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Distribution of Microorganisms Isolated from Blood Cultures and Evaluation of Antibiotic Resistance Rates in Patients Diagnosed with Cancer

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ABSTRACT

Objective: Cancer patients are a high-risk population for infections caused by various bacterial agents. Specifically, bloodstream infections (BSIs) can lead to severe complications and even mortality in cancer patients. This study aimed to identify the predominant bacterial species causing bacteremia and assess the prevalence of antibiotic resistance among cancer patients receiving treatment at our hospital.

Materials and Methods: Retrospective analysis was conducted on data from cancer patients diagnosed between January 2020 and June. The microorganisms isolated from blood cultures of cancer patients were identified using the matrix-assisted laser desorption ionization (MALDI) Biotyper Microflex LT device. The antimicrobial susceptibility profiles of the bacteria were examined using the BD Phoenix 100. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) 22.0 program.

Results: The study included a total of 158 bacterial isolates grown from blood cultures of 133 patients across different populations. Gram-positive bacteria were detected in 54.4% (86) of the isolates, while gram-negative bacteria were found in 40.5% (64) of the isolates. The extended spectrum beta-lactamase (ESBL) positivity rate was 41.2% (14/34) in *Escherichia coli* isolates and 25% (3/12) in *Klebsiella pneumoniae* isolates. Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified in only one bacterial strain. Nine (26.5%) *E. coli* isolates and three (25%) *K. pneumoniae* isolates were determined to be multi-drug resistant (MDR).

Conclusion: BSIs remain a significant health issue in cancer patients. Analyzing MDR isolates and resistance profiles through routine bacterial surveillance in cancer patients can provide guidance for antimicrobial therapy. Furthermore, regularly sharing the obtained data can enhance treatment success.

Keywords: Bloodstream infections, cancer, antibiotic resistance, population.

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INTRODUCTION

Bacterial bloodstream infections (BSIs) significantly contribute to morbidity and mortality, often leading to complications in immunosuppressed oncology patients undergoing chemotherapy. Deaths resulting from microbial infections have a considerable impact on the survival rates of cancer patients.[1,2] Factors influencing the epidemiology of infection include increased neutropenia, the use of corticosteroids or cytotoxic chemotherapeutic agents, chemoprophylaxis, empirical antibiotic therapy, the presence of a central venous catheter, environmental factors, and the length of hospital stay. Additionally, various factors such as nutritional disorders, alterations in intestinal flora, mucosal lesions, deterioration of skin integrity after invasive procedures and operations, or damage to epithelial surfaces contribute to the development of infections.[3,4]

In patients with febrile neutropenia (FN), BSI rates differ significantly. Rates were observed to be 16.4% in patients with solid tumors and notably higher at 76.9% in patients with hematological malignancies.[5] The reason for this disparity is the increased utilization of cytotoxic chemotherapeutic agents that suppress the hematopoietic system and disrupt the host's protective mechanisms.[2]

Accurate identification of the infectious agent and prompt initiation of appropriate antibiotic therapy are of paramount importance for the prognosis of the disease in cancer patients.[6] The most common clinical bacterial isolates found in cancer patients include *Staphylococcus aureus, Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Escherichia coli*.[1]

BSIs and antimicrobial resistance often result in treatment failure and persistent infections in cancer patients.[1] Empirical selection of antimicrobial agents is particularly critical due to the increasing prevalence of multidrug-resistant (MDR) pathogens in today's world, where therapeutic options are limited. Hence, it is necessary to determine the frequency of infectious agents and their resistance status in cancer patients.

The data presented in the literature on this topic are limited. However, there are reports indicating an increase in the incidence of bacterial infections resistant to antimicrobial drugs in cancer patients. The objective of this investigation was to identify the dominant bacterial species causing bacteremia and evaluate the prevalence of antibiotic resistance among cancer patients receiving care at our hospital.

MATERIALS AND METHODS

Ethical Considerations

This study protocol received approval from the Sivas Cumhuriyet University Non-Invasive Clinical Research Ethics Committee (date: 21.09.2022, decision No: 2022-09/19).

Table 1. Distribution of cancer patients by age groups

Age groups	Patients	
	n	%
20–35	5	3.8
35–50	20	15.0
50–65	44	33.1
>65	64	48.1
Total	133	

Collection of Patient Data

The study was conducted at a tertiary research and training hospital with a total bed capacity of 1100, including 450 internal medicine polyclinics, 390 surgical medicine polyclinics, 190 intensive-care polyclinics, and 70 pediatric services polyclinics. Retrospective analysis was performed on data from patients diagnosed with cancer between January 2020 and June 2022, retrieved from the laboratory registry system.

Blood samples (8–10 ml) from the patients were inoculated into Becton Dickinson (BD) BACTEC Plus Aerobic medium (Becton Dickinson, USA) culture bottles and incubated in the BD BACTEC 9120 (Becton Dickinson, Sparks, USA) culture device. From the bottles in which the device showed a growth signal, the samples were transferred onto blood agar and incubated in an oven for 24–48 hours. The microorganisms isolated after incubation were identified using the Matrix-Assisted Laser Desorption/Ionization (MALDI) Biotyper Microflex LT (Bruker Daltonics, Germany). The antimicrobial susceptibility of the bacteria was examined using the BD Phoenix 100 (Becton Dickinson, Sparks, USA). Antimicrobial susceptibility profiles were evaluated based on the recommendations of the current European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. If the same microorganism was grown multiple times in a patient's blood culture, only the initial growth of the microorganism was considered for evaluation. Statistical analysis of the research was performed using IBM Statistical Package for the Social Sciences (SPSS) 22.0 (IBM Co., Armonk, NY, USA). Numerical variables are presented as frequencies (percentages).

RESULTS

A total of 133 patients, of whom 76 (57.1%) were male and 57 (42.9%) were female, were included in the study. The age range of the patients varied from 22 to 85 years. Among the patients, 33.1% were in the 50–65 age range, while 48.1% were over 65 years old (Table 1). The types of cancer detected in the patients included hematological malignancies (27%), lung cancer (13.5%), and colon cancer (10.5%) (Table 2).

Table 2. Distribution of patients by cancer types

Cancer types	Patients n	Patients %
Hematological malignancy	36	27.0
Acute myeloid leukemia	15	11.2
Non-hodgkin lymphoma	8	6.0
Multiple myeloma	5	3.8
Chronic lymphocytic leukemia	4	3.0
Acute lymphoblastic leukemia	2	1.5
Chronic myeloid leukemia	2	1.5
Lung cancer	18	13.5
Colon cancer	14	10.5
Gastric cancer	13	9.8
Brain cancer	10	7.5
Pancreatic cancer	8	6.0
Breast cancer	7	5.3
Bladder cancer	7	5.3
Prostate cancer	5	3.8
Ovarian cancer	4	3.0
Other	11	8.2
Total	133	

The study included a total of 158 bacterial isolates grown from blood cultures of the 133 patients. Gram-positive bacteria were detected in 54.4% (86) of the isolates, while gram-negative bacteria were found in 40.5% (64) of the isolates. Coagulase-negative staphylococci (CoNS) were the most prevalent strain (34.2%) among the Gram-positive isolates, followed by *Enterococcus species* as the second dominant strain (8.2%), and *Staphylococcus aureus* as the third dominant strain (4.4%). Additionally, *Escherichia coli* (21.5%) was identified as the most dominant gram-negative bacterium. *K. pneumoniae* (7.6%) and *P. aeruginosa* (3.2%) were also detected as other prominent gram-negative bacteria. The distribution of microorganisms, as well as Gram-positive and Gram-negative bacteria, is presented in Figure 1.

The Extended Spectrum Beta-Lactamase (ESBL) positivity rate was 41.2% (14/34) in *E. coli* isolates, while it was 25% (3/12) in *K. pneumoniae* isolates. Only one bacterial strain was identified as Methicillin-resistant *S. aureus* (MRSA). Additionally, three bacterial strains were identified as vancomycin-resistant *Enterococcus faecium* (VRE) (Table 3).

The antibiotic resistance profiles of the isolated bacteria (*E. coli*, *K. pneumoniae*, and *S. aureus*) are shown in Table 4. Imipenem or meropenem resistance was not detected in *E. coli* and *K. pneu-*

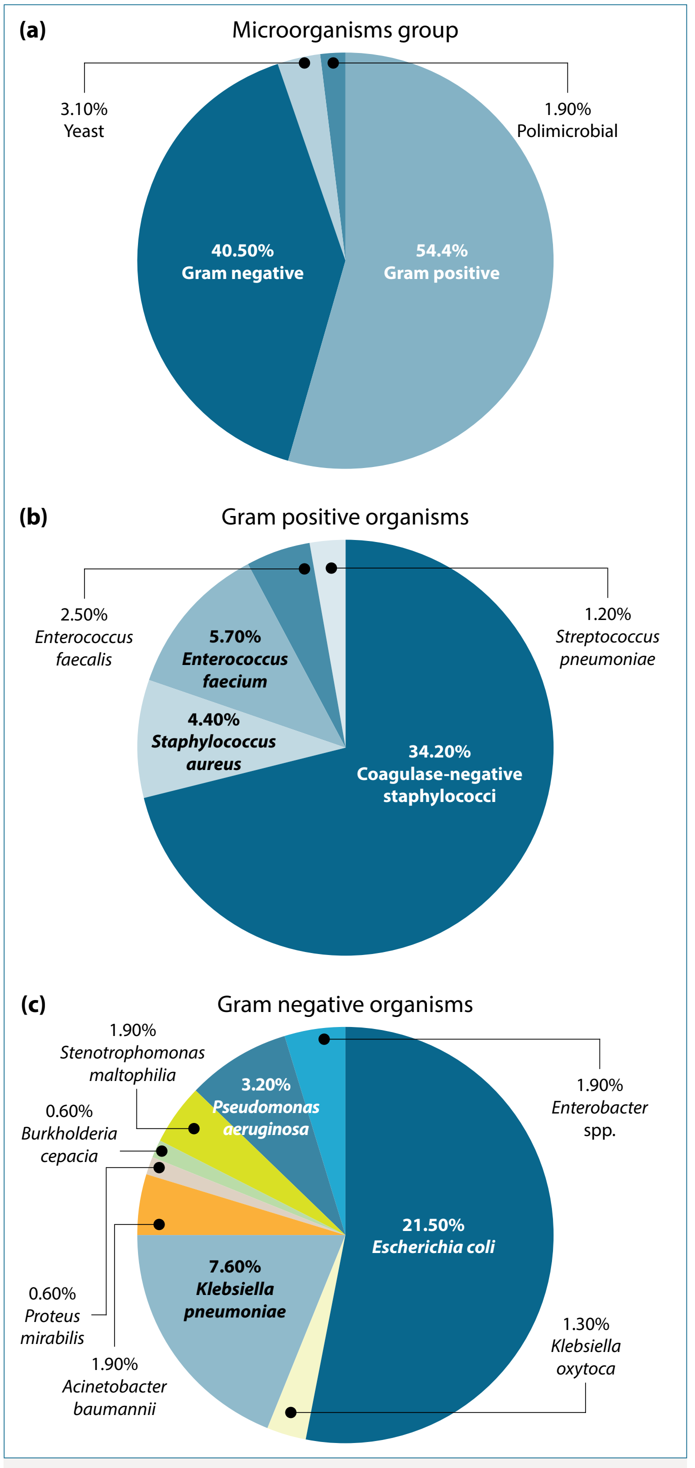

Figure 1. Distribution and percentages of pathogens. **(a)** Percentages of gram-positive, gram-negative, yeast pathogens, and polymicrobial growth. **(b)** Percentages of gram-positive bacteria infecting cancer patients' bloodstreams. **(c)** Percentages of gram-negative bacteria infecting cancer patients' bloodstreams.

Table 3. Distribution and antibiotic resistance profile of isolated microorganisms

Pathogens and resistance	Pathogens	
	n	%
Gram-negative pathogens	**64**	**40.5**
Acinetobacter baumannii	3	1.9
CR	3	
Colistin resistance	–	
Klebsiella pneumoniae	12	7.6
ESBL	3	
CR	2	
Klebsiella oxytoca	2	1.3
ESBL	1	
Escherichia coli	34	21.5
ESBL	14	
CR	2	
Pseudomonas aeruginosa	5	3.2
CR	–	
Enterobacter species	3	1.9
Stenotrophomonas maltophilia	3	1.9
Burkholderia cepacia	1	0.6
Proteus mirabilis	1	0.6
Gram-positive pathogens	**86**	**54.4**
Staphylococcus aureus	7	4.4
Methicillin-susceptible	6	
Methicillin-resistant	1	
Coagulase-negative staphylococci	54	34.2
Streptococcus pneumoniae	2	1.2
Enterococcus faecalis	4	2.5
Enterococcus faecium	9	5.7
VR	3	
Other	10	6.3
Yeast	5	3.1
Candida albicans	2	
Candida parapsilosis	2	
Candida tropicalis	1	
Polymicrobial	3	1.9
Total	**158**	

CR: Carbapenem resistance; ESBL: Extended-Spectrum β-Lactamase-producing; VR: Vancomycin-resistant.

moniae bacterial isolates. Amikacin resistance was detected in only one *E. coli* bacterial isolate. The antibacterial effect of penicillin was low (14.3%) against *S. aureus*, but the effects of other antibiotics were high. The MDR rate was determined as 6% (nine (26.5%) *E. coli* and three (25%) *K. pneumoniae* isolates).

DISCUSSION

With the use of chemotherapeutic drugs in cancer patients, there is an increase in bloodstream infections due to immune system suppression, invasive procedures, and long-term hospitalizations. However, the development of antimicrobial resistance limits the activity of empirical antibiotics in cancer patients, which is quite worrying. The frequent and uncontrolled use of antibiotics leads to a substantial increase in resistance rates, calling for urgent action. Previous studies have stated that Gram-negative bacteria are the predominant pathogens that frequently cause bloodstream infections (BSIs) in cancer patients.[7] However, it has been reported that there is an increase in Gram-positive bacteria, and these bacteria have gradually become dominant in the last 20 years.[8,9] It is thought that the effective prophylactic antibiotic agents, such as fluoroquinolones used in the treatment of gram-negative bacteria, may be responsible for this change.[10] In this study, it was determined that Gram-positive bacteria were more frequently isolated than Gram-negative bacteria in patients diagnosed with cancer at our hospital.

In a study by Worku et al.,[1] which investigated the bacterial profiles in cancer patients in Ethiopia, it was reported that Gram-positive bacteria were frequently isolated, consistent with the results of our study. S. aureus was the dominant strain (61.1%), followed by CoNS (48.5%). The most frequently isolated gram-negative bacteria were *K. pneumoniae* (47%) and *P. aeruginosa* (29.5%). Additionally, multidrug resistance was detected in 17.1% of bacterial isolates. Previous reports have indicated that Gram-negative bacterial isolates have a higher prevalence of MDR compared to Gram-positive isolates. In our study, a 6% rate of MDR resistance was found, and all of this ratio was determined as Gram-negative bacterial isolates.

In a study conducted in Türkiye, Sacar et al.[11] reported that Gram-negative organisms were isolated in 58.4% of cancer patients. In another study by Kara et al.,[12] Gram-negative bacteria were detected at a rate of 52.6%. Consistent with our study, Kara et al.[12] found that *E. coli* (17.3%) and *Klebsiella spp.* (11%) (Gram-negative bacteria), and CoNS (10.4%) (Gram-positive bacteria) were the most frequently isolated bacteria.

In a study conducted by Haddad et al.[2] in Lebanon, Gram-negative microorganisms were reported to be isolated most frequently in bloodstream infections of cancer patients. The rates of bacteria were determined as follows; *E. coli* (45.6%), *P. aeruginosa* (7.5%), and *A. baumannii* (4.0%). Most of these microorganisms have been reported to be MDR (61%) isolates.

Table 4. Resistance profile of bacterial isolates

Antibiotics	Number of resistant isolates (%)		
	***E. coli* (34)**	***K. pneumoniae* (12)**	***S. aureus* (7)**
Amikacin	1 (2.9)	0	0
Amoxicillin/Clavulanate	–	–	1 (14.3)
Gentamicin	4 (11.8)	3 (25)	–
Penicillin G	–	–	6 (85.7)
Ampicillin/Sulbactam	17 (50)	7 (58.3)	–
Ceftazidime	11 (32.4)	2 (16.7)	–
Ceftriaxone	14 (41.2)	3 (25)	–
Cefepime	10 (29.4)	2 (16.7)	–
Methicillin	–	–	1 (14.3)
Erythromycin	–	–	1 (14.3)
Clindamycin	–	–	1 (14.3)
Tetracycline	–	–	1 (14.3)
Ciprofloxacin	10 (29.4)	4 (33.3)	0
Levofloxacin	10 (29.4)	4 (33.3)	0
Ertapenem	2 (5.9)	2 (16.7)	–
Imipenem	0	0	–
Meropenem	0	0	–
Piperacillin/Tazobactam	11 (32.4)	5 (41.7)	–
Trimethoprim/Sulfamethoxazole	14 (41.2)	4 (33.3)	0
Vancomycin	–	–	0
Teicoplanin	–	–	0
Linezolid	–	–	0
Daptomycin	–	–	0

In a recent study carried out in Palestine, the distribution of microorganisms and the antimicrobial resistance status isolated from blood cultures of patients with solid organ malignancies were investigated. Similar to our study results, 52.6% Gram-positive bacteria and 39.7% Gram-negative bacteria were detected in this study. Additionally, CoNS (33.7%), *Enterococcus* (6.9%), and *S. aureus* (4.3%) among gram-positive bacteria, and *E. coli* (18.1%), *Klebsiella spp*. (15.5%), and *P. aeruginosa* among gram-negative bacteria (5.2%) were reported as the most frequently isolated microorganisms. These results are also consistent with our study.[13]

Amanati et al.[14] determined that gram-negative bacteria (63.3%) isolated from bloodstream infections in cancer patients were more prevalent than gram-positive bacteria (36.7%) in their study. Similarly, in our study, it was stated that *E. coli* was the most common among gram-negative bacteria, and CoNS were the most common among gram-positive bacteria. It has also been reported that species such as *Acinetobacter spp*., *Pseudomonas spp*., *E. coli*, and *K. pneumoniae* are ESBL producers. However, in our study, resistance to imipenem and meropenem was not detected in *E. coli* and *K. pneumoniae* isolates. Nevertheless, resistance to ertapenem was determined in 5.9% of *E. coli* isolates and 16.7% of *K. pneumoniae* isolates. Additionally, for cephalosporin group antibiotics, the resistance rates were found to be 29–41% for *E. coli* isolates and 16–25% for *K. pneumoniae* isolates. In the study by Rabayah et al.,[13] carbapenem resistance was reported at 27.8% for *Klebsiella spp*., although no carbapenem resistance was detected in *E. coli* isolates. Furthermore, very-high cephalosporin-resistance was detected in both *E. coli* isolates (50–52%) and *K. pneumoniae* isolates (40–45%). The methicillin-resistance rate in S. aureus isolates was 40% (2/5) in the same study, and the MRSA rate was 24.8% (7/30) in the study by Kara et al.[12] In our study, the MRSA rate was found 14.3% (1/7).

In a study conducted in China by Liang et al.[15] in patients with hematological malignancies, the ESBL positivity rate was reported as 45.4%. It has been stated that higher resistance rates were detected among ESBL-positive (+) isolates for many antibiotics. Kara et al.[12] reported an ESBL production rate of 45% for *E. coli* and 58% for *Klebsiella spp*. In our study, similar to this study, the ESBL positivity rate was 41.2% (14/34) in *E. coli* isolates and 25% (3/12) in *K. pneumoniae* isolates. The high rates of ESBL positivity detected in Gram-negative bacterial isolates and the accompanying increased antibiotic resistance lead to treatment failure.

Limitation

There are some limitations of our study. Firstly, since this study was retrospective, some variables such as chemotherapeutic protocols, pre-hospital antibiotic therapy, and certain clinical and laboratory test results could not be analyzed. Therefore, the results of the study were not associated with these variables. Secondly, our research was conducted using data collected from a single center. Therefore, a prospective multicenter study is needed to further validate the results.

CONCLUSION

Bloodstream infections pose a significant health concern, leading to increased morbidity and mortality rates in cancer patients. This study aimed to investigate the bacterial composition and level of antibiotic resistance in bloodstream infections among cancer patients. It was determined that Gram-positive bacteria were more prevalent in blood cultures from cancer patients. The most frequently detected bacterium in the study was CoNS, followed by *E. coli*, *Enterococcus sp*., *K. pneumoniae*, and *S. aureus*. It was determined that the isolated bacteria were sensitive to many antibiotics, and the MDR ratio was low. This result is promising for our hospital. These studies reveal the changes in MDR isolates and resistance data over the years. With routine bacterial surveillance for cancer patients, it can assist in regulating antimicrobial treatment protocols and, consequently, increase treatment success. Additionally, it can be stated that the results of our study are effective in terms of sharing regional and current data.

Peer-review: Externally peer-reviewed.

Ethics Committee Approval: The Sivas Cumhuriyet University Non-Invasive Clinical Research Ethics Committee granted approval for this study (date: 21.09.2022, number: 2022-09/19).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Author Contributions: Concept – AHTK, FÇ; Design – AHTK, FÇ; Supervision – MH, AHTK; Resource – MH, FÇ; Materials – MH, FÇ; Data Collection and/or Processing – AHTK, MH; Analysis and/or Interpretation – AHTK, FÇ; Literature Search – RA, ZÇ; Writing – RA, ZÇ; Critical Reviews – RA, ZÇ.

Conflict of Interest: The authors have no conflict of interest to declare.

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