



# Analysis of Blood Culture Results and Antibiotic Sensitivities in Adult Patients Applying to a Training and Research Hospital in Istanbul

## İstanbul'da Bir Eğitim ve Araştırma Hastanesine Başvuran Erişkin Hastaların Kan Kültürü Sonuçları ve Antibiyotik Duyarlılıklarının Analizi

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### ABSTRACT

**Objectives:** Sepsis is a life-threatening condition caused by microorganisms entering the bloodstream and spreading very rapidly. In sepsis guidelines, starting early antibiotic treatment is one of the main steps of treatment. Therefore, it is necessary to know the antibiotics to which the agents are susceptible. Our study aimed to determine the antibiotic susceptibility and resistance of microorganisms grown in blood cultures obtained from patients admitted to the emergency department of our hospital and treated in the inpatient ward or intensive care unit.

**Methods:** The blood cultures in our hospital in the 1-year period between 2018 and 2019 were analyzed retrospectively. The age and gender of the patients from whom the blood cultures were obtained, the microorganisms grown, and their antibiotic susceptibility/resistance were recorded and analyzed statistically.

**Results:** A total of 1232 blood cultures were included in the study, and growth was observed in 182 blood cultures. *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, and *Acinetobacter baumannii* were isolated most frequently. The antibiotics to which staphylococci were most susceptible were trimethoprim-sulfamethoxazole, vancomycin, and gentamicin, while the highest resistance was found to ertapenem and penicillin. Methicillin-resistant coagulase-negative Staphylococcus (MRCNS) was 54.1%, and methicillin-resistant *Staphylococcus aureus* (MRSA) was 28%. For *Escherichia coli*, ceftriaxone resistance was 72%, ciprofloxacin resistance was 68.4%, while 82.4% were susceptible to gentamicin, and 100% to carbapenems. Multidrug resistance was 61%.

**Conclusion:** In our study, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, and *Acinetobacter baumannii* were isolated most frequently from blood cultures, respectively. *Escherichia coli* was highly resistant to ciprofloxacin and ceftriaxone but susceptible to aminoglycosides and carbapenems. We also found that multidrug resistance was quite high. Early initiation of appropriate antibiotics in the treatment of sepsis and bacteremia reduces mortality. Therefore, it is important to determine the most frequently isolated pathogens and their antibiotic susceptibility and resistance status.

**Keywords:** Antibiogram; Antibiotic resistance; Blood culture; Multidrug resistance; Sepsis.

### ÖZET

**Amaç:** Mikroorganizmaların kana karışıp çok hızlı bir şekilde yayılarak oluşturduğu ve hayatı tehdit eden durum, sepsis olarak adlandırılır. Sepsis kılavuzlarında erken antibiyotik tedavisine başlamak, tedavinin temel basamaklarından biridir. Bu nedenle, etkenlerin duyarlı olduğu antibiyotiklerin bilinmesi gereklidir. Çalışmamızın amacı, hastanemiz acil servisine başvurmuş ve yataklı servis veya yoğun bakım ünitesinde tedavi görmüş hastalardan alınan kan kültürlerinde üreyen mikroorganizmaların duyarlı ve dirençli olduğu antibiyotiklerin belirlenmesidir.

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**Yöntem:** Hastanemizde 2018-2019 arası 1 yıllık dönemde alınan kan kültürü sonuçları retrospektif olarak incelendi. Kan kültürlerinin alındığı hastaların yaşı, cinsiyeti, üreyen mikroorganizmalar ve duyarlı/dirençli oldukları antibiyotikler kaydedilerek istatistiksel olarak analiz edildi.

**Bulgular:** Toplam 1232 kan kültürü çalışmaya dahil edildi, 182 kan kültüründe üreme gözlemlendi. En sık izole edilen patojenler sırasıyla; *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis* ve *Acinetobacter baumannii*'dir. Staflokokların en duyarlı olduğu antibiyotikler trimetoprim-sülfametoksazol, vankomisin ve gentamisin iken en yüksek direnç ertapenem ve penisiline karşı bulundu. Metisiline dirençli koagülaz negatif staflokoklar (MRKNS) %54.1, metisiline dirençli *Staphylococcus aureus* (MRSA) oranı %28 idi. *Escherichia coli* için seftriakson direnci %72, siprofloksasin direnci %68.4 iken gentamisine %82.4, karbapenemlere %100 duyarlıydı. Çoklu ilaç direnci %61 idi.

**Sonuç:** Çalışmamızda kan kültürlerinden sırasıyla en sık *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis* ve *Acinetobacter baumannii* izole edildi. Staflokoklarda ve enterokoklarda vankomisin direnci gözlenmedi. *Escherichia coli*'nin siprofloksasin ve seftriakson direncinin yüksek olduğu, aminoglikozid ve karbapenemlere duyarlı olduğu gözlemlendi. Ayrıca çoklu ilaç direncinin oldukça yüksek olduğunu tespit ettik. Sepsis ve bakteriyemi tedavisinde erken dönemde uygun antibiyotik başlayabilmek mortaliteyi azaltır. Hastalardan en sık izole edilen patojenleri ve bu patojenlerin antibiyotik duyarlılık ve direnç durumunu belirlemek bu nedenle önemlidir.

**Anahtar sözcükler:** Antibiyogram; Antibiyotik direnci; Çoklu ilaç direnci; Kan kültürü; Sepsis.

Sepsis ranks among the top causes of mortality and morbidity in both developed and developing countries.<sup>[1-4]</sup> Early diagnosis and treatment of sepsis significantly decrease mortality rates. Pathogens causing the infection can be detected by blood culture.<sup>[5,6]</sup> Studies have shown that mortality rates increase due to delays in appropriate antibiotic treatment.<sup>[3,4,7]</sup> Therefore, clinicians often have to start empirical treatment without waiting for blood culture results.

In the literature, gram-positive cocci and gram-negative bacilli have been reported as the leading pathogens obtained from blood cultures.<sup>[2,8]</sup> In addition to bacteria, Candida-type fungi are also detected as causative agents.<sup>[2,8]</sup> The distribution and antibiotic resistance status of microorganisms obtained from blood cultures vary according to the geographical region, type, and size of the hospital, and the antibiotic protocol applied.<sup>[9]</sup> Increasing antibiotic resistance due to incorrect dosage and duration of antibiotics is one of the significant public health problems worldwide.<sup>[10,11]</sup> Therefore, determining the causative microorganisms and antibiotic resistance rates in regions and even in individual hospitals is necessary for the correct selection of empirical treatments. Thus, we believe our study may guide clinicians in determining empirical treatment for patients with sepsis.

This study aimed to show the pathogens grown from blood cultures of various patients admitted to the emergency department, inpatient ward, and intensive care units of Fatih Sultan Mehmet Training and Research Hospital in Türkiye, and the antibiotic resistance rates of these pathogens.

## Methods

Our study was conducted as a retrospective observational cross-sectional study at Fatih Sultan Mehmet Training and

Research Hospital. Within the scope of the study, blood cultures obtained from patients admitted to the emergency department, inpatient wards, or intensive care unit of Fatih Sultan Mehmet Training and Research Hospital between January 2018 and January 2019 were retrospectively evaluated. Patients whose blood cultures were obtained from the hospital data system within the specified date range were screened. In patients who had multiple blood cultures, only the first blood culture results were considered.

The demographic data of the patients, the clinic where the blood culture was requested (emergency department, intensive care unit, or inpatient ward), the presence of growth in the blood culture, the causative pathogen(s), and antibiotic resistance status were analyzed and statistically evaluated.

Blood culture samples sent to the microbiology laboratory of our hospital are incubated for 5 days with the BACT/ALERT 3D automated system according to the evaluation procedure. The incubation period of samples with suspected Brucella is extended to 20 days. At the end of this period, culture bottles with positive signals are inoculated onto media and incubated at 37°C for 24-48 hours. The isolated microorganisms are identified using conventional methods (gram staining, catalase, coagulase, and oxidase tests) and the VITEK 2 kit system. Antibiotic susceptibility analysis is performed by the Kirby-Bauer disk diffusion method and according to Clinical Laboratory Standards Institute (CLSI) guidelines. Cefoxitin and oxacillin disks are used for the evaluation of methicillin resistance of staphylococcal strains by disk diffusion method, and ceftazidime disk is used for the evaluation of extended-spectrum beta-lactamase (ESBL) positivity of Enterobacteriaceae. The vancomycin resistance status of enterococci is also evaluated using the disk diffusion method.

Bacterial pathogens were defined as multidrug-resistant (MDR) if resistant to at least one agent in three or more antibiotic groups, extensively drug-resistant (XDR) if susceptible to only one or two antibiotic groups, and pan-resistant (PDR) if resistant to all tested antibiotics.<sup>[12]</sup>

## Data Analysis

Statistical Package for the Social Sciences (SPSS) version 26 program was used for statistical analysis. Mean, standard deviation, percentage, median, minimum, and maximum values were used for the descriptive analysis of the data. The normality of quantitative data was tested using the Shapiro-Wilk test and graphical analysis. The Kruskal-Wallis test and Dunn-Bonferroni test were used to compare non-normally distributed quantitative variables between more than two groups. Pearson chi-square test, Fisher's exact test, and Fisher-Freeman-Halton test were used to compare qualitative data. Statistical significance was accepted as  $p < 0.05$ .

The study has been approved by the scientific committee of our hospital with the consent letter numbered 17073117-050.06 and dated 2019.

The study was conducted under the Helsinki Declaration.

## Results

Between January 2018 and January 2019, blood cultures were obtained from 3,942 patients at Fatih Sultan Mehmet Education and Research Hospital, and blood cultures of 1,232 patients who met the study criteria were included in the study. Among the patients included in the study, 49.8% ( $n=614$ ) were female. The ages of the patients from whom blood cultures were obtained ranged between 17 and 100 years, with a mean age of  $66.04 \pm 18.70$  years. Demographic data and the distribution of cultures according to services are given in Table 1.

While no growth was observed in 70.9% ( $n=873$ ) of the cultures, contamination was observed in 14.4% ( $n=177$ ), and growth was observed in 14.8% ( $n=182$ ). Descriptive characteristics according to the results of the cultures are given in Table 2.

There was a statistically significant difference between the ages of the cases according to the culture results ( $p=0.001$ ). The ages of the cases with no growth were significantly lower than those with contamination and growth ( $p=0.046$ ;  $p=0.001$ ).

Table 1. Distribution of Descriptive Characteristics

|                                         |             |
|-----------------------------------------|-------------|
| Age                                     |             |
| Mean±Sd                                 | 66.04±18.70 |
| Median (Min-Max)                        | 70 (17-100) |
| Sex                                     |             |
| Female                                  | 614 (49.8)  |
| Male                                    | 618 (50.2)  |
| The service sent the blood culture test |             |
| ICU                                     | 627 (50.9)  |
| Internal Medicine                       | 182 (14.8)  |
| Emergency service                       | 176 (14.3)  |
| Infectious disease service              | 88 (7.1)    |
| Neurology                               | 63 (5.1)    |
| General surgery                         | 30 (2.4)    |
| Urology                                 | 6 (0.5)     |
| Ophthalmology                           | 3 (0.2)     |
| ENT                                     | 5 (0.4)     |
| Neurosurgery                            | 27 (2.2)    |
| Orthopedic                              | 10 (0.8)    |
| Physical therapy and rehabilitation     | 15 (1.2)    |

ICU: Intensive care unit; ENT: Ear nose throat.

The distribution of culture results of the cases according to gender did not show a statistically significant difference ( $p > 0.05$ ).

There was a statistically significant difference between the rates of growth in blood cultures according to the service where blood cultures were taken ( $p=0.004$ ). Both contamination and growth rates were significantly higher in blood cultures obtained in the emergency department compared to those obtained in the anesthesia, infection, and internal medicine departments. The rate of contamination in blood cultures taken in the neurology service was significantly higher than in the infection service.

Of the cases with growth, 59.9% ( $n=109$ ) were gram-positive, 38.4% ( $n=70$ ) were gram-negative, and 1.7% ( $n=3$ ) were fungal. The distribution of pathogens with growth is summarized in Table 3. When the culture results of the cases included in the study were analyzed, *Staphylococcus epidermidis* (*Staph. Epidermidis*) was the most common pathogen with 19.2% ( $n=35$ ), followed by *Staphylococcus aureus* (*Staph. Aureus*) with 11.5% ( $n=21$ ), *Enterococcus faecalis* with 11% ( $n=20$ ), *Escherichia coli* (*E. coli*) with 11% ( $n=20$ ), and *Acinetobacter baumannii* with 11.0% ( $n=20$ ).

The pathogens that grew according to the culture results and their antibiotic resistance status are given in Tables 4 and 5.

Table 2. Evaluation of Descriptive Characteristics According to Culture Results

|                                         | Blood culture results        |                                  |                             | p                    |
|-----------------------------------------|------------------------------|----------------------------------|-----------------------------|----------------------|
|                                         | No growth<br>(n=873 (%70,9)) | Contamination<br>(n=177 (%14,4)) | Pathogen<br>(n=182 (%14,8)) |                      |
| Age                                     |                              |                                  |                             |                      |
| Median±SD                               | 64.59±19.03                  | 68.55±17.58                      | 70.53±17.20                 | <sup>a</sup> 0.001** |
| Sex                                     |                              |                                  |                             |                      |
| Female                                  | 444 (72.3)                   | 75 (12.2)                        | 95 (15.5)                   | <sup>b</sup> 0.095   |
| Male                                    | 429 (69.4)                   | 102 (16.5)                       | 87 (14.1)                   |                      |
| The service sent the blood culture test |                              |                                  |                             |                      |
| Emergency department                    | 94 (53.4)                    | 41 (23.3)                        | 41 (23.3)                   | <sup>c</sup> 0.004** |
| ICU                                     | 460 (73.4)                   | 82 (13.1)                        | 85 (13.6)                   |                      |
| Infectious disease                      | 69 (78.4)                    | 8 (9.1)                          | 11 (12.5)                   |                      |
| Internal medicine                       | 139 (76.4)                   | 21 (11.5)                        | 22 (12.1)                   |                      |
| Neurology                               | 38 (60.3)                    | 13 (20.6)                        | 12 (19.0)                   |                      |
| Urology                                 | 5 (83.3)                     | 1 (16.7)                         | 0 (0.0)                     |                      |
| General surgery                         | 22 (73.3)                    | 2 (6.6)                          | 6 (20.0)                    |                      |
| Ophthalmology                           | 2 (66.7)                     | 0 (0.0)                          | 1 (33.3)                    |                      |
| ENT                                     | 4 (80.0)                     | 1 (20.0)                         | 0 (0.0)                     |                      |
| Neurosurgery                            | 20 (74.0)                    | 4 (15.0)                         | 3 (11.0)                    |                      |
| Orthopedic                              | 9 (90.0)                     | 1 (10.0)                         | 0 (0.0)                     |                      |
| Physical therapy and rehabilitation     | 11 (73.3)                    | 3 (20.0)                         | 1 (6.7)                     |                      |

<sup>a</sup>Chi-Square Test; <sup>b</sup>Fisher Exact Test; <sup>c</sup>Fisher Freeman Halton Test; \*\*p<0,01; ICU: Intensive care unit; ENT: Ear nose throat.

Table 3. Distribution of Culture Results

| Results (n=182)             |           |
|-----------------------------|-----------|
| Staphylococcus epidermidis  | 35 (19.2) |
| Staphylococcus aureus       | 21 (11.5) |
| Escheria Coli               | 20 (11.0) |
| Enterococcus faecalis       | 20 (11.0) |
| Acinetobacter baumannii     | 20 (11.0) |
| Klebsiella                  | 17 (9.3)  |
| Staphylococcus hominis      | 8 (4.4)   |
| Staphylococcus haemolyticus | 7 (3.8)   |
| Pseudomonas aeruginosa      | 5 (2.7)   |
| Staphylococcus capitis      | 5 (2.7)   |
| Enterococcus faecium        | 4 (2.2)   |
| Staf lugdunensis            | 3 (1.6)   |
| Candida albicans            | 2 (1.1)   |
| Brucella melitensis         | 2 (1.1)   |
| Staphylococcus sciuri       | 2 (1.1)   |
| Enterobacter cloacae        | 1 (0.5)   |
| Citrobacter freundii        | 1 (0.5)   |
| Enterococcus gallinarum     | 1 (0.5)   |
| Morganella morganii         | 1 (0.5)   |
| Proteus mirabilis           | 1 (0.5)   |
| Pseudomonas stutzeri        | 1 (0.5)   |
| Candida tropicalis          | 1 (0.5)   |
| Salmonella                  | 1 (0.5)   |
| Staphylococcus schleiferi   | 1 (0.5)   |
| Streptococcus mitis         | 1 (0.5)   |
| Streptococcus pneumoniae    | 1 (0.5)   |

Methicillin-resistant *Staphylococcus aureus* (MRSA) was 28% (n=6), while Methicillin-resistant coagulase-negative staphylococcus (MRCNS) was 54.1% (n=33). *Staph. Aureus* was 81% (n=17) resistant to penicillin and 100% (n=21) resistant to ertapenem. Resistance to ertapenem in coagulase-negative staphylococci (CNS) was 98.4% (n=60). The ESBL positivity was 55% (n=11) for *E. coli* and 64.7% (n=11) for *Klebsiella*.

## Discussion

Sepsis is recognized as one of the most common causes of death worldwide. Early antibiotic treatment is one of the main steps in sepsis guidelines.<sup>[1-4]</sup> The most appropriate antibiotic should be selected according to the suspected site of infection and the agent. To use the most appropriate drug at the optimal dose, it is necessary to demonstrate the presence of infection and to identify the bacteria. Blood culture is the gold standard test for the diagnosis of systemic infection and bacteremia.<sup>[3,13,14]</sup>

When blood cultures are evaluated, the results are reported as positive, negative, or contaminated. Although it is stated in the literature that the contamination rate should be less than 3%, the Clinical and Laboratory Standards Institute (CLSI) states that a rate of less than 1% is more appropriate.

Table 4. Antibiotic resistance status of the most frequently isolated Gram-positive bacteria

| Antibiotics                   | Staf.Epidermidis*<br>n (%) | Staf.Aureus<br>n (%) | Enterococcus<br>n (%) |
|-------------------------------|----------------------------|----------------------|-----------------------|
| Penicillin                    | -                          | 17/21 (81)           | -                     |
| Ampicillin                    | -                          | -                    | 5/25 (20)             |
| Amoxicillin-clavulanate       | 0 (100 sensitive)          | -                    | -                     |
| Mupirocin                     | 1/3 (33.3)                 | 0 (100 sensitive)    | -                     |
| Fucidic acid                  | 15/28 (53.6)               | -                    | -                     |
| Clindamycin                   | 17/31 (54.8)               | 9/22 (40,9)          | -                     |
| Ciprofloxacin                 | -                          | -                    | 13/25 (55)            |
| Levofloxacin                  | 23/29 (79.3)               | 7/24 (29.7)          | 8/15 (54)             |
| Linezolid                     | 3/21 (14.3)                | 0 (100 sensitive)    | 0 (100 sensitive)     |
| Vankomycin                    | 0 (100 sensitive)          | 0 (100 sensitive)    | 0 (100 sensitive)     |
| Teikoplanin                   | 1/5 (20)                   | 0 (100 sensitive)    | 0 (100 sensitive)     |
| Fusidic acid                  | 15/28 (53.6)               | 4/20 (20)            | -                     |
| Daptomycin                    | 0 (100 sensitive)          | -                    | -                     |
| Trimethoprim-Sülfomethoxazole | 4/34 (11.8)                | 0 (100 sensitive)    | 8/24 (33)             |

(%) indicates the percentage of isolates resistant to the antibiotic. A dash (-) means that the antibiotic has not been tested or is not applicable. \*Staf: Staphylococcus.

Table 5. Antibiotic resistance status of the most frequently isolated Gram-negative bacteria

| Antibiotics             | E.Coli<br>n (%)   | Klebsiella<br>n (%) | P. aeruginosa<br>n (%) | Acinetobacter<br>n (%) |
|-------------------------|-------------------|---------------------|------------------------|------------------------|
| Gentamycin              | 3/17 (17.6)       | 4/15 (26.7)         | 0 (100 sensitive)      | 11/15 (73.3)           |
| Trim-Smx&               | 12/17 (70.6)      | 11/16 (68.8)        | -                      | 13/19 (68.4)           |
| Ciprofloxacin           | 13/19 (68.4)      | 9/16 (56.3)         | 1/4 (25)               | 17/19 (89.5)           |
| Levofloxacin            | -                 | -                   | 1/4 (25)               | 15/16 (93.8)           |
| Amikacin                | 0 (100 sensitive) | 2/11 (18.2)         | -                      | 9/12 (75)              |
| Amoxicillin-clavulanate | 13//18 (72.2)     | 9/16 (56.3)         | -                      | -                      |
| Ceftriaxone             | 13/18 (72.2)      | 13/17 (76.5)        | -                      | -                      |
| Tigecycline             | 0 (100 sensitive) | 0 (100 sensitive)   | -                      | 0 (100 sensitive)      |
| Ampicillin              | 9/13 (69.2)       | 15/15 (100)         | -                      | -                      |
| Pip-Tazo+               | 3/15 (20)         | 9/16 (56.3)         | 0 (100 sensitive)      | 12/14 (85.7)           |
| Ertapenem               | 1/14 (7.1)        | 6/13 (46.2)         | -                      | -                      |
| Meropenem               | 1//15 (6.7)       | 6/13 (46.2)         | -                      | 15/16 (93.8)           |
| İmipenem                | 0 (100 sensitive) | 2/6 (33.3)          | 0 (100 sensitive)      | 14/15 (93.3)           |
| Colistin                | 0 (100 sensitive) | -                   | 0 (100 sensitive)      | -                      |
| Cefuroxime axetil       | -                 | 13/17 (76.5)        | -                      | -                      |
| Cefepime                | -                 | -                   | 0 (100 sensitive)      | -                      |
| Ceftazidime             | -                 | -                   | 0 (100 sensitive)      | -                      |

(%) indicates the percentage of isolates resistant to the antibiotic. Dash (-) means that the antibiotic was not tested or not applicable. \*E.coli: Escheria coli, &: Trim-SMX: Trimethoprim-Sulfumethazoksazol, +:Pip-Tazo: Piperacillin-Tazocin.

[13-15] Studies have shown that patients whose culture results were evaluated as contamination received up to 41% higher rates of antibiotic treatment compared to patients with negative cultures, which resulted in drug reactions, antibiotic

resistance, intravenous antibiotic treatment, and increased hospitalization time as well as increased treatment costs. [13-16] In our study, 14.4% (n=177) of the cultures were evaluated as contaminated. This rate is considerably higher than



acceptable rates. There may be different causes of contamination. One of the most common causes may be practitioner error (hand hygiene), insufficient disinfection of the area to be sampled, sampling from the patient's existing catheter, the medium used for blood culture, not changing the tip of the syringe while transferring the sample to the culture bottle. It may also be due to bacteria; for example, clinical correlation should also be questioned before considering contamination in agents such as coagulase-negative staph, *Propionibacterium acnes*, *Micrococcus*. Since the data in our study were obtained retrospectively from the data system, we could not determine which of these factors was responsible for the high contamination rate. But this result indicates that sample collection techniques for blood culture should be reviewed and training and algorithms should be organized in this regard.

Blood culture results may vary between countries and regions. According to the European Center for Disease Prevention and Control (ECDC) 2020 report, the most frequently isolated bacteria from blood cultures were *E. coli*(41.3%), *S. aureus*(21.9%), *K. pneumoniae*(11.9%), *E. faecalis*(8.4%), *P. aeruginosa*(6.2%), *E. faecium*(5.5%), *S. pneumoniae*(2.6%) and *Acinetobacter species*(2.3%).<sup>[17]</sup> According to the National Antimicrobial Resistance Surveillance System (NARSS) 2016 data, the most frequently isolated bacteria in Türkiye were *E. coli*(23.8%), *Enterococci*(18.9%), *K. pneumoniae*(17.6%), and *Staph. aureus*(15.5%), *A. baumannii*(15.1%) and *P. aeruginosa*(8%).<sup>[18]</sup> *Staph. epidermidis* were excluded from this report.

While studies conducted in our country have shown that Gram-negative bacteria are the most common,<sup>[19]</sup> there are also studies showing that Gram-positive bacteria are isolated more frequently.<sup>[20,21]</sup> In the study by Şay et al.,<sup>[19]</sup> enterococci were the most common Gram-positive bacteria, while in the studies by Arabacı et al.<sup>[20]</sup> and Bıçak et al.<sup>[8]</sup> *Staph. epidermidis* was the most common bacteria (23.9% and 17.7%, respectively). In the study of Er et al.<sup>[21]</sup> *Staph. aureus*(38.3%) was observed most frequently.<sup>[8,19-21]</sup> When our results were analyzed, Gram-positive bacteria were isolated most frequently, *Staph. epidermidis* was the most frequently isolated Gram-positive bacterium, and *E. coli* was the most frequently isolated Gram-negative bacterium.

Although in some studies *Staph. epidermidis* growth is considered as contamination with skin flora, *Corynebacterium* and micrococci are reported as contamination from skin flora bacteria in our hospital. We think that the laboratory

should contact the clinician before reporting the culture growth result as contamination or growth, and a decision should be made after evaluating the focus of infection and the possible agent together.

When evaluated in terms of Gram-negative bacteria, *E. Coli*, *Acinetobacter species*, *Klebsiella*, and *Pseudomonas species* were most frequently observed in our study, and the frequency of these agents was similar to studies conducted in our country.<sup>[8,19,20]</sup>

Fungi are opportunistic infections and cause infection in conditions such as increased use of broad-spectrum antibiotics and suppression of the immune system. The fungal infection may originate from the endogenous flora of the patient or may be hospital-acquired.<sup>[22]</sup> In the literature, it is observed that fungi cause bacteremia between 4.8%,<sup>[19]</sup> 3.3%,<sup>[21]</sup> and 2.9%.<sup>[8]</sup> In our study, the rate was 1.6%. One of the reasons for this low rate may be that the first blood cultures of the patients were included in the study. In intensive care patients and patients with prolonged hospitalization and antibiotic use, the frequency of fungi may increase in repeated blood cultures.

Inappropriate antibiotic use is one of the most important problems in terms of antibiotic resistance development.<sup>[10,11]</sup> According to World Health Organization (WHO) 2019 data, resistance to at least one of the most commonly used antibiotics varies between 0-82%. Therefore, it is very important to know the regionally changing antibiotic resistance patterns.<sup>[10,11]</sup>

The rate of MRSA isolated from blood cultures was reported as 12.11% in the WHO 2019 report.<sup>[10]</sup> In studies conducted in our country, the MRSA rate was reported in a wide range of 15.76% to 71%.<sup>[8,19,21]</sup> Although MRSA was significantly higher than the WHO data with 28%(N:6) in our study, it is similar to the studies conducted in our country. In our study, *Staph. aureus* was 100% susceptible to trimethoprim-sulfamethoxazole, vancomycin, linezolid, teicoplanin, and mupirocin, while its resistance to penicillin was high. In coagulase-negative staphylococci, resistance to vancomycin, daptomycin, and amoxicillin-clavulanic acid was not observed, while the highest resistance was observed to levofloxacin and clindamycin reported as contamination from skin flora bacteria.

In a study evaluating five-year (2014-2018) culture results, it was observed that ESBL resistance increased from 39% to 75% for *E. coli* and from 23% to 73% for *Klebsiella*. In addition,

although ESBL-positive *E. coli* cases were highly susceptible to carbapenem group antibiotics, carbapenem resistance was reported to be an important problem for *Klebsiella*.<sup>[20]</sup>

In this study, we found that aminoglycoside resistance was 17-26% in *Klebsiella*, 17% in *E. coli*, and 75% in *Acinetobacter*. The carbapenem resistance rate was quite high in *Acinetobacter*, while resistance to tigecycline was not observed in our study. The fact that patients with *Acinetobacter* isolates are mostly hospitalized in intensive care units and that these patients usually use multiple antibiotics may be the reason for the high resistance rates in these patients.

Although there is no precise definition for multidrug resistance, one of the most accepted definitions is "resistance to three or more antibiotics." Pan resistance can be seen as a type of multidrug resistance and is defined as the observation of resistance to all antibiotics studied.<sup>[12]</sup> In the studies conducted, these rates vary according to the countries, the wards where the patients are hospitalized, and the pathogens that have grown. In a study conducted in India, the MDR rate was 37.1% and the XDR rate was 13.8%, while the MDR rate in *Enterobacter* isolated from patients hospitalized in an intensive care unit in Saudi Arabia was 57% and the XDR rate was 3%, and in a study conducted in China, MDR *Acinetobacter* rate was 19.7%.<sup>[23-25]</sup> In a study conducted in our country in which isolates obtained from patients in intensive care units were evaluated, it was reported that the prevalent drug resistance in *Acinetobacter* increased from 52% in 2012 to 72% in 2018.<sup>[26]</sup> In our study, multidrug resistance (MDR) was 61%(n=111) and pan resistance was 3.3%(n=6). Although this high rate of multidrug resistance is quite alarming, it supports the necessity of conscious antibiotic use by knowing the regional antibiotic resistance and susceptibility.

Since this is a retrospective, single-center study, the results cannot be generalized. In addition, pediatric patients could not be included in the study since there was no pediatric service in our hospital.

## Conclusion

In our study, the most commonly isolated pathogens from patients were coagulase-negative staphylococcus, *Staph. aureus*, *E. coli*, *Enterococcus faecalis*, and *Acinetobacter*, respectively. Vancomycin resistance was not observed in *Staphylococcus* and *Enterococcus*. High resistance was observed in *E. coli* against commonly used drugs such as ciprofloxacin

and ceftriaxone. In addition, while carbapenem resistance was high in *Acinetobacter*, no resistance was observed against tigecycline. Moreover, the high rates of multidrug resistance against the pathogens cultured are concerning. This highlights the importance of conscious antibiotic selection for the causative agent.

Early initiation of appropriate antibiotics in the treatment of sepsis and bacteremia reduces mortality. The pathogens isolated and their antibiotic susceptibility may vary by country and region. Therefore, we believe that our study is important in determining the antibiotic susceptibility and resistance status of pathogens and contributing to conscious antibiotic use.

## Disclosures

**Ethics Committee Approval:** Scientific committee of Fatih Sultan Mehmet Education and Research Hospital - 17073117-050.06/2019.

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