

Original Article



Etiology of Bacteremia in Children With Hemato-Oncologic Diseases From 2013 to 2023: A Single Center Study

Sun Woo Park ,¹ Ji Young Park ,² Hyoung Soo Choi ,^{1,3} Hyunju Lee ^{1,3}

¹Department of Pediatrics, Seoul National University Bundang Hospital, Seongnam, the Republic of Korea

²Department of Pediatrics, Chung-Ang University Hospital, College of Medicine, Chung-Ang University, Seoul, the Republic of Korea

³Department of Pediatrics, Seoul National University College of Medicine, Seoul, the Republic of Korea

OPEN ACCESS

Received: Oct 27, 2023

Revised: Mar 26, 2024

Accepted: Mar 26, 2024

Published online: Apr 3, 2024

Correspondence to

Hyunju Lee

Department of Pediatrics, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, the Republic of Korea.

Email: hyunjulee@snuhb.org

© 2024 The Korean Society of Pediatric Infectious Diseases

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Sun Woo Park

<https://orcid.org/0000-0002-3112-7528>

Ji Young Park

<https://orcid.org/0000-0002-6777-0494>

Hyoung Soo Choi

<https://orcid.org/0000-0002-4837-164X>

Hyunju Lee

<https://orcid.org/0000-0003-0107-0724>

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ABSTRACT

Purpose: This study aimed to identify the pathogens of bloodstream infection in children with underlying hemato-oncologic diseases, analyze susceptibility patterns, compare temporal trends with those of previous studies, and assess empirical antimicrobial therapy.

Methods: Retrospective review study of children bacteremia in hemato-oncologic diseases was conducted at Seoul National University Bundang Hospital from January 2013 to July 2023.

Results: Overall, 98 episodes of bacteremia were observed in 74 patients. Among pathogens isolated, 57.1% (n=56) were Gram-positive bacteria, 38.8% (n=38) were Gram-negative bacteria, and 4.1% (n=4) were *Candida* spp. The most common Gram-positive bacteria were coagulase-negative staphylococci (n=21, 21.4%) and *Staphylococcus aureus*, (n=14, 14.3%) whereas the most common Gram-negative bacteria were *Klebsiella pneumoniae* (n=16, 16.3%) and *Escherichia coli* (n=10, 10.2%). The susceptibility of Gram-positive bacteria to penicillin, oxacillin, and vancomycin was 11.5%, 32.7%, and 94.2%, respectively and the susceptibility of Gram-negative bacteria to cefotaxime, piperacillin/tazobactam, imipenem, gentamicin, and amikacin was 68.6%, 80%, 97.1%, 82.9%, and 91.4%, respectively. Methicillin-resistant *S. aureus* was detected in 1 strain and among Gram-negative strains, extended spectrum β -lactamase accounted for 28.9% (12/38). When analyzing the antibiotic susceptibility and empirical antibiotics, the mismatch rate was 25.5% (n=25). The mortality rate of children within 30 days of bacteremia was 7.1% (n=7).

Conclusions: Empirical antibiotic therapy for bacteremia in children with hemato-oncologic diseases should be based on the local antibiogram in each institution and continuous monitoring is necessary.

Keywords: Bacteremia; Hematology; Neoplasm; Children

INTRODUCTION

Due to recent improvements in diagnosis and treatment, the long-term survival rate of pediatric hemato-oncology patients is increasing, along with an increased risk of infection due to changes in the immune system and compromised defense mechanisms.^{1,2)} Among the various opportunistic infections that may occur, bacteremia is one of the most life-threatening complications for hemato-oncologic children.³⁻⁵⁾

Author Contributions

Conceptualization: Park SW, Park JY, Lee H; Data curation: Park SW, Lee H; Formal analysis: Park SW, Choi HS, Lee H; Funding acquisition: Lee H; Investigation: Park SW, Lee H; Methodology: Park SW, Park JY, Lee H; Project administration: Park SW, Lee H; Resources: Park SW, Lee H; Software: Park SW, Lee H; Supervision: Choi HS, Lee H; Validation: Park SW, Choi HS, Lee H; Visualization: Park SW, Choi HS, Lee H; Writing - original draft: Park SW; Writing - review & editing: Park SW, Choi HS, Lee H.

A marked pattern has been observed in causative pathogens for bacteremia in hemato-oncologic children over time. For example, in the 1960s to 1970s, Gram-negative bacteria were the most common pathogen. Since the 1980s, an increased incidence of Gram-positive bacteremia secondary to oral mucositis has been recorded due to the widespread use of chemotherapeutic agents (such as cytosine arabinoside), persistent neutropenia, increased long-term catheter use, prophylactic antibiotic use (such as trimethoprim-sulfamethoxazole and fluoroquinolone).^{6,13)}

This study aimed to analyze the distribution of bacteremia pathogens and findings in antimicrobial susceptibilities in children with hemato-oncologic diseases. Therefore, hemato-oncologic patients diagnosed with bacteremia between 2013 and 2023 were analyzed, and we compared the antimicrobial susceptibility with the empirical antibiotics to assess the appropriateness of antibiotic treatment in these patients.

MATERIALS AND METHODS

1. Study population and hospital setting

The study was conducted by retrospectively reviewing the medical records of children with bacteremia and underlying hemato-oncologic diseases from January 1, 2013, to July 31, 2023, at Seoul National University Bundang Hospital. For each case of bacteremia, the specific pathogen, as well as antibiotic susceptibility, preceding infection, presence of neutropenia, use of central line and treatment course, were reviewed.

2. Definition

Bacteremia was defined as having a positive bacterial growth in blood culture results. If follow-up blood culture tests taken within 14 days from the same child revealed the same pathogen, it was considered a single case of bacteremia. Polymicrobial bacteremia was defined as a case in which two or more bacteria were separated from blood culture samples obtained simultaneously or within 24 hours; superinfection was defined as the case in which two or more bacteria were separated at intervals of 24 hours to 14 days.¹⁴⁾

Fever was measured from the axilla or tympanic membrane and was defined as a body temperature over 38.0°C for >1 hour or a long-lasting body temperature over 38.3°C. Neutropenia was defined as absolute neutrophil count <1,000/uL. Underlying diseases were classified as hematologic and non-hematologic malignancies. Patients receiving peripheral blood stem cell transplantation (PBSCT) treatment or those who received PBSCT in the past were defined as the post-PBSCT group, and patients who have completed chemotherapy or ceased immunosuppressant treatment were defined as the off-therapy group. Mortality was defined as the death of the patient within 30 days of contracting bacteremia. Long term catheter included both chemoport and hickman catheter. Central line bloodstream infection was defined as a bloodstream infection that occurs when a central line is maintained for more than two days and established on the day or the day before the infection, with a recognized pathogen isolated from one or more blood cultures, with no other related site of infection.

3. Data collection

Date of birth, sex, underlying disease, presence of neutropenia, presence of long-term catheter, date of PBSCT, and the date of blood culture were extracted from hospital databases and medical records. Microbiological data, treatment course, and date of negative blood

culture were retrieved from medical records. This study was approved by the Institutional Review Board (IRB) of SNUBH (IRB no. B-2308-845-107).

4. Statistical analysis

Blood was collected into a Bactec blood culture bottle (Becton Dickinson, Sparks, MD, USA) and incubated using a Bactec 9240 blood culture system. An antibiotic susceptibility test using Vitek-2 (bioMérieux, Marcy-l'Étoile, France) and Microscan (Siemens Healthcare, Sacramento, CA, USA) was conducted to determine the minimum inhibitory concentration. Descriptive analyses were performed to characterize the patient population by reporting the median values and interquartile ranges (IQRs) or percentages. Categorical data were calculated using χ^2 test and statistical analyses were performed using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). A *P*-value <0.05 was considered significant.

RESULTS

1. Demographics and clinical characteristics

Between January 2013 and July 2023, 74 children with 98 episodes of bacteremia were identified. Polymicrobial bacteria was found in 2 cases (2.0%).

The demographics and clinical characteristics of patients with bacteremia are summarized in **Table 1**. A total of 60 (61.2%) children were male, and the median age was 10.6 years (IQR, 8.8; range, 2 months–18 years). Among all episodes of bacteremia, 67.3% (n=66) occurred in patients with long-term catheters.

Of the 74 patients, the most common underlying disease was hematologic malignancy (n=71, 72.4%) and within the hematologic malignancy, acute lymphoblastic leukemia (ALL) was the most common (n=26, 26.5%), followed by acute myeloblastic leukemia (n=23, 23.5%), and non-Hodgkin lymphoma (n=14, 14.3%). The most common diagnoses within non-hematologic malignancy were osteosarcoma (n=7, 7.1%) and neuroblastoma (n=5, 5.1%).

2. Distribution of pathogens causing bacteremia

Table 2 summarizes the pathogens causing bacteremia in children with hemato-oncologic malignancies. A total of 98 pathogens were identified, among which 57.1% (n=56) were Gram-positive bacteria, 38.8% (n=38) were Gram-negative bacteria, and 4.1% (n=4) were *Candida* spp. The most common pathogens were coagulase-negative *staphylococci* (CoNS) (n=21, 21.4%), *Klebsiella pneumoniae* (n=16, 16.3%), *Staphylococcus aureus* (n=14, 14.3%), viridans streptococcus group (n=13, 13.3%), and *Escherichia coli* (n=10, 10.2%). Among 21 cases of CoNS, 3 cases were *S. epidermidis*, and whether the patient had true infection was determined by having fever > 38.3°C following isolated pathogen from blood culture, and having no other infection focus. Among 14 cases of *S. aureus*, 13 cases were methicillin-susceptible *S. aureus* and one case was methicillin-resistant *S. aureus*.

Overall, 70.4% (n=69) patients had neutropenia at the time of bacteremia diagnosis, of these 46.4% (n=32) were Gram-positive bacteria, 49.3% (n=34) were Gram-negative bacteria, and 4.3% (n=3) were *Candida* spp. Among 29 patients who developed bacteremia without neutropenia, 82.8% (n=24) were Gram-positive bacteria, 13.8% (n=4) were Gram-negative bacteria, and 3.4% (n=1) was *Candida* spp., showing the distribution difference of Gram-positive and Gram-negative bacteria by whether the patient had neutropenia. Among patients

Table 1. Clinical characteristics of pediatric hemato-oncological patients with bacteremia

Characteristics	No. of episodes	Percentage (%)
Total	98	100
Sex		
Male	60	61.2
Female	38	38.8
Age, median (IQR, range) (yr)	10.6 (8.8, 2 mon–18 yr)	
Long-term catheter	66	67.3
Underlying disease		
Hematologic malignancy		
Acute lymphoblastic leukemia	26	26.5
Acute myelogenous leukemia	23	23.5
Non-Hodgkin lymphoma	14	14.3
Hodgkin lymphoma	3	3.1
Hemophagocytic lymphohistiocytosis	2	2
Langerhand cell histiocytosis	2	2
Juvenile myelomonocytic leukemia	1	1
HSCT in hematologic malignancy	13	13.3
Subtotal	71	72.4
Non-hematologic malignancy		
Osteosarcoma	7	7.1
Neuroblastoma	5	5.1
Rhabdomyosarcoma	2	2
Primitive neuroectodermal tumor	2	2
Brain stem glioma	1	1
Germ cell ovarian cancer	1	1
Immature teratoma	1	1
Medulloblastoma	1	1
HSCT in non-hematologic malignancy	3	3.1
Subtotal	20	20.4
Non-malignant hematologic disease		
Aplastic anemia	5	5.1
Idiopathic thrombocytopenic purpura	1	1
Venous thromboembolism	1	1
HSCT in non-malignancy hematologic disease	4	4.1
Subtotal	7	7.1

Abbreviations: IQR, interquartile range; HSCT, hematopoietic stem cell transplantation.

who had neutropenia, *K. pneumoniae*, CoNS, and *E. coli* were the most common bacteria. On the other hand, among patients who had bacteremia without neutropenia, CoNS, *S. aureus*, and viridans streptococcus group were the most common bacteria found (**Table 2**). There were five cases of Gram-negative bacteria isolated from patients without neutropenia. Among these five cases, two patients were under 1 year old, and had just undergone 1st chemotherapy after diagnosed with LCH. And also, one patient had underlying precursor B-cell ALL, and had uncontrolled GVHD after receiving PBSCT. She had bacteremia two days before her death due to GVHD complication, the results of which revealed *Candida tropicalis*.

Of 98 cases in total, only one case of bacteremia occurred on the PBSCT infusion day. All the other patients who has undergone PBSCT had bacteremia at least two months before or after infusion day. There were no bacteremia that occurred during high dose chemotherapy, or during biological agent administration (ex. Eculizumab, Rituximab). Pathogen distribution also differed by whether the patient had a long-term catheter. Among patients without long-term catheter, *S. aureus* and *E. coli* and among those with a long-term catheter, *K. pneumoniae* and CoNS, viridans streptococcus group were most common. Among 66 bacteremia cases with patients having long term catheter, three cases of CRBSI was found in total; one case of *K. pneumoniae*, one case of *E. coli*, and one case of *S. aureus*.

Table 2. Pathogens in blood stream infections of pediatric hemato-oncological patients with or without neutropenia

Variables	No. of pathogens (%)						P-value
	Total	%	Neutropenia	%	Without neutropenia	%	
Gram-positive bacteria							
Coagulase-negative staphylococci	21	21.4	10	10.2	11	11.2	
<i>Staphylococcus aureus</i>	14	14.3	8	8.2	6	6.1	
Viridans streptococci	13	13.3	9	9.2	4	4.1	
<i>Enterococcus faecium</i>	4	4.1	3	3.1	1	1	
<i>Enterococcus faecalis</i>	1	1	0	0	1	1	
Others*	3	3.1	2	2	1	1	
Subtotal	56	57.1	32	32.7	24	24.5	0.0009
Gram-negative bacteria							
<i>Klebsiella pneumoniae</i>	16	16.3	15	15.3	1	1	
<i>Escherichia coli</i>	10	10.2	9	9.2	1	1	
<i>Enterobacter cloacae</i>	6	6.1	5	5.1	1	1	
<i>Pseudomonas aeruginosa</i>	2	2	2	2	0	0	
<i>Acinetobacter baumannii</i>	1	1	1	1	0	0	
Others†	3	3.1	2	2	1	1	
Subtotal	38	38.8	34	34.7	4	4.1	0.0001
Fungus							
<i>Candida tropicalis</i>	3	3.1	2	2	1	1	
<i>Candida krusei</i>	1	1	1	1	0	0	
Subtotal	4	4.1	3	3.1	1	1	0.8372
Total	98	100	69	70.4	29	29.6	0.0033

*Others: *Corynebacterium* species (n=2), *Streptococcus agalactiae* (n=1); †Others: *Haemophilus parainfluenzae* (n=1), *Citrobacter freundii* (n=1), *Burkholderia* species (n=1).

There were patients who accompanied focal infections with bacteremia. The most common focal infection was perianal abscess (n=5, 5.1%), enteritis (n=4, 4.1%), pneumonia (n=2, 2.0%), fungus ball (n=2, 2.0%), postoperative wound abscess (n=1, 1.0%). Among these, only the postoperative wound abscess was considered as the origin of bacteremia.

3. Antibiotic susceptibility of pathogens causing bacteremia

Antimicrobial susceptibility testing results were available for all cases. **Tables 3** and **4** summarize the susceptibility testing results for Gram-positive and Gram-negative bacteria. Among 54 Gram-positive bacteria in which antimicrobial susceptibility results were available, the susceptibility to penicillin, oxacillin, and vancomycin was 14.8% (n=8), 31.5% (n=17), and 94.4% (n=51), respectively. Among four cases of *Enterococcus faecium*, three cases were resistant to vancomycin. And all other Gram-positive bacteria were susceptible to vancomycin (**Table 3**).

Among 37 Gram-negative bacteria in which antimicrobial susceptibility results were available, the antimicrobial susceptibility to cefotaxime, piperacillin/tazobactam, imipenem, gentamicin, and amikacin were 70.3% (n=26), 81.1% (n=30), 94.6% (n=35), 81.1% (n=30),

Table 3. Antimicrobial susceptibilities of Gram-positive bacteria causing blood stream infection

Variables	No. of strains susceptible to (%)								
	Total (%)	Penicillin	%	Oxacillin	%	Ampicillin	%	Vancomycin	%
Coagulase-negative staphylococci	21 (38.9)	0	0	4	19.0	ND	ND	21	100
<i>Staphylococcus aureus</i>	14 (25.9)	1	7.1	13	92.9	ND	ND	14	100
Viridans streptococci	13 (24.0)	5	38.5	ND	ND	ND	ND	13	100
<i>Enterococcus faecium</i>	4 (7.4)	ND	ND	ND	ND	0	0	1	25.0
<i>Enterococcus faecalis</i>	1 (1.9)	1	100	ND	ND	1	1	1	100
<i>Streptococcus agalactiae</i>	1 (1.9)	1	100	ND	ND	ND	ND	1	100
Total*	54	8	14.8	17	31.5	1	1.9	51	94.4

Abbreviation: ND, not definite.

*Data not available for *Corynebacterium* species (n=2).

Table 4. Antimicrobial susceptibilities of Gram-negative bacteria causing blood stream infection

Variables	No. of strains susceptible to (%)											
	Total	%	Cefotaxime	%	Piperacillin/Tazobactam	%	Imipenem	%	Gentamicin	%	Amikacin	%
<i>Klebsiella pneumoniae</i>	16	43.2	9	56.3	11	68.8	16	100.0	14	87.5	14	87.5
<i>Escherichia coli</i>	10	27.0	8	80.0	9	90.0	10	100.0	7	70.0	9	90.0
Enterobacter species	6	16.2	4	66.7	5	83.3	5	83.3	5	83.3	6	100.0
<i>Pseudomonas aeruginosa</i>	2	5.4	2*	100.0	2	100.0	2	100.0	2	100.0	2	100.0
<i>Acinetobacter baumannii</i>	1	2.7	1*	100.0	1	100.0	1	100.0	1	100.0	1	100.0
Others [†]	2	5.5	2	100.0	2	100.0	1	50.0	1	50.0	1	50.0
Total [‡]	37	100.0	26	70.3	30	81.1	35	94.6	30	81.1	33	89.2

*Ceftazidime; [†]Others: *Citrobacter freundii* (n=1), Burkholderia species (n=1); [‡]Data not available for *Haemophilus parainfluenzae* (n=1).

and 89.2% (n=33), respectively (**Table 4**). The most common Gram-negative bacteria were *Klebsiella* species and *E. coli*, which showed 56.3%, and 80% of susceptibility to cefotaxime, respectively, 68.8%, and 90% to piperacillin/tazobactam, respectively, and 87.5%, and 90% to amikacin, respectively (**Table 4**). The overall susceptibility of Gram-negative bacteria to imipenem was 94.6%, with only one resistant pathogen (Enterobacter species) of 35 pathogens. There were 12 pathogens producing extended spectrum β -lactamase (ESBL), among which seven were *K. pneumoniae*, two were *E. coli*, two were Enterobacter species, and one was Coagulase negative Staphylococcus. These accounted for 43.7% (7/16) of *K. pneumoniae*, 20% (2/10) of *E. coli*, and 33.3% (2/6) of Enterobacter species.

For all 98 episodes, antimicrobial susceptibility of the pathogen isolated to the antibiotics being administered at the point of bacteremia was also assessed. For 74.5% (n=73) episodes of bacteremia, susceptible antibiotics were being administered to the patient, 25.5% (n=25) episodes had unmatching antibiotics, and 10.2% (n=10) episodes were non assessable.

4. Clinical course of hemato-oncologic diseases patients with bacteremia

All 98 episodes were analyzed, and septic shock was observed in 14.3% (n=14) cases. Among all cases, 11.2% (n=11) received intensive care unit (ICU) care, and total mortality was 7.1% (n=7), 4 of which had Gram-positive bacteria (*E. faecium*: 2, CoNS: 1, Corynebacterium: 1), 2 of which had fungus (*Candida tropicalis*), and 1 of which had Gram-negative bacteria (*K. pneumoniae*) isolated. Among seven mortality cases, five patients had underlying precursor B-cell ALL, with immunocompromised state at the point of bacteremia. Among these five patients, one patient showed septic shock features with bacteremia, and therefore received ICU care including continuous renal replacement therapy. Also, one patient had underlying neuroblastoma with multiple metastasis, and was receiving palliative care at the point of bacteremia. The mortality of this patient was not directly due to bacteremia, whereas all other six cases of mortality was due to bacteremia.

DISCUSSION

Surveillance of bacteremia is imperative for the treatment and management of hemato-oncologic patients who are vulnerable to infection. Identifying the demographic characteristics of patients who experienced bacteremia and analyzing the pathogen distribution and antimicrobial susceptibility may help treat patients who need more intensive monitoring for bacteremia management. Surveillance of pathogens and antibiograms is important to develop guidelines regarding appropriate antibiotic use.

Monitoring antibiotic resistance is essential to optimize empiric antibiotic use. Antibiotic resistance has emerged as an important issue in hospital settings because of the extensive use and misuse of antibiotics.¹⁵⁾

This study aimed to identify the pathogens of bloodstream infection in children with underlying hemato-oncologic diseases from January 2013 to July 2023, analyze susceptibility patterns of microorganisms, compare temporal trends of the pathogen and antimicrobial susceptibility with those of previous studies, and finally assess empirical antimicrobial therapy.

In our hospital, hemato-oncologic patients with fever obtain blood cultures immediately from both central and peripheral lines, and are administered with piperacillin/tazobactam as initial empirical antibiotics. According to a previous study among children in Korea,¹⁶⁾ the incidence of Gram-negative bacteria was higher than Gram-positive bacteria, and the mortality rate of Gram-positive bacteria and Gram-negative bacteria was similar. Therefore, piperacillin/tazobactam was administered as initial empirical antibiotics. Between 2013 and 2023, the frequency of Gram-positive bacteria was higher than Gram-negative bacteria. Among Gram-positive bacteria, CoNS was the most common pathogen observed, accounting for 21.4% of all bacteremia. This is likely due to their ability to colonize human skin and mucous membranes, which may provide many opportunities to become pathogens in predisposed patients, such as hemato-oncologic patients and patients with catheters.

For Gram-positive bacteria, the antimicrobial susceptibility to penicillin was low (14.8%), along with the susceptibility of oxacillin (31.5%). Susceptibility to vancomycin was 94.4%, with 3 episodes of vancomycin-resistant *E. faecium* isolated.

For Gram-negative bacteria, the susceptibility to amikacin, cefotaxime, piperacillin/tazobactam, imipenem, and gentamycin was 89.2%, 70.3%, 81.1%, 94.6%, and 81.1%, respectively, which showed similar susceptibility proportions compared to a recent study that was previously conducted in another hospital.¹⁴⁾

Among Gram-negative bacteria, the distribution of ESBL-producing bacteria during study period accounted for 43.7% of *K. pneumoniae* and 20% of *E. coli*. According to a previous study conducted in another hospital from 2011 to 2015, the ESBL-producing bacteria accounted for 27.4% of *K. pneumoniae* and 12.9% of *E. coli*. For ESBL producing bacteremia with susceptibility to piperacillin/tazobactam, antibiotics were changed to cefepime or carbapenem,¹⁷⁾ and there were no carbapenem-resistant-enterobacteriaceae or carbapenemase-producing-enterobacteriaceae positive pathogens or no multi-drug resistant *Acinetobacter baumannii* pathogens isolated. The results of pathogen distribution and antibiotics susceptibility in this previous study was similar to our study. A total of three vancomycin resistant enterococci cases were found in total, two of which had kept empirical antibiotics due to clinical response and improving patient state, and 1 of which empirical antibiotics have been changed from vancomycin and meropenem to linezolid. All three cases of bacteremia were treated successfully, without any mortality cases.

There were four cases of *Candida* spp. in total; two cases with *C. tropicalis* infection had no associated focal infection, but both patients had moderate GVHD after recent PBST. These 2 patients received IV Ambisome as initial antifungal agent, but one of them expired within 7 days. *C. krusei* was isolated in 1 cases, from a patient with perianal inflammation. IV Caspofungin was administered for this patient as initial antifungal agent, and the bacteremia was successfully treated within 2 weeks.

Antibiotics are changed promptly according to the Gram stain and final culture reports. In our study, the empirical antibiotics used were inappropriate in 25.5% (n=25) cases, most of which were piperacillin/tazobactam.

This study had some limitations. First, because this was a retrospective cohort study at a single institution, the total number of patients included was small and thus could not represent the general hemato-oncologic patient population in Korea. Second, as this study included no control group of patients without bacteremia, the statistical significance of the contributing factors leading to the increased risk of bacteremia could not be identified.

In our cohort of children of hemato-oncologic disease with bacteremia, during 2013 to 2023, Gram-positive bacteria were more common compared with Gram-negative bacteria with CoNS the most common followed by *K. pneumonia*, *S. aureus*, viridans streptococci and *E. coli*, regardless of Gram stain. For *S. aureus* induced bacteremia, clinicians changed empirical antibiotics according to the susceptibility results. Also, differences in pathogen distribution were found in children according to neutropenia state or long-term catheters. Nevertheless, the incidence of septic shock and mortality rate in patients with Gram-positive bacteria showed no difference from those of Gram-negative bacteria. In the analysis of appropriateness of empirical antibiotics, 74.5% of episodes were found to be on susceptible antibiotics. Therefore, based on the results from this study, we believe our hospital can keep using current treatment guidelines for empirical antibiotics. Empirical antibiotic therapy for bacteremia in children with hemato-oncologic diseases should be based on the local antibiogram in each institution and continuous monitoring is necessary.

ACKNOWLEDGEMENTS

We would like to thank the team at the Department of Laboratory medicine of SNUBH for their support and providing bacteremia-surveillance data in this analysis.

REFERENCES

1. Viscoli C, Varnier O, Machetti M. Infections in patients with febrile neutropenia: epidemiology, microbiology, and risk stratification. *Clin Infect Dis* 2005;40 Suppl 4:S240-5. [PUBMED](#) | [CROSSREF](#)
2. Pizzo PA. Management of fever in patients with cancer and treatment-induced neutropenia. *N Engl J Med* 1993;328:1323-32. [PUBMED](#) | [CROSSREF](#)
3. Klastersky J, Ameye L, Maertens J, Georgala A, Muanza F, Aoun M, et al. Bacteraemia in febrile neutropenic cancer patients. *Int J Antimicrob Agents* 2007;30 Suppl 1:S51-9. [PUBMED](#) | [CROSSREF](#)
4. Nørgaard M, Larsson H, Pedersen G, Schönheyder HC, Sørensen HT. Risk of bacteraemia and mortality in patients with haematological malignancies. *Clin Microbiol Infect* 2006;12:217-23. [PUBMED](#) | [CROSSREF](#)
5. Aust C, Tolfvenstam T, Broliden K, Ljungman P, Kalin M, Giske CG, et al. Bacteremia in Swedish hematological patients with febrile neutropenia: bacterial spectrum and antimicrobial resistance patterns. *Scand J Infect Dis* 2013;45:285-91. [PUBMED](#) | [CROSSREF](#)
6. Singer C, Kaplan MH, Armstrong D. Bacteremia and fungemia complicating neoplastic disease. A study of 364 cases. *Am J Med* 1977;62:731-42. [PUBMED](#) | [CROSSREF](#)
7. Zinner SH. Changing epidemiology of infections in patients with neutropenia and cancer: emphasis on gram-positive and resistant bacteria. *Clin Infect Dis* 1999;29:490-4. [PUBMED](#) | [CROSSREF](#)
8. Wisplinghoff H, Seifert H, Wenzel RP, Edmond MB. Current trends in the epidemiology of nosocomial bloodstream infections in patients with hematological malignancies and solid neoplasms in hospitals in the United States. *Clin Infect Dis* 2003;36:1103-10. [PUBMED](#) | [CROSSREF](#)

9. Ramphal R. Changes in the etiology of bacteremia in febrile neutropenic patients and the susceptibilities of the currently isolated pathogens. *Clin Infect Dis* 2004;39 Suppl 1:S25-31. [PUBMED](#) | [CROSSREF](#)
10. Gudiol C, Bodro M, Simonetti A, Tubau F, González-Barca E, Ciscal M, et al. Changing aetiology, clinical features, antimicrobial resistance, and outcomes of bloodstream infection in neutropenic cancer patients. *Clin Microbiol Infect* 2013;19:474-9. [PUBMED](#) | [CROSSREF](#)
11. Elting LS, Bodey GP, Keefe BH. Septicemia and shock syndrome due to viridans streptococci: a case-control study of predisposing factors. *Clin Infect Dis* 1992;14:1201-7. [PUBMED](#) | [CROSSREF](#)
12. Cordonnier C, Buzyn A, Leverger G, Herbrecht R, Hunault M, Leclercq R, et al. Epidemiology and risk factors for gram-positive coccal infections in neutropenia: toward a more targeted antibiotic strategy. *Clin Infect Dis* 2003;36:149-58. [PUBMED](#) | [CROSSREF](#)
13. Kim SH, Lee YA, Eun BW, Kim NH, Lee JA, Kang HJ, et al. Etiological agents isolated from blood in children with hemato-oncologic diseases (2002–2005). *Korean J Pediatr* 2007;50:56-64. [CROSSREF](#)
14. Kang JE, Seok JY, Yun KW, Kang HJ, Choi EH, Park KD, et al. Etiological agents in bacteremia of children with hemato-oncologic diseases (2006–2010): a single center study. *Korean J Pediatr Infect Dis* 2012;19:131-40. [CROSSREF](#)
15. Hsu JF, Tsai MH, Huang HR, Lien R, Chu SM, Huang CB. Risk factors of catheter-related bloodstream infection with percutaneously inserted central venous catheters in very low birth weight infants: a center's experience in Taiwan. *Pediatr Neonatol* 2010;51:336-42. [PUBMED](#) | [CROSSREF](#)
16. Park JY, Yun KW, Kang HJ, Park KD, Shin HY, Lee HJ, et al. Etiology of bacteremia in children with hemato-oncologic diseases from a single center from 2011 to 2015. *Pediatr Infect Vaccine* 2017;24:71-8. [CROSSREF](#)
17. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America 2023 guidance on the treatment of antimicrobial resistant gram-negative infections. *Clin Infect Dis*, in press 2023. [PUBMED](#) | [CROSSREF](#)

요약

목적: 본 연구는 2013년부터 2023년까지 최근 10년간 분당서울대학교병원 소아 혈액종양 환자들에게 발생한 균혈증 발생 숫자를 확인하고, 원인균 발생 빈도 및 분포와 이들의 항생제 감수성을 분석하면서 경험적 항생제를 선택하는 데에 필요한 치료 지침의 기초 자료로 활용하고자 수행되었다.

방법: 2013년 1월부터 2023년 7월까지 분당서울대학교병원에 입원한 환자 중 기저혈액종양질환이 있으면서 혈류감염이 발생한 환자들을 대상으로 후향적 의무기록 분석을 하였다.

결과: 10년의 연구 기간동안 총 74명의 환자에서 98례의 혈류감염이 확인되었고, 이 중 그람 양성균, 그람 음성균, 진균이 각각 57.1% (n=56), 38.8% (n=38), 4.1% (n=4)이었다. 가장 흔한 그람 양성균은 coagulase-negative staphylococci (n=21, 21.4%) 와 *Staphylococcus aureus* (n=14, 14.3%) 였고, 가장 흔한 그람 음성균은 *Klebsiella* species (n=16, 16.3%) 와 *Escherichia coli* (n=10, 10.2%) 였다. 전체 사망한 환자들 중 균혈증 발생으로부터 30일 이내로 사망한 사례는 총 6건 (6.1%) 이었다.

결론: 본 연구는 혈액종양질환을 진단받은 소아 환자들에게서 발생한 균혈증의 원인균 분포 및 각 원인균의 항생제 분포를 분석하였다. 연구결과를 토대로, 연구자들은 현재 사용하는 경험적 항생제 가이드라인을 유지할 수 있다는 점을 알 수 있었다. 소아 혈액종양질환 환자들에게서 발생한 균혈증에서 사용해야 할 적절한 경험적 항생제는 각 기관별로 조사한 항생제 감수성 양상에 기초하여 결정되어야 하며, 지속적인 모니터링은 반드시 이루어져야 한다.