin-Methylene Blue (EMB) ve %5 koyun kanlı agarlara ekimleri yapıldı. Ekimi yapılan kültürler 24-48 saat süresince 35°C'de etüvde inkübasyona bırakıldı. Üreme saptanan kültürlerdeki mikroorganizmaların identifikasyon ve antibiyotik duyarlılık testleri (ADT) için VİTEK 2 (Biomerieux) kompakt otomatize sitemi kullanıldı.

Bulgular: Kan kültürlerinin 691 (%8,8)'inde üreme saptanmıştır. İzole edilen mikroorganizmaların 392 (%56,7)'sini gram negatif bakteriler, 295 (%42,7)'ini gram pozitif bakteriler ve 4 (%0,6)'ünü ise *Candida* türleri oluşturmaktadır. En sık izole edilen bakteriler sırasıyla; Koagülaz negatif stafilokoklar (KNS) (%21,1), *Escherichia coli* (%15,2), *Klebsiella pneumoniae* (%11,9), *Staphylococccus aureus* (%11,4) idi. *Escherichia coli* dağılımına bakıldığı zaman genişlemiş spektrumlu beta-laktamaz (GSBL) oranı 2020 yılında artış göstermiştir fakat bunun istatistiksel olarak anlamlı olmadığı anlaşılmıştır. GSBL pozitif *K. pneumoniae* türleri ise yıllar içerisinde anlamlı derecede artış göstermiş ve 2019 yılında en yüksek (%69,6) seviyeye ulaşmıştır. *Pseudomonas aeruginosa* için ÇİD (çoklu ilaç dirençli) oranı %13 olarak belirlenmiştir. *Acinetobacter baumannii* için ÇİD oranı ise %97 olarak bulunmuştur. İzole edilen *Staphylococcus aureus* suşlarının %30,4'ü metisilin dirençli *Staphylococccus aureus* (MRSA) idi.

Sonuç: KDE'dan izole edilen mikroorganizmaların ve duyarlılıklarının en kısa sürede belirlenmesi kritik öneme sahiptir. Ayrıca, aktif sürveyans sistemleri KDE'nın yönetimine yardımcı olmaktadır.

Anahtar Kelimeler: Kan Kültürü, Enfeksiyon, Antimikrobiyal Duyarlılık, Direnç, Kuzey Kıbrıs.

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INTRODUCTION

Bloodstream infections (BSI) can cause serious clinical consequences such as sepsis and multiple organ failure, so it is considered as the most important cause of morbidity and mortality. Therefore, application of rapid and appropriate empirical therapy is critical for patients. Management of these types of infections becomes more complicated when antimicrobial resistance increases (1,2). There is a parallel increase in microorganisms isolated from BSI due to reasons such as the frequent use of invasive interventions, the increase in the use of broad-spectrum antibiotics, cancer surgery, organ transplantation applications and the increase in immunosuppressive treatments (3). Bacteremia caused by bacteria with multiple antibiotic resistance extends the hospitalization period of patients, increases the mortality rate, creates the risk of other infections and increases the cost per patient in hospitals and healthcare institutions (4).

Although the ratio of bacteremia varies between 20-30%, this rate can be up to 50% in patients with sepsis and multiple organ failure. The estimated mortality rate of bacteremia due to hospital is accepted as 15-30%. In addition, bacteria have resistance issues against antibiotics due to the increasing use of antibiotics. There are some resistant bacteria which causes treatment failures and increase in mortality rates. These are; methicillin resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii*, *Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella pneumoniae* which produces extended spectrum beta-lactamases (ESBL), and carbapenemase-forming *Enterobacteriaceae* (5-7).

Blood cultures, which are accepted as gold standard in the diagnosis of bacteremia, play an important role in identifying infections, determining antibiotic susceptibility parameters and in the treatment process. The distribution of microorganisms isolated from blood cultures and antibiotic resistance rates vary according to years and geographic regions, as well as different results can occur between hospitals in the same region or even in different departments within the same hospital. Therefore, it is important to know and follow the effective microorganisms and resistance patterns in order to guide appropriate and correct empirical treatment (8-10).

Surveillance systems are used in developed countries to monitor changing infection trends. These surveillance systems provide entire data on microorganisms and provide clues about the clinical significance, etiological trends and antimicrobial resistance patterns of all infections, including BSI. Active surveillance systems are not available in most developing countries where infectious diseases are more prevalent (2).

The main purpose of this study is to examine the distribution of microorganisms grown in blood cultures and their antimicrobial resistance rates in order to guide clinicians in the appropriate and correct empirical treatment of BSI. In addition, it is among our goals to determine infection prevention policies by shedding light on surveillance studies that are not carried out in our country.

MATERIAL AND METHODS

Study Design: Microorganisms isolated from 7.866 blood cultures sent to Microbiology Laboratory of Near East University (NEU) Hospital between January 2016 and December 2020 were retrospectively evaluated. Only one result was included in the study if the same bacteria replicated in more than one blood culture of the same patient.

Bacterial Identification and Antibiotic Susceptibility Test: BACTEC 9120 (Becton, Dickinson and Company Sparks, USA) automated blood culture system was used to detect growth in blood cultures. Blood samples of 8-10 mL from adult patients and 1-3 mL from infant and pediatric patients were taken and transferred to BD BACTEC Plus Aerobic/F and BD BACTEC Peds Plus/F culture bottles, respectively, and the samples were incubated on the device for seven days. If a positive signal was obtained during the incubation, samples were taken from blood culture bottles with a sterile syringe and cultivated on Eosin-Methylene Blue (EMB) and 5% sheep blood agars. The cultivated cultures were left to incubate at 35°C for 24-48 hours. VITEK 2 (Biomerieux) compact automated system was used for identification and antibiotic susceptibility tests (AST) of microorganisms in cultures with growth. VITEK 2 GN and VITEK 2 GP cards used for identification. Also, VITEK 2 AST-N325, VITEK 2 AST-N327, VITEK 2 AST-N326, VITEK 2 AST-P641 and VITEK 2 AST-P640 cards were used to measure antibiotic susceptibility. ADT was evaluated according to the EUCAST (European Committee on Antimicrobial Susceptibility Testing) criteria and antibiotics detected as intermediate were considered as resistant. Coagulase negative staphylococci (CNS) growth samples which were in a single blood culture bottle and *Micrococcus* spp. growth samples were considered as contamination. Resistance to one antibiotic from at least three different antibiotic groups is accepted as 'Multi Drug Resistant' (MDR), and resistance to all other antibiotics except one or two antibiotics is accepted as 'Extreme Drug Resistant' (XDR).

Statistical Analysis: SPSS (Statistical Package of the Social Sciences) Demo Ver 22 (SPSS Inc., Chicago, IL, USA) program was used for all statistical analysis of the data. In order to determine statistical significance, Pearson Chi-square, Fisher's Exact Test and One-Way ANOVA tests were used and $p<0.05$ values were considered significant.

Ethical Approval: Ethics committee approval was obtained for our study with the project number NEU/2021/88-1292 at the meeting held by the NEU Scientific Research Ethics Committee on 25.02.2021.

RESULTS

A total of 7.866 blood culture tests were carried out in a 5-year period from January 2016 to December 2020 in our laboratory. There were 4,590 (58.4%) blood samples from male and 3.276 (41.6%) blood samples from female and the age average was 59.25±24.44 (0-100 years old). Growth was detected in 691 (8.8%) of blood cultures which are 367 (53.1%) of these patients were male and 324 (46.9%) female, and their mean age was 66.15±19.82 (0-100 years old). While there was no growth in 6,531 (83%) of the samples, 644 (8.2%) of them were accepted as contamination. It was determined that the mean age of the patients with growth was significantly higher than those without growth (p<0.001). In parallel with this, it can be seen in the Table 1, it was found that the most growth of blood cultures has seen at patients who are aged >60 and the least growth has seen at the patients who are 21-40 years old due to the analysis performed among age groups (p<0.001). Accordingly, it is seen that the risk of BSI may increase with age. In addition, a significant relationship was observed between the growth in blood cultures and gender, and it was found that the growth in female was higher than in male as shown in Table 1 (p=0.002).

Table 1. Evaluation of blood culture results

	Blood Culture Positive	Blood Culture Negative	*P*
Gender			
Male	367 (%8.7)	3867 (%91.3)	0.002
Female	324 (%10.8)	2664 (%89.2)	
Age Group			
0-20	42 (%5.5)	726 (%94.5)	<0.001
21-40	17 (%2.5)	669 (%97.5)	
41-60	130 (%10.6)	1099 (%89.4)	
>60	502 (%11.1)	4037 (%88.9)	
Year			
2016	89 (%8.2)	990 (%91.8)	0.009
2017	162 (%9.5)	1545 (%90.5)	
2018	155 (%9.8)	1429 (%90.2)	
2019	170 (%11.8)	1275 (%88.2)	
2020	115 (%8.2)	1292 (%91.8)	
Season			
Spring	158 (%8.4)	1723 (%91.6)	0.007
Summer	196 (%11.0)	1583 (%89.0)	
Autumn	178 (%10.6)	1500 (%89.4)	
Winter	159 (%8.4)	1725 (%91.6)	

It can be seen that from Table 1, the growth in blood cultures was the highest in 2019 (170, 11.8%) and there was a significant decrease in growth (115, 8.2%) in 2020 (p=0.020). In addition, it was observed that BSI were most common in the summer months when compared within the seasons (p=0.005). In blood cultures of patients who have been sent blood samples were isolated the most is shown in Figure 1. These are; CNS (146/691, 21.1%), *Escherichia coli* (105/691, 15.2%), *Klebsiella pneumoniae* (82/691, 11.9%), *Staphylococccus aureus* (79/691, 11.4%), *Pseudomonas aeruginosa* (54/691, 7.8%), *Enterococcus faecalis* (43/691, 6.2%) and *Acinetobacter baumannii* (33/691, 4.8%) respectively.

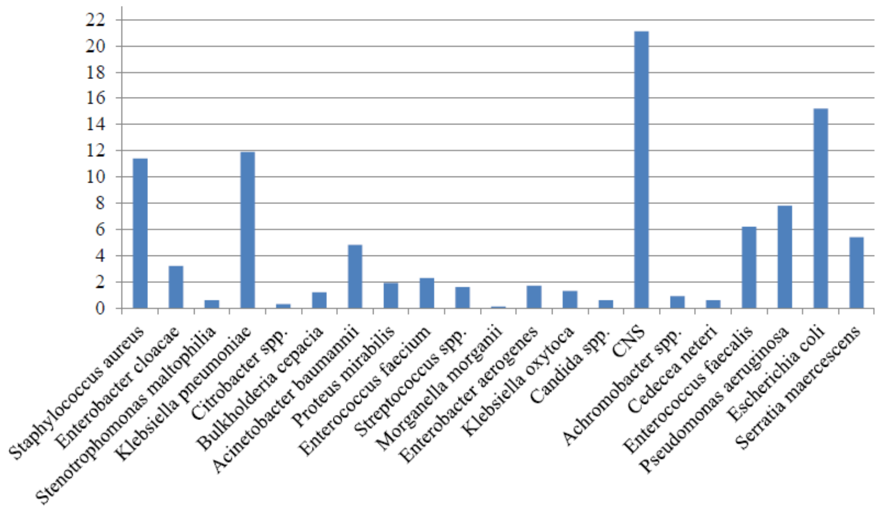

Figure 1. Distribution of microorganisms isolated in blood cultures (%)

The species of the microorganisms found from blood cultures are; 392 (56.7%) gram-negative, 295 (42.7%) gram-positive and 4 (0.6%) *Candida* species. 287 (73.2%) were *Enterobacterales* and 105 (26.8%) were non-fermenting gram-negative bacteria among the gram-negative bacteria. When the antibiotic sensitivities in *Escherichia coli* are examined, it is seen that the most resistant antibiotics are ciprofloxacin (64.1%), trimethoprim-sulfamethoxazole (59.8%) and cefepime (58.1%). The most sensitive antibiotics were found as meropenem (97.1%), imipenem (96.7%) and amikacin (96.2%). It was determined that *Klebsiella pneumoniae* isolates were most resistant to cefepime (55.7%), ceftazidime (53.2%) and aztreonam (53.1%) antibiotics. What is more, amikacin (95.1%), imipenem (83.9%) and gentamicin (81.2%) antibiotics were the most effective antibiotics against *Klebsiella pneumoniae* isolates. Table 2 shows the antibiotic resistance rates and ESBL positivity in the most frequently isolated *Enterobacterales*.

Table 2. Antibiotic resistance rates in the most frequently isolated in blood cultures, n (%)

Antibiotic	*Escherichia coli*	*Klebsiella pneumoniae*	*Enterobacter* spp.	*Serratia marcescens*
Amikacin	4/105 (3.8)	4/82 (4.9)	0/32 (0.0)	1/37 (2.7)
Aztreonam	46/88 (52.3)	34/64 (53.1)	8/30 (26.7)	3/36 (8.3)
Cefepime	61/105 (58.1)	44/79 (55.7)	14/32 (43.8)	4/37 (10.8)
Ceftazidime	57/102 (55.9)	42/79 (53.2)	15/32 (46.9)	2/36 (5.6)
Ceftriaxone	54/97 (55.7)	40/77 (51.9)	22/31 (71.0)	2/22 (9.1)
Ciprofloxacin	66/103 (64.1)	40/79 (50.6)	9/33 (27.3)	1/37 (2.7)
Ertapenem	6/97 (6.2)	18/75 (24.0)	14/31 (45.2)	1/22 (4.6)
Gentamicin	21/103 (20.4)	15/80 (18.8)	7/34 (20.6)	1/37 (2.7)
Imipenem	3/92 (3.3)	10/62 (16.1)	7/31 (22.6)	14/36 (38.9)
Meropenem	3/105 (2.9)	16/80 (20.0)	7/32 (21.9)	2/37 (5.4)
PTZ	18/105 (17.1)	25/78 (32.1)	17/32 (53.1)	2/37 (5.4)
SXT	61/102 (59.8)	39/81 (48.1)	10/29 (34.5)	1/37 (2.7)
ESBL	59/105 (56.2)	44/82 (53.7)	-	-

Abbreviations: PTZ, piperacillin-tazobactam; SXT, trimethoprime-sulfametoxazole; ESBL, extended spectrum beta lactamase

When the ESBL distribution in *Escherichia coli* is examined, it can be seen that it increased in 2020, but this is not statistically meaningful (p=0.188). ESBL positive *Klebsiella pneumoniae* blood samples were found to be at very low rates (1/13, 7.7%) in 2016, but showed a significant increase over the years, reaching the highest level (16/23, 69.6%) in 2019 (p=0.007) (Table 3).

Table 3. ESBL positivity by years of the most commonly grown *Enterobacterales* in blood cultures, n (%)

	2016	2017	2018	2019	2020	p
Escherichia coli ESBL +	12/23 (52.2)	10/21 (47.6)	12/19 (63.2)	14/29 (48.3)	11/13 (84.6)	0.188
Klebsiella pneumoniae ESBL +	1/13 (7.7)	15/24 (62.5)	3/6 (50.0)	16/23 (69.6)	9/16 (56.3)	0.007

Abbreviation: ESBL, extended spectrum beta lactamase

The distribution of non-fermenting *Pseudomonas aeruginosa* and *Acinetobacter baumannii* over the years is shown in Figure 2, which are the most common isolated bacteria in blood cultures. When the resistance rates were examined, it was determined that amikacin (98.1%), meropenem (96.1%), colistin (92%), imipenem (90.2%) and gentamicin (90%) antibiotics were the most effective options in the treatment of *Pseudomonas aeruginosa*. MDR rate for *Pseudomonas aeruginosa* was determined to be 13%. The most sensitive antibiotics for isolated *Acinetobacter baumannii* are tigecycline (94.1%) and colistin (90.9%), respectively. In addition, MDR rate for *Acinetobacter baumannii* was found to be 97% (Table 4).

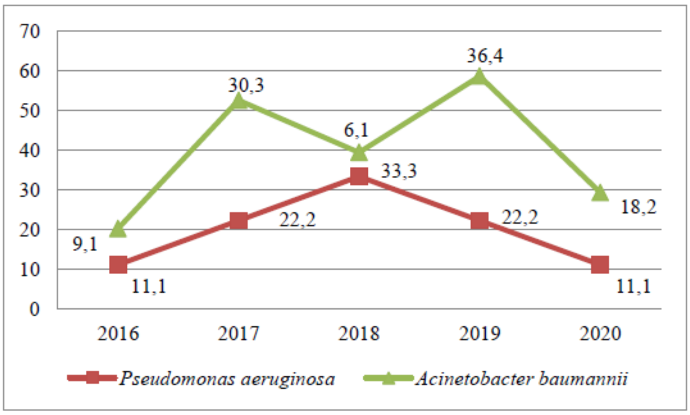

Figure 2. Distribution of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* over the years (%)

Table 4. Antibiotic resistance rates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

Antibiotic	*Pseudomonas aeruginosa* n (%)	*Acinetobacter baumannii* n (%)
Amikacin	1/53 (1.9)	28/30 (93.3)
Aztreonam	28/53 (52.9)	-
Cefepime	19/52 (36.6)	-
Ceftazidime	15/49 (30.6)	-
Ciprofloxacin	9/48 (18.8)	28/29 (96.6)
Colistin	4/50 (8.0)	3/33 (9.1)
Gentamicin	5/50 (10.0)	26/28 (92.9)
Imipenem	5/51 (9.8)	29/30 (96.7)
Meropenem	2/52 (3.9)	31/32 (96.9)
PZT	12/53 (22.6)	-
Tigecycline	-	1/17 (5.9)
SXT	-	24/28 (85.7)
MDR	7/54 (13)	32/33 (97)

Abbreviations: PTZ, piperacillin-tazobactam; SXT, trimethoprime-sulfametoxazole; MDR, multiple drug resistant

The gram-positive isolated in this study were CNS (146/295, 45.9%), *Staphylococcus aureus* (79/295, 26.8%), *Enterococcus faecalis* (43/295, 14.6%), *Enterococcus faecium* (16/295, 5.4%) and S*treptococcus* spp. (11/295, 3.7%). The rate of MRSA among this patients is 30.4% (24/79). The Table 5 indicates that MRSA was detected at the highest rate (6/9, 66.7%) in a statistically significant in 2019 when looked by years (p=0.021). The most resistant antibiotics in blood samples with MRSA were erythromycin (15/16, 93.7%), tetracycline (15/23, 65.2%) and clindamycin (13/22, 59.1%).

Table 5. Distribution of *Staphylococcus aureus* in blood cultures over the years, n (%)

	2016	2017	2018	2019	2020	*P*
MSSA	13 (%72.2)	8 (%61.5)	24 (%88.9)	3 (%33.3)	7 (%58.3)	0.021
MRSA	5 (%27.8)	5 (%38.5)	3 (%11.1)	6 (%66.7)	5 (%41.7)	

Abbreviations: MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*

Despite this, vancomycin and linezolid resistance were not found in any of the MRSA isolates, while resistance to daptomycin, rifampin, and teicoplanin was 5.6%, 8.3%, and 13.0%, respectively. A statistically significant difference was observed between methicillin resistance and clindamycin, daptomycin, erythromycin, teicoplanin, and tetracycline antibiotic resistances in all *Staphylococcus aureus* isolates. This is shown in Table 6 as p=0.000, p=0.025, p=0.000, p=0.027, p=0.000, respectively.

Table 6. Resistance rates in MRSA isolates detected in blood cultures, n (%)

Antibiotic	MRSA	MSSA	*P*
Ciprofloxacin	6/20 (30.0)	4/49 (8.2)	0.029*
Clindamycin	13/22 (59.1)	2/53 (3.8)	<0.001*
Daptomycin	1/18 (5.6)	0/51 (0.0)	0.025*
Erythromycin	15/16 (93.7)	6/40 (15.0)	<0.001*
Linezolid	0/21 (0.0)	0/53 (0.0)	-
Rifampin	1/12 (8.3)	3/38 (7.9)	0.269
Teicoplanin	3/23 (13.0)	0/53 (0.0)	0.027*
Tetracycline	15/23 (65.2)	9/52 (17.3)	0.000*
SXT	4/22 (18.2)	9/55 (16.4)	0.094
Vankomycin	0/24 (0.0)	0/55 (0.0)	-

*Statistically significant
Abbreviations: MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*; SXT, trimethoprime-sulfametoxazole

In our study, ESBL positive *Escherichia coli* and *Klebsiella pneumoniae* and MRSA isolates were evaluated according to age groups in patients who requested blood culture. Accordingly, it was determined that ESBL positivity increased significantly with age and ESBL positive bacteria were grown most frequently in the age group >60. However, it can be seen that from the Table 7, there was no significant relationship between the growth of MRSA in blood cultures and age groups (p=0.115).

Table 7. Distribution of ESBL and MRSA positivity by age groups, n (%)

	0-20	21-40	41-60	>60	*P*
ESBL positive	1/8 (12.5)	1/2 (50.0)	17/38 (44.7)	84/139 (60.4)	0.028*
ESBL negative	7/8 (87.5)	1/2 (50.0)	21/38 (55.3)	55/139 (39.6)	
MRSA	1/11 (9.1)	1/5 (20.0)	9/18 (50.0)	13/45 (28.9)	0.115
MSSA	10/11 (90.9)	4/5 (80.0)	9/18 (50.0)	32/45 (71.1)	

* Statistically significant
Abbreviations: ESBL, extended spectrum beta lactamase; MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*

Furthermore, it was determined that the most samples with any microorganism in blood cultures were sent from the intensive care department.

The distribution of blood cultures with growth detected according to the departments is shown in Table 8.

Table 8. Distribution of blood cultures with growth detected according to hospital department, n (%)

Department	*E. coli*	*K. pneumoniae*	*P. aeruginosa*	*A. baumannii*	*S. aureus*	*E. faecalis*
Emergency	-	2 (2.4)	-	-	4 (5.1)	-
Neurology	-	-	1 (1.9)	-	4 (5.1)	1 (2.3)
Cardiology	8 (7.6)	2 (2.4)	-	1 (3.0)	9 (11.4)	2 (4.7)
Child Health and Diseases	1 (1.0)	1 (1.2)	-	-	2 (2.5)	-
Intensive Care	45 (42.9)	53 (64.6)	37 (68.5)	29 (87.9)	25 (31.6)	28 (65.1)
Chest Diseases and Allergy	5 (4.8)	1 (1.2)	5 (9.3)	2 (6.1)	2 (2.5)	3 (7.0)
Internal Medicine	7 (6.7)	8 (9.8)	2 (3.7)	-	13 (16.5)	3 (7.0)
Geriatrics	7 (6.7)	-	1 (1.9)	-	2 (2.5)	-
Dialysis	2 (1.9)	2 (2.4)	-	-	2 (2.5)	-
Infection Diseases	18 (17.1)	10 (12.2)	2 (3.7)	-	16 (20.3)	4 (9.3)
Oncology	5 (4.8)	2 (2.4)	4 (7.4)	1 (3.0)	-	2 (4.7)
Urology	1 (1.0)	-	-	-	-	-
Obstetrics	1 (1.0)	-	-	-	-	-
Gastroenterology	3 (2.9)	-	-	-	-	-
General Surgery	2 (1.9)	-	-	-	-	-
Brain Surgery	-	1 (1.2)	1 (1.9)	-	-	-
Orthopedics and Traumatology	-	-	1 (1.9)	-	-	-

DISCUSSION

Failure to apply early and appropriate antibiotic treatment in BSI may cause an increase in mortality, morbidity and costs (1). Approximately 30 million people are affected by these infections each year and causes death of 6 million people. In addition, it is important to determine of hospital surveillance for the management of BSI besides detection and identification of the causative pathogen and performing ADT on time (11). According to the researches have been conducted, inappropriate antibiotic treatments significantly increase mortality rates in patients with bacteremia, and the importance of appropriate empirical treatment in such cases has been emphasized (12).

Furthermore, positivity rates detected in blood cultures vary in many of the studies carried out. According to the study of Müderris et al., bacterial growth was detected in 18.3% (8.248/45.071) of the blood samples sent to the laboratory (12). In a study conducted in Izmir, Turkey, it was reported that positive signals were received in 15.2% (327/2.148) of blood cultures (13). In another study conducted by Şafak et al., growth was detected in 24.3% (2.809/11.559) blood culture samples (3). The isolation of bacteria in blood cultures taken from febrile patients was determined as 28% (144/514) (14), whereas, blood culture positivity was reported at a rate of 16% (3.949/24.694) in another research (11). Despite all these studies discussed before with high positivity, the positivity obtained from blood cultures is observed at lower rates in some studies. A study carried out by Prakash et al., a total number of 7.579 blood cultures were examined and 5% (n: 382) positivity was found (15). In addition, only 9.2% (n: 132) of 1.440 blood cultures were found to be positivity in a study conducted by Gohel et al. (16). The observed positive growth of our study was at a relatively low rate (8.8%) compared to the most similar studies in the literature.

It is obvious that, as the age increases, the isolations in blood cultures also increase significantly in this research. Accordingly, it was determined that BSI is most common in patients 41-60 and over 60 years old (10.6% and 11.1% respectively). Reports in the literature indicates that BSI is associated with age groups. The increase in these infections with advanced age may be due to reasons such as malnutrition, immunosuppression, decreased cognitive functions, increased comorbidity and the associated increase in the rate of referrals to health institutions (5). Sepsis and septic shock can be seen in all age groups. However, especially it is more common in elderly patients. In addition, newborns are more susceptible to these infections due to their weak immunological barriers (17). According to a research conducted by

Kante et al., growth in the blood cultures with a rate of 25% has been determined at the patients over 60 years of age (18). However, there are some studies showing that isolation rates in blood cultures decrease as age increases. For example, Sweta et al. found 4.6% blood culture positivity in patients over 64 years old and 38.7% in newborns (19). What is more, Nazir et al. determined the most common rate of blood culture positivity in newborns with a rate of 25.6% and this is followed by 22.1% of blood culture positivity at the age of 60 and above (17). Also, a research carried out by Bolukçu et al. reported that age over 65 is not related with blood culture positivity (20).

The researches about this topic indicates that BSIs are more common in male. According to the studies conducted by Kalın-Ünüvar et al. (5), Akyıldız et al. (8) and Kante et al. (18), it was reported that these infections are more common in male than in female. However, the rate of positivity detected in blood cultures was higher in female in our study.

Climate and seasonal changes can affect the diagnosis of infections in humans and direct infection prevention struggles. Studies about this area have emphasized that gram-negative bacteria cause more frequent infections during the summer months (21). According to a study conducted by Chazan et al., it was shown that BSI caused by *Escherichia coli* increased significantly in the summer months (22). Similarly, in the study carried out by Rodrigues et al., it was indicated that BSI caused by *Klebsiella* spp. and *Acinetobacter baumannii* increased significantly in the summer season (23). Parallel to all these, infections detected in blood cultures were observed to be seen more frequently in the summer season compared to other seasons in our study.

During this study, gram-negative bacteria were reproduced in 392 (56.7%) of the blood culture samples, 295 (42.7%) of them reproduced gram-positive and 4 (0.6%) *Candida* species reproduced. *Escherichia coli* (15.2%) from gram-negative and CNS (21.1%) among gram-positive were the most frequently isolated bacteria. In a study, gram-positive (67.3%) were isolated more frequently than gram-negative (29.4%) in blood cultures (24). Differently in another study, 64.3% of 224 blood samples had gram-negative and 35.7% had gram-positive reproduced. In the same study, *Escherichia coli* (59.7%) was the most frequently isolated bacteria among gram-negatives (25). In a study conducted by Keihanian et al., 225 samples were reproduced in blood cultures which gram-negative and gram-positives were detected at a rate of 64% and 36%, respectively. In the same study, the most frequently isolated bacterium was *Pseudomonas aeruginosa* (29.3%) unlike the others (4).

As stated by the World Health Organization (WHO), there is an increase in *Enterobacteriaceae* species that produce ESBL in parallel with the increasing rates of antimicrobial resistance worldwide (26,27). The ineffectiveness of most antibiotics in infections developed by ESBL-producing bacteria causes increased mortality and serious economic losses (8). In the studies conducted, it has been proven that ESBL positivity in *Escherichia coli* and *Klebsiella pneumoniae* strains is a risk factor that increases mortality (28,29). In a study carried out by Anggraini et al., ESBL producing *Escherichia coli* and *Klebsiella pneumoniae* rates were determined as 62.2% and 66.2%, respectively (30). In another study, the rate of ESBL positive *Escherichia coli* was 80% and the rate of ESBL positive *Klebsiella pneumoniae* was 85% (31). However, ESBL positivity rate in *Escherichia coli* and *Klebsiella pneumoniae* strains was 56.2% and 53.7% in our study, respectively. In addition, it was found that ESBL positive rate was at the highest rate (84.6%) in 2020 when looking at the distribution of ESBL positive *Escherichia coli* over the years, but this was not statistically significant. Despite this, ESBL-positive *Klebsiella pneumoniae* is observed to have progressed increasingly between 2016-2019 and reached the highest level (69.6%) in 2019. The ESBL rates obtained in this study were found to be relatively low compared to similar studies. However, it is important that the frequency of ESBL should be considered in the empirical treatment of ESBL positive *Enterobacteriaceae* infections.

Pseudomonas aeruginosa is held responsible for 3-7% of bloodstream infections. In addition, it is known that it progresses with high morbidity and mortality (27-48%) in critically ill patients. MDR is a common feature of hospital-acquired *Pseudomonas aeruginosa* strains (32). In our study, the most resistant antibiotic of *Pseudomonas aeruginosa* isolates was aztreonam (52.9%) and the most sensitive was amikacin (98.1%). In addition, the frequency of MDR in *Pseudomonas aeruginosa* isolates was 13%. In a research conducted by Choi et al., it was found that the most resistant antibiotic was aztreonam (50%), and the most sensitive was colistin (100%) and amikacin (96%) just similar to this research. In the same study, the rate of MDR *Pseudomonas aeruginosa* was 22% (33). In a study carried out by Coşar et al., it was stated that the most resistant antibiotic was aztreonam (51.7%) and the most effective antibiotic was amikacin (89.3%) to *Pseudomonas aeruginosa* (6).

The mortality rate in patients with bacteremia caused by *Acinetobacter baumannii* exceeds 50% (34). The bacteria's high antibiotic resistance and ability to survive on inanimate, dry surfaces lead to epidemics in hospitals. It has now been reported that *Acinetobacter baumannii* is resistant to almost all antibiotics, including colistin, tigecycline and polymylcin B. In recent years, an increase has been detected in the rate of resistance it developed against carbapenem group antibiotics, which are frequently preferred in the treatment of serious infections (35,36). The rate of *Acinetobacter baumannii* isolated from blood cultures was 4.8% (33/691) in this study. In a study conducted in Turkey, *Acinetobacter baumannii* was the second factor (16.7%) detected in blood cultures (10). In another study, the incidence of *Acinetobacter baumannii* in blood cultures was found to be 11.3% (1). This rate was found to be lower in our study compared to the literature. However, 97% of *Acinetobacter baumannii* strains isolated from blood cultures were found to be MDR and 84.8% were XDR, and this rate considered as high. In a study carried out by Al-Mously et al., the rate of MDR *Acinetobacter baumannii* in BSI was reported as 69%. In the same study, it was emphasized that the most effective antibiotics against *Acinetobacter baumannii* were colistin (99.5%) and tigecycline (96.1%) (37). In the light of the data obtained, it is clear that it is a situation that requires urgent action when it is considered that the bloodstream infection caused by MDR and XDR *Acinetobacter baumannii* may have an effect on mortality.

Gram-positive bacteria (especially *Staphylococcus* spp.) are frequently isolated in BSI. One of the most important factors of bacteremia caused by gram-positive bacteria is *Staphylococcus aureus* (38,39). The effects of MRSA bacteremias on the mortality of patients hospitalized in vital departments such as intensive care must be considered (7). MRSA strains are resistant to all beta-lactam antibiotics (except ceftaroline and ceftobiprol), but also to macrolides, lincosamides, quinolones and aminoglycosides (38). MRSA isolates are considered reservoirs for MDR genes, and limitations in their treatment lead to serious health problems (40). In a study conducted by Kula-Atik et al., 20.367 blood cultures were examined and *Staphylococcus aureus* was isolated in 8.6% (n: 390) of them and 41% (n: 160) of these strains were found to be MRSA (38). Gu et al. determined the incidence of *Staphylococcus aureus* as 7.4% in the blood culture of 2.760 patients, and found that 44.2% of them were MRSA (41). In another study conducted in Turkey, the prevalence of MRSA in blood cultures was determined as 50.8% (40). According to the data of Turkey, the frequency of *Staphylococcus aureus* in blood cultures varies between 4.9-38.3%. The frequency of MRSA is between 12.2% and 71.7% (10). The frequency of *Staphylococcus aureus* and MRSA in this study was 11.4% and 30.4%, respectively. Furthermore, it is obvious that BSI caused by MRSA does not progress at a high level in our hospital when compared with the literature. Despite this, while the rate of MRSA detected in 2019 was 66.7% alarming, thanks to the infection control measures taken, this rate was reduced to 41.7% in 2020.

Limitations: The reference methodology for detecting colistin susceptibility according to EUCAST (European Committee on Antimicrobial Susceptibility Testing) criteria is the broth microdilution (BMD) method. While some of the studies conducted that automated systems were insufficient for colistin susceptibility tests, it was reported that these systems were sufficient in some studies (42,43). Despite this, the fact that the BMD method was not applied is considered as a limitation of our study.

CONCLUSION

Determination of microorganisms isolated from blood cultures and antibiotic resistance conditions guides the clinician for empirical treatment. Although bacteria isolated from blood cultures and antibiotic susceptibility rates that are effective against them vary depending on both geographic characteristics and seasons, they may vary even among different institutions in the same country. These types of studies should be carried out at certain time intervals in each institution and the most common factors of each institution should be determined. Thus, in addition to the detected factors, antibiotic susceptibility patterns against them can also be determined. Since the resistance conditions of the factors causing bacteremia may change over time, it will be easier for the clinician to follow the antibiotic resistance rates of the factors regularly and carefully in order to determine the correct treatment strategy. Active surveillance systems play a important role for monitoring BSIs.

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