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Bloodstream Infections in Hematologic Malignancies: Clinical Features and Pathogen Profile from a 2023 Study at Dr. Soetomo General Hospital, Surabaya

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ABSTRACT

Infection remains a major complication and a leading cause of death in patients with hematologic malignancies (HMs), with bloodstream infection (BSI) being one of the most critical complications. This happens due to profound immunosuppression caused by the disease and chemotherapy. Myelosuppression and neutropenia significantly increase the risk of infection in these patients. This retrospective descriptive study analyzed 129 patients with HMs and positive blood cultures at Dr. Soetomo General Hospital, Surabaya, in 2023 to describe the clinical profile and pathogen distribution. The findings showed that most patients were male, aged 19-59 years, and most were diagnosed with acute lymphocytic leukemia (ALL) and had a history of chemotherapy exposure. Hematologic profile showed high rates of anemia, thrombocytopenia, and neutropenia. A total of 142 isolates showed Gram-positive bacteria were the most common pathogens, with Staphylococcus aureus as the predominant species, and most infections being monomicrobial. Antibiotic susceptibility tests showed variable resistance patterns. These findings highlight the vulnerability of patients with HMs to severe infections and the need for optimized infection prevention and surveillance of local pathogen and antibiotic sensitivity patterns.

Keywords: hematologic malignancy; bloodstream infection pathogen; neutropenia

INTRODUCTION

Hematologic malignancies (HMs) consist of diverse cancers arising from the bone marrow and lymphoid tissues [1]. Despite advances in diagnosis and therapy, infectious complications remain one of the major causes of mortality in patients with HMs. Patients with HMs experience immunosuppression, largely due to the disease itself and chemotherapy exposure. Chemotherapy causes myelosuppression and neutropenia [2]. This significantly increases their susceptibility to severe infections, including bloodstream infections (BSIs) [3]. Latest studies have shown that Gram-negative bacteria are the predominant cause of BSI in the last few years [4]. However, the epidemiology of BSI-causing pathogens varies by geographic area [3]. Early administration of appropriate antibiotics is critical in the management of infections. Although the use of antimicrobial agents has significantly reduced patient mortality, it has also led to the emergence of multidrug-resistant (MDR) bacteria [5].

Local data on BSI among patients with HMs remains limited in Indonesia. Given the geographic variation in microbial profiles and antibiotic resistance patterns, institution-specific data are crucial to inform clinical decision-making and antimicrobial stewardship.

Therefore, this study aims to describe clinical characteristics and pathogen distribution of HM patients with BSI at Dr. Soetomo General Hospital in 2023, providing updated evidence to support improved prevention and management of BSI in this high-risk patient population.

METHODS

This study used a descriptive method and a retrospective design. Secondary data were collected from the medical records of patients with HMs at Dr. Soetomo General Hospital, Surabaya, Indonesia, between January and December 2023.

This study had received ethical clearance from the Ethics Committee of Dr. Soetomo General Hospital, Surabaya. Using a total sampling technique, 129 eligible patients were identified based on the inclusion criteria. The variables assessed in this study included: patient age and sex, HM type, hematologic profile: hemoglobin, platelet count, and absolute neutrophil count (ANC), chemotherapy exposure and regimen, bloodstream infection pathogen, and antibiotic susceptibility patterns. The collected data were analyzed descriptively.

RESULTS

During January - December of 2023, a total of 2,605 patients with HMs were registered at Dr. Soetomo General Hospital, Surabaya. Out of 2,605 patients, 749 patients had microbiological laboratory data.

After removing duplicate medical records (n=273), 476 patients remained, among whom 393 had blood culture done. The results showed that 258 patients had negative results. After applying the inclusion and exclusion criteria, 135 patients were eligible. Potential skin contaminant isolates were reassessed using the criteria of present clinical infection signs, which include: fever of ≥38°Ç dyspnea (respiratory rate of >20 breaths/min), decreased consciousness (Glasgow Coma Scale <15), and signs of shock (systolic blood pressure ≤90 mmHg; capillary refill time >2 seconds; cold, clammy, and pale extremities) [6, 7]. There were 46 isolates considered potential contaminants. From 46, 40 isolates were classified as probable bloodstream infection, while 6 isolates without clinical infection signs were excluded (Table 1). Following this evaluation, the final analytic cohort consisted of 129 patients with BSI.

TABLE 1: Classification of Potential Contaminant Isolates.

Isolates	Contaminants (n)	Probable BSI (n)	Total (n)
Aerococcus viridans	0	1	1
Bacillus cereus	0	1	1
Bacillus spp	0	3	3
Bacillus subtilis	1	0	1
Corynebacterium jeikeium	0	1	1
Corynebacterium matruchotii	0	1	1
Corynebacterium pseudodiphtericum	0	1	1
Corynebacterium species	1	0	1
Micrococcus luteus	0	1	1
Staphylococcus epidermidis	1	18	19
Staphylococcus gallolyticus ssp pasteurianus/infantarius	0	1	1
Staphylococcus haemolyticus	2	3	5
Staphylococcus hominis	0	4	4
Staphylococcus schleiferi	1	0	1
Staphylococcus warneri	0	1	1
Streptococcus constellatus	0	1	1
Streptococcus mitis	0	2	2

Clinical Characteristics of HM Patients with BSI

A total of 129 patients with hematologic malignancies and positive blood cultures were included in the analysis. The majority of the patients were male (53.49%), and the largest proportion of patients were in the 19-59 years age group (28.68%), followed by children aged <5 years (26.36%) (Table 2).

TABLE 2: Age Distribution of Hematologic Malignancy Patients with BSI.

Age Group	Number of Patients (n)	Percentage (%)
<5 years	34	26.36
5-9 years	21	16.28
10-18 years	26	20.16
19-59 years	37	28.68
≥60 years	11	8.53
Total	**129**	**100**

Regarding underlying malignancy, acute lymphocytic leukemia (ALL) was the most common diagnosis among the patients, accounting for 49.61% of cases. Followed by non-Hodgkin's lymphoma (18.60%) and acute myeloid leukemia (16.28%).

TABLE 3: Distribution of Hematologic Malignancy Types Among Patients with BSI.

Type of Hematologic Malignancy	Number of Patients (n)	Percentage (%)
Acute Lymphocytic Leukemia	64	49.61
Acute Myeloid Leukemia	21	16.28
Chronic Lymphocytic Leukemia	2	1.55
Chronic Myeloid Leukemia	4	5.43
Non-Hodgkin's Lymphoma	24	18.60
Hodgkin's Lymphoma	3	2.33
Multiple Myeloma	8	6.20
Total	**129**	**100**

Hematologic Profile of HM Patients with BSI

The hematologic profile showed that most of the patients experienced hematologic abnormalities. Anemia was observed in 78.29% of patients (Table 3), thrombocytopenia in 76.74% (Table 4), and neutropenia in 47.29% based on absolute neutrophil count (ANC) (Table 5).

TABLE 4: Hemoglobin Levels Among Hematologic Malignancy Patients with BSI.

Hemoglobin Level	Number of Patients (n)	Percentage (%)
Anemia	101	78.29
Normal	27	20.93
Polycythemia	1	0.78
Total	**129**	**100**

TABLE 5: Platelet Count Of Hematologic Malignancy Patients with BSI.

Platelet Count	Number of Patients (n)	Percentage (%)
Thrombocytopenia	99	76.74
Normal	26	20.16
Thrombocytosis	4	3.10
Total	**129**	**100**

TABLE 6: Absolute Neutrophil Count Profile Of Hematologic Malignancy Patients with BSI.

Absolute Neutrophil Count	Number of Patients (n)	Percentage (%)
Neutropenia	61	47.29
Normal	33	25.28
Neutrophilia	35	27.13
Total	**129**	**100**

Chemotherapy Exposure Among HM Patients with BSI

Based on therapy modalities, more than half of the patients (59.69%) had gone through chemotherapy at the time of BSI, whereas 39.53% had not yet received any cancer therapy (Table 7). Patients with ALL made up the largest proportion of patients who received chemotherapy (Table 8).

TABLE 7: Types Of Therapy In Hematologic Malignancy Patients with BSI.

Types of Therapy	Number of Patients (n)	Percentage (%)
Chemotherapy	77	59.69
Chemotherapy and Radiotherapy	1	0.78
Not Yet Receiving Therapy	51	39.53
Total	**129**	**100**

TABLE 8: Distribution of Therapy Types In HM Patients with BSI Based on Type of Malignancy.

Type of Hematologic Malignancy	Chemotherapy (n)	Chemotherapy and Radiotherapy (n)	Not Yet Receiving Therapy (n)	Total (n)
Acute Lymphocytic Leukemia	46	0	18	64
Acute Myeloid Leukemia	8	0	13	21
Chronic Lymphocytic Leukemia	0	0	2	2
Chronic Myeloid Leukemia	7	0	0	7
Non-Hodgkin's Lymphoma	2	1	0	3
Hodgkin's Lymphoma	10	0	14	24
Multiple Myeloma	4	0	4	8
Total	**77**	**1**	**51**	**129**

A total of 151 chemotherapy agent uses were recorded. The most frequently used agent classes were antimetabolites (31.79%) and anti-tubulin agents (31.13%) (Table 9). Among 49 patients receiving combination chemotherapy, two-agent regimens were most common. The most frequent combination was DNA-interactive agents with anti-tubulin agents (24.49%) (Table 10).

TABLE 9: Chemotherapy Agents Used in Hematologic Malignancy Patients with BSI.

Chemotherapy Agents	Number of Uses (n)	Percentage (%)
DNA-interactive agents	33	21.85
Antimetabolite agents	48	31.79
Anti-tubulin agents	47	31.13
Monoclonal antibody agents	3	1.99
Tyrosine kinase inhibitors	4	2.65
Enzymatic agents	16	10.60
Total	**151**	**100**

TABLE 10: Distribution of Combination Chemotherapy Agents Use in Hematologic Malignancy Patients with BSI.

Number of Chemotherapy Agents (n)	Combination of Chemotherapy Agents	Number of Uses (n)	Percentage (%)
2	Antimetabolite agents, anti-tubulin agents	7	14.29
2	Antimetabolite agents, tyrosine kinase inhibitors	2	4.08
2	DNA-interactive agents, antimetabolite agents	5	10.20
2	DNA-interactive agents, enzymatic agents	1	2.04
2	DNA-interactive agents, anti-tubulin agents	12	24.49
2	Anti-tubulin agents, enzymatic agents	4	8.16
3	Antimetabolite agents, anti-tubulin agents, enzymatic agents	3	6.12
3	DNA-interactive agents, antimetabolite agents, anti-tubulin agents	6	12.24
3	DNA-interactive agents, anti-tubulin agents, monoclonal antibody agents	3	6.12
4	DNA-interactive agents, antimetabolite agents, anti-tubulin agents, enzymatic agents	6	12.24
Total		**49**	**100**

Microbiological Profile of BSIs

Data from the blood cultures identified a total of 142 isolates from 129 patients, reflecting the presence of polymicrobial infections in some cases. The predominant pathogens were Gram-positive bacteria (57.04%), followed by Gram-negative bacteria (41.55%) and fungi (1.41%) (Table 11).

At the species level, the most frequent pathogens were Staphylococcus aureus (14.08%), Staphylococcus epidermidis (12.68%), and Pseudomonas aeruginosa (9.15%) (Table 12). Most of the infections were monomicrobial (91.47%), while 6.98% and 1.55% of patients had two and three pathogens, respectively (Table 13).

TABLE 11: Distribution of BSI-Causing Pathogen Types in Patients with Hematologic Malignancies.

Types of Pathogens	Number of Isolates (n)	Percentage (%)
Gram-Positive Bacteria	81	57.04
Gram-Negative Bacteria	59	41.55
Fungi	2	1.41
Total	**142**	**100**

TABLE 12: Distribution of BSI-Causing Pathogens in Patients with Hematologic Malignancies.

Types of Pathogens Causing BSI	Genus/Species of Pathogens Causing Bloodstream Infections	Number of Isolates (n)	Percentage (%)
Bacteria		140	98.59
Gram-Positive		81	57.04
	Bacillus spp	3	2.11
	Bacillus cereus	1	0.70
	Corynebacterium matruchotii	1	0.70
	Corynebacterium jeikeium	1	0.70
	Corynebacterium pseudodiphtericum	1	0.70
	Aerococcus viridans	1	0.70
	Streptococcus constellatus	1	0.70
	Streptococcus mitis	2	1.41
	Streptococcus pneumoniae	1	0.70
	Streptococcus porcinus	1	0.70
	Staphylococcus aureus	20	14.08
	*Methicillin-Resistant Staphylococcus aureus (*MRSA*)*	6	4.23
	Staphylococcus epidermidis	18	12.68
	Staphylococcus equorum	1	0.70
	Staphylococcus gallolyticus ssp pasteurianus/infantarius	1	0.70
	Staphylococcus haemolyticus	3	2.11
	Staphylococcus hominis	4	2.82
	Staphylococcus coagulase negative	7	4.93
	Staphylococcus warneri	1	0.70
	Enterococcus faecalis	3	2.11
	Micrococcus luteus	1	0.70
	Streptococcus dysgalactiae ssp dysgalactiae	2	1.41
	Streptococcus pyogenes	1	0.70
Gram-Negative		59	41.55
	Acinetobacter baumanii	1	0.70%
	Aeromonas veronii bv sobria	2	1.41%
	Klebsiella pneumoniae	3	2.11%
	Klebsiella pneumoniae ESBL	5	3.52%
	Klebsiella ozaenae	1	0.70%
	Enterobacter cloacae	2	1.41%
	Escherichia coli	9	6.34%
	Escherichia coli CRE	2	1.41%
	Escherichia coli ESBL	5	3.52%
	Pseudomonas aeruginosa	13	9.15%

	Pseudomonas aeruginosa MDRO	1	0.70%
	Pseudomonas putida	2	1.41%
	Salmonella enterica	1	0.70%
	Salmonella enterica ssp enterica sv typhi	1	0.70%
	Salmonella species	7	4.93%
	Proteus mirabilis	2	1.41%
	Moraxella species	1	0.70%
	Moraxella catharhalis	1	0.70%
Fungi		2	1.41%
	Candida tropicalis	1	0.70%
	Candida albicans	1	0.70%

TABLE 13: Distribution of Patients by Number of Pathogen Types Causing Infection.

Number of Pathogens Causing Infection	Number of Patients (n)	Percentage (%)
1	118	91.47
2	9	6.98
3	2	1.55
Total	**129**	**100**

Antibiotic susceptibility testing was analyzed for pathogens with ≥ 5 isolates. Interpretation of these findings is limited by the small number of isolates analyzed. Among Gram-negative bacteria, E. coli demonstrated high susceptibility to aminoglycosides and carbapenems but low susceptibility to ampicillin and trimethoprim–sulfamethoxazole. ESBL-producing E. coli and Klebsiella pneumoniae showed low susceptibility to β- β-lactams and cephalosporins, with preserved susceptibility to amikacin and carbapenems. Pseudomonas aeruginosa exhibited the highest susceptibility to amikacin, meropenem, and cefoperazone–sulbactam.

Salmonella species were susceptible to most tested antibiotics, except aminoglycosides and tigecycline (Table 14). Among Gram-positive bacteria, MRSA isolates showed high susceptibility to linezolid and vancomycin, with low susceptibility to β-lactam antibiotics. Non-MRSA S. aureus demonstrated higher overall susceptibility, including to oxacillin and cefoxitin. Coagulase-negative staphylococci showed variable susceptibility but retained high susceptibility to linezolid and vancomycin. Staphylococcus epidermidis exhibited high resistance to penicillin G and ampicillin, with better susceptibility to fosfomycin and linezolid (Table 15)

TABLE 14: Antibiotic Sensitivity Testing of Gram-Negative Bacterial Pathogens.

Isolates	Note	AMK	AMC	AMP	SAM	ATM	CFZ	FEP	CSL	CTX	FOX	CAZ	CRO	CHL	CIP	GM	IPM	LVX	MEM	Mfx	TZP	TET	TGC	SXT
Escherichia coli	N Susceptible	9	9	3	5	9	9	7	9	9	7	9	8	9		9	8	8	9	9	9	6	6	4
	N Tested	9	9	9	9	9	9	9	9	9	9	9	8	9		9	9	8	9	9	9	9	8	8
	% Susceptible	100	100	33	56	100	100	78	100	100	78	100	100	100		100	89	100	100	100	100	67	75	50
Escherichia coli ESBL	N Susceptible	5	2	0	0	0	0	0		0		0		3		2	5		5	1	0	2		4
	N Tested	5	5	5	5	5	5	5		5		5		5		5	5		5	5	5	5		5
	% Susceptible	100	40	0	0	0	0	0		0		0		60		40	100		100	20	0	40		80
Klebsiella pneumoniae ESBL	N Susceptible	5	1	0	0	1	0	0	3	2		1	1	3		0	4	3	4	4	0	2	1	0
	N Tested	5	5	5	5	5	5	5	5	5		5	5	5		5	5	5	5	5	5	5	5	5
	% Susceptible	100	20	0	0	20	0	0	60	40		20	20	60		0	80	60	80	80	0	40	20	0
Pseudomonas aeruginosa	N Susceptible	12	0	0	0	7	0	10	10	0	0	8	1	0	10	9	10	9	13		10	0	0	0
	N Tested	12	13	13	13	13	13	13	11	13	8	13	13	13	13	12	13	12	13		13	13	12	13
	% Susceptible	100	0	0	0	54	0	77	91	0	0	62	8	0	77	75	77	75	100		77	0	0	0
Salmonella species	N Susceptible	0	6	3	3	6	0	6	6	6	6	6	6	7		0	6	6	6	6	7	6	2	6
	N Tested	7	7	7	7	7	7	7	7	7	6	7	7	7		7	7	7	7	7	7	7	7	6
	% Susceptible	0	86	43	43	86	0	86	86	86	100	86	86	100		0	86	86	86	86	100	86	29	100

*AMK=Amikacin; AMC=Amoxicillin-Clavulanate; AMP=Ampicillin; SAM=Ampicillin-Sulbactam; ATM=Aztreonam; CFZ=Cefazolin; FEP=Cefepime; CSL=Cefoperazone-Sulbactam; CTX=Cefotaxime; FOX=Cefoxitin, CAZ=Ceftazidime; CRO=Ceftriaxone; CHL=Chloramphenicol; CIP=Ciprofloxacin; GM=Gentamicin; IPM=Imipenem; LVX=Levofloxacin; MEM=Meropenem; Mfx=Moxifloxacin; TZP=Piperacillin-Tazobactam; TET=Tetracycline; TGC=Tigecycline; SXT=Trimethoprim-Sulfamethoxazole.

TABLE 15: Antibiotic Sensitivity Testing of Gram-Positive Bacterial Pathogens.

Isolates	Note	AMC	AMP	FOX	CRO	CXM	CHL	CIP	CLI	ERY	FOT	GM	LVX	LZD	OX	PenG	RIF	TEI	TET	SXT	VAN
Methicillin-Resistant Staphylococcus aureus	N Susceptible	0	0		0		5	1	5	5		4	1	6	0	0	5		1	4	5
	N Tested	5	6		6		6	6	6	6		6	6	6	6	6	5		5	6	6
	% Susceptible	0	0		0		83	17	83	83		67	17	100	0	0	100		20	67	83
Staphylococcus aureus	N Susceptible	9	0	17	17		15	18	18	20		19	13	20	20	1	16	10	14	17	18
	N Tested	10	18	17	17		17	20	20	20		20	16	20	20	19	16	10	20	19	20
	% Susceptible	90	0	100	100		88	90	90	100		95	81	100	100	5	100	100	70	89	90
Staphylococcus coagulase-negative	N Susceptible			2			4	3	0	2		3	2	6	2				5		6
	N Tested			7			6	7	6	7		7	5	6	7				7		7
	% Susceptible			29			67	43	0	29		43	40	100	29				71		86
Staphylococcus epidermidis	N Susceptible	2	0	3	2		10	8	4	2	6	11	9	13	3	0	8	4	7	5	9
	N Tested	9	17	12	11		17	17	15	17	6	17	17	17	17	17	15	6	16	17	17
	% Susceptible	22	0	25	18		59	47	27	12	100	65	53	76	18	0	53	67	44	29	53

*AMC=Amoxicillin-Clavulanate; AMP=Ampicillin; FOX=Cefoxitin; CRO=Ceftriaxone; CXM=Cefuroxime; CHL=Chloramphenicol; CIP=Ciprofloxacin; CLI=Clindamycin; ERY=Erythromycin; FOT=Fosfomycin; GM=Gentamicin; LVX=Levofloxacin; LZD=Linezolid; OX=Oxacillin; PenG=Penicillin G; RIF=Rifampin; TEI=Teicoplanin; TET=Tetracycline; SXT=Trimethoprim- Sulfamethoxazole; VAN=Vancomycin.

DISCUSSION

Clinical Characteristics of HM Patients with BSI

Patient characteristics showed the majority were male and within the age range of 19-59 years old, similar to the demographic profiles in prior studies that report a dominance of young to middle-aged adults and males in the population of patients with HM [8, 9]. The high proportion of BSI cases in this age group could be associated with immunity factors and the presence of comorbidities, which could contribute to susceptibility to infections [9]. This number also reflects the burden of HMs among working-age adults.

Other studies have highlighted the sex-related differences in infection susceptibility. According to Zhang et al. (2025), there is growing evidence that males are more prone to infection than females. This is possibly due to estrogen having a role in inhibiting certain microbial virulence factors. Social factors may also contribute, as hygiene practices are generally poorer among males, increasing their risk of infection [10]. Khateb et al. (2025) also suggested that the higher incidence of BSIs in males may be partly explained by differences in the immune function of the two sexes, with females generally exhibiting stronger immunoreactivity. One of the proposed explanations is the immunological role of the X chromosome. However, these differences are multifactorial and call for further research to clarify the relative contributions of biological and social determinants [9].

Based on HM type, this study found that a total of 64 patients (49.61%) had a diagnosis of acute lymphocytic leukemia (ALL). The higher BSI incidence among ALL patients can be explained by several pathophysiological mechanisms. In acute leukemia, abnormal blast cells proliferate and replace normal hematopoietic cells in the bone marrow, impairing normal hematopoiesis and resulting in neutropenia, anemia, and thrombocytopenia. Severe neutropenia is a well-established risk factor for infections. Additionally, ALL patients typically go through intensive chemotherapy, which carries the risk of profound myelosuppression and gastrointestinal mucosal damage, increasing the risk of microbial translocation into the bloodstream [11]. These effects collectively increase the risk of infection. Prior research also showed that infections are the most common adverse event in ALL patients and remain a leading cause of death, especially during induction therapy [12]. Overall, these findings emphasize that patients with ALL are at elevated risk for BSIs, highlighting the need for strengthened infection prevention strategies and monitoring throughout the course of their treatment.

Hematologic profile of HM Patients with BSI

Hematologic profile in this study includes hemoglobin, platelet count, and absolute neutrophil count (ANC). The results demonstrated the high degree of immunosuppression in this demographic. Anemia, thrombocytopenia, and neutropenia were prevalent, consistent with the known complications of marrow infiltration by cancer cells and chemotherapy-induced myelosuppression. Anemia in patients with HMs is a multifactorial condition resulting from marrow infiltration and chronic inflammation driven by the increase of pro-inflammatory cytokines such as IL-6 and TNF-α. These cytokines stimulate the production of hepcidin, which then inhibits the absorption of iron in the intestines and the release of iron from macrophages, resulting in anemia of chronic disease. The myelosuppressive effect of chemotherapy contributes by damaging hematopoietic progenitor cells in the bone marrow, leading to decreased erythrocyte production [13].

The high prevalence of thrombocytopenia observed in this study is consistent with previous research reporting that thrombocytopenia occurred in 43.2% of patients with nosocomial BSIs and was associated with increased mortality in intensive care unit (ICU) settings. Although that study was conducted in an ICU population, the underlying mechanisms of thrombocytopenia are comparable, involving impaired bone marrow production, increased peripheral consumption due to coagulation activation, and immune-mediated platelet destruction during systemic infection [14]. In patients with HMs, thrombocytopenia may develop as a complication of infection progressing to sepsis. The immune response in sepsis leads to the release of inflammatory mediators such as IL-6, IL-8, and TNF-α, which promote platelet activation and aggregation, thereby increasing peripheral consumption. Moreover, excessive activation of the coagulation system may result in disseminated intravascular coagulation (DIC), further accelerating platelet destruction [14, 15].

In addition to infection-related mechanisms, thrombocytopenia in patients with HMs may also arise from disease progression and treatment-related factors. Bone marrow infiltration by malignant cells and cytotoxic effects of chemotherapy can directly suppress platelet production, contributing to thrombocytopenia independent of infection [16]. Therefore, the high rate of thrombocytopenia observed in this study likely reflects a combination of direct effects of the underlying HM and the host response to severe infection. Nevertheless, studies specifically evaluating the relationship between thrombocytopenia and bloodstream infections in patients with hematologic malignancies remain limited, highlighting the need for further investigation.

In this study, neutropenia was classified without stratification by severity due to differences in normal reference ranges between pediatric and adult populations. This approach ensured analytical consistency and minimized age-related laboratory bias. Previous studies have shown that up to 93.2% of hematologic malignancy patients with BSIs experience severe neutropenia (ANC <500/μL), identifying neutropenia as the most common risk factor for BSI, with the risk of infection increasing

with both the severity and duration of neutropenia [17].

Neutropenia represents a major risk factor for infection due to the central role of neutrophils in innate immunity, including chemotaxis, phagocytosis, degranulation, reactive oxygen species production, formation of neutrophil extracellular traps, and immune regulation [2,18]. Quantitative or functional impairment of neutrophils predisposes patients to recurrent and severe infections, particularly when neutropenia persists for more than one week [8, 19].

In patients with HMs, neutropenia results from overlapping mechanisms. Bone marrow infiltration by malignant cells disrupts hematopoiesis and impairs neutrophil maturation, leading to reduced peripheral counts even prior to chemotherapy. Immune-mediated peripheral destruction, splenic sequestration, chronic infection, nutritional deficiencies, and drug-related toxicity also contribute. Furthermore, chemotherapy-induced neutropenia remains a common complication of cytotoxic therapy, as these agents suppress dividing progenitor cells in the bone marrow, resulting in decreased neutrophil production [19, 20]. The high proportion of patients with concurrent cytopenia highlights their vulnerability to invasive pathogens and BSIs.

Chemotherapy Exposure and Treatment-Related Factors

This study found that chemotherapy exposure was present in 59.26% of patients. Most treatment-naïve patients in this study were newly diagnosed with HMs or presented for the first time to the emergency department in severe clinical condition or with complications. As a result, chemotherapy had not yet been initiated because patients were not clinically stable enough, and some patients experienced further deterioration during stabilization and did not proceed to chemotherapy. These findings suggest that BSIs may occur as an initial manifestation or as a pre-treatment complication in severely ill patients with HMs. This study's results are supported by a study by Zimmer et al. (2022), which reported 68% of patients with BSIs preceded by febrile neutropenia had received chemotherapy without transplantation [21]. Chemotherapy-induced neutropenia remains the most common risk factor for BSIs in this population [17].

Chemotherapy remained the most common treatment modality. ALL patients accounted for the highest proportion of patients receiving chemotherapy, followed by non-Hodgkin lymphoma (NHL) and acute myeloid leukemia (AML), while many untreated patients also belonged to the ALL and NHL groups. These findings are consistent with previous studies showing that chemotherapy-induced neutropenia is the most important risk factor for bloodstream infections in patients with HMs [17, 21, 22]. Although ALL has not consistently been reported as the predominant subgroup in prior literature, the high proportion observed in this study warrants further investigation. The increased risk of BSIs during chemotherapy can be attributed to chemotherapy-induced myelosuppression, resulting in neutropenia, anemia, and thrombocytopenia, as well as gastrointestinal mucosal injury that facilitates bacterial translocation into the bloodstream [23].

The most frequently used drug class was antimetabolite agents. These findings are consistent with a previous study by Rusu et al. (2018), which reported that cytarabine, an antimetabolite agent, was associated with the highest incidence of infection among 463 patients with HMs [24]. In this study, the antimetabolite agents used included cytarabine, methotrexate, hydroxyurea, and 6-mercaptopurine. Antimetabolites act by inhibiting essential metabolic pathways involved in DNA and RNA synthesis, thereby disrupting cancer cell replication and inducing apoptosis. A major adverse effect of this drug class is myelosuppression [25]. Myelosuppression results in reduced blood cell production, leading to neutropenia, anemia, and thrombocytopenia, with neutropenia being a key factor increasing susceptibility to infection [3].

The onset and duration of neutropenia vary depending on the chemotherapeutic agent and regimen intensity, with more intensive regimens causing more severe and prolonged neutropenia [26]. Accordingly, the high proportion of antimetabolite use in this study may represent an important predisposing factor for bloodstream infections through chemotherapy-induced neutropenia.

Regarding the use of combinations of chemotherapy agents, this study found that two-agent combination chemotherapy was the most commonly used regimen among HM patients with BSI, particularly combinations of DNA-interactive and anti-tubulin agents (24.49%). Most patients in this cohort were diagnosed with ALL (49.61%) or NHL (18.60%), consistent with standard treatment protocols such as CHOP for lymphoma and daunorubicin–cytarabine–based regimens for acute leukemia [27, 28].

Furthermore, survivors of diffuse large B-cell lymphoma treated with R-CHOP have a 1.5-fold increased risk of infection, particularly within the first two years after therapy, likely due to persistent immunosuppression, including neutropenia and hypogammaglobulinemia [29]. Overall, these findings highlight the need for close hematologic monitoring, early detection of neutropenia, and effective infection prevention strategies in patients receiving intensive chemotherapy.

Microbiological Profile of BSIs

The microbiological profile of BSIs in this study was characterized by a predominance of Gram-positive bacteria, with Staphylococcus aureus as the most frequently isolated pathogen. There is variation in previous studies regarding the etiology of BSIs. However, this finding is consistent with some reports from other studies, where Gram-positive

bacteria remain the leading causes of BSI [30, 31]. The dominance of these pathogens is commonly attributed to skin flora colonization and the frequent use of invasive devices, such as central venous catheters, which serve as major portals of entry in immunocompromised patients [30,32]. The identification of Staphylococcus epidermidis further supports the role of device-associated and healthcare-related infections in this population.

With respect to infection patterns, the majority of BSIs in this study were monomicrobial, while polymicrobial infections were relatively uncommon. These findings are consistent with previous studies reporting that most bloodstream infection episodes in patients with HMs are monomicrobial, while polymicrobial infections occur in only a small proportion of cases (13.2%). This suggests that BSIs in patients with HMs generally originate from a single primary source [23]. Infections caused by more than one pathogen generally require specific predisposing conditions, such as severe immunosuppression, the use of invasive devices, or the presence of secondary infection. Facchin et al. (2022) reported that most patients with polymicrobial infections had severe neutropenia (89%) and nearly all had central venous catheter use (97%). In addition, prolonged neutropenia and the presence of infection foci in other organs, such as the lungs or abdomen, also act as predisposing factors [30].

Antibiotic susceptibility testing revealed the presence of clinically significant resistant organisms, including ESBL-producing E. coli and K. pneumoniae, as well as multidrug-resistant Pseudomonas aeruginosa. These findings are of particular concern, as antimicrobial resistance has been shown to adversely affect treatment outcomes in HM patients with BSI. Previous studies have demonstrated that inappropriate initial empirical therapy significantly increases mortality in this population [4], emphasizing the critical role of local antimicrobial susceptibility data in guiding empirical treatment decisions. The resistance patterns observed in this study highlight the importance of continuous microbiological surveillance and robust antimicrobial stewardship programs to optimize empirical therapy while minimizing the development of further resistance. Overall, the microbiological findings of this study illustrate a complex pathogen landscape shaped by host immunosuppression, healthcare exposure, and antimicrobial pressure. These results reinforce the need for institution-specific infection prevention strategies, careful management of invasive devices, and the routine integration of local pathogen and resistance data into empirical treatment guidelines for bloodstream infections in patients with HMs.

CONCLUSION

This study demonstrates that BSIs among patients with HMs at Dr. Soetomo General Hospital Surabaya in 2023 mainly affected adults aged 19-59 years, were more frequent in males, and were most commonly associated with ALL. The majority of patients displayed hematologic abnormalities, including anemia, thrombocytopenia, and neutropenia, reflecting their high degree of immunosuppression. Microbiologically, most BSIs were monomicrobial and primarily caused by Gram-positive bacteria, particularly Staphylococcus aureus, although Gram-negative bacteria and MDR organisms were also detected.

The results of this study emphasize the importance of targeted strategies for infection prevention and the use of institution-specific pathogen and antimicrobial resistance data to guide empirical therapy for BSIs. Future studies incorporating clinical outcomes and risk factor analysis are warranted to improve infection control and management strategies in patients with HMs.

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Conflict Of Interest

The authors declare no conflicts of interest related to this study.

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