

## Microbial and Antimicrobial Susceptibility Profile of Pediatric Hematological Malignancy Patients at a Tertiary Hospital

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### Abstract

Neutropenia is a major predisposing factor for infection in pediatric patients with hematological malignancies. In Indonesia, data on microbial patterns and antibiotic resistance in this group remain limited, highlighting the need for local data to guide empirical therapy. This study aimed to determine the microbial and antibiotic susceptibility profile of pediatric patients with hematological malignancies. A cross-sectional descriptive study was conducted in the pediatric ward of Dr. Hasan Sadikin General Hospital, Bandung, from April to June 2024. Data were collected retrospectively using total sampling from medical records and registers of patients diagnosed with hematological malignancies (subgroups I and II) between January 2021 and December 2022. Microbial identification and antibiotic susceptibility profiles were performed using an automated colorimetry method. A total of 33 bacterial isolates were identified, with Gram-negative bacteria being the most frequent (75.8%). The predominant isolates were *Escherichia coli* (39.4%), *Klebsiella pneumoniae* (15.15%), and *Staphylococcus hominis* (12.1%). From all isolates, 69.7% were multidrug-resistant organisms (MDROs). About 62.5% of Gram-positive bacteria were methicillin-resistant coagulase-negative Staphylococci (MRCoNS), while 48% and 24% of Gram-negative bacteria were extended-spectrum  $\beta$ -lactamase (ESBL) and carbapenem-resistant, respectively. Gram-positive bacteria showed 100% sensitivity to Linezolid, Tigecycline, and Vancomycin, while Gram-negative bacteria showed the highest sensitivity to Amikacin. *Escherichia coli*, as the most frequent isolate, showed 100% sensitivity to Tigecycline. In conclusion, Gram-negative bacteria were the predominant organisms, with *Escherichia coli* being the most common isolate. The antibiotic susceptibility test showed a high proportion of MDROs and decreased susceptibility levels in 2022 compared to 2021.

**Keywords:** Antimicrobial susceptibility, hematological malignancy, microbial profile, pediatric

### Introduction

Malignancy is one of the focus topics for non-communicable diseases in Indonesia. According to the World Health Organization (WHO) malignancy profile published in 2020, 7,574 cases of childhood malignancy were reported nationwide, with acute lymphoblastic leukemia as the most common type, followed by Hodgkin lymphoma, Wilms tumor, central nervous system low-grade tumors, retinoblastoma, and

Burkitt lymphoma.<sup>1</sup> Malignancy remains one of the leading causes of mortality in children. Infections represent a major source of morbidity and mortality, particularly among pediatric patients with hematological malignancies such as acute leukemia. The administration of intensive combination chemotherapy induces immunosuppression, resulting in an increased incidence of infectious complications.<sup>2</sup> This weakened immunity is characterized by fewer specific components of white blood cells, particularly neutrophils, a condition known as neutropenia. Neutropenia is the primary predisposing factor for infections in patients with hematological malignancies. This condition may occur with or without fever, and febrile

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neutropenia is considered an oncological emergency.<sup>3,4</sup>

The management of neutropenia includes risk assessment, diagnostic evaluation, and initiation of antibiotic treatment. Antibiotics are selected based on local microbial patterns and antibiotic susceptibility within the healthcare institution and will be adjusted according to culture results.<sup>3,5</sup> In most cases, cultures of neutropenic patients with malignancies are negative; hence, treatment is continued based on the microbial patterns and antibiotic susceptibility at the healthcare institution.

International and national data describing microbial patterns and antibiotic susceptibility among pediatrics patients with hematological malignancies in Indonesia remain limited, particularly at Dr. Hasan Sadikin General Hospital, Bandung, remain limited. The absence of updated, institution-specific data may compromise optimal empirical antibiotic selection. The novelty of this study lies in the provision of recent local data on microbial profiles and antibiotic susceptibility patterns specific to pediatric patients with hematological malignancies in a tertiary referral center in Indonesia. Therefore, this study aimed to determine the microbial pattern and antibiotic susceptibility among pediatric patients with hematological malignancies at Dr. Hasan Sadikin General Hospital, Bandung.

## Methods

This is a descriptive study with a cross-sectional method conducted at Dr. Hasan Sadikin General Hospital, Bandung, from April to June 2024. Approval was received from the Health Research Ethics Committee of Universitas Padjadjaran (No. 456/UN6.KEP/EC/202).

The study population comprised pediatric patients registered in the database from January 1, 2021, to December 31, 2022, with a diagnosis of hematological malignancy. Diagnoses were classified into diagnostic subgroup I, including leukemia, myeloproliferative disorders, myelodysplastic syndromes, and diagnostic subgroup II, including lymphoma and reticuloendothelial neoplasms. Data were collected from the registry data and medical records using a total sampling method retrospectively. The inclusion criteria for this study were patients undergoing chemotherapy, had neutropenia defined as an absolute neutrophil count  $<500/\text{mm}^3$ , underwent

a culture testing, and received antibiotic susceptibility testing. Exclusion criteria include inaccessible data, incomplete data, and culture results indicating fungal infection.

Collected variables included sex, age, hematological malignancy, and hematological laboratory parameters, including leukocyte count, hemoglobin level, and platelet count. Laboratory values were categorized as increased, normal, or decreased based on normal values for pediatrics. Normal leukocyte ranges were defined as 0–30 days ( $9.100\text{--}34.000/\text{mm}^3$ ), 1–23 months ( $6.000\text{--}1.000/\text{mm}^3$ ), 2–9 years ( $4.000\text{--}12.000/\text{mm}^3$ ), and 10–17 years ( $4.000\text{--}10.500/\text{mm}^3$ ). Normal range of hemoglobin is as follows; 0–30 days ( $15\text{--}25\text{g/dL}$ ), 1–23 months ( $10.5\text{--}14\text{g/dL}$ ), 2–9 years ( $11.5\text{--}14.5\text{g/dL}$ ), 10–17 years, females ( $12.5\text{--}15\text{g/dL}$ ) and males ( $12.5\text{--}16.1\text{g/dL}$ ). Finally, the normal range of platelet number is between  $150\text{--}400 \times 10^9/\text{L}$ .<sup>6,7</sup>

Bacterial identification and antibiotic susceptibility testing (AST) were performed using an automated microbiology analyzer with a colorimetric method (Vitek 2 Compact, Biomerieux, France). Bacterial identification followed WHO and Clinical and Laboratory Standards Institute (CLSI) guidelines. According to the CLSI guidelines, the AST result was validated and interpreted as susceptible, intermediate and resistant.<sup>8</sup> Culture results were categorized into Gram-positive bacteria (GPB) and Gram-negative bacteria (GNB). Meanwhile, the AST results for GPB, GNB, and predominant isolates were reclassified according to WHO AWaRe classification namely Access (Amikacin, Ampicillin, Ampicillin/Sulbactam, Amoxicillin/Clavulanic Acid, Benzylpenicillin, Cefadroxil, Cefazolin, Cephalothin, Chloramphenicol, Ciprofloxacin, Clindamycin, Co-trimoxazole, Gentamicin, Tetracycline), Watch (Cefepime, Cefixime, Cefoperazone, Cefotaxime, Ceftazidime, Ceftriaxone, Cefuroxime, Cephalothin, Ciprofloxacin, Clindamycin, Co-trimoxazole, Ertapenem, Erythromycin, Levofloxacin, Meropenem, Moxifloxacin, Piperacillin/Tazobactam, Vancomycin), and Reserve (Aztreonam, Linezolid, Tigecycline).<sup>9</sup>

Data were collected and processed using Microsoft Excel 2019, with frequency and percentage calculations for each variable presented in the tables and figures.

## Results

During the study period, 294 patients were

**Table 1. Characteristics of Patients Based on Hematological Malignancy and Neutropenia**

Variable	Total		2021		2022	
	n	%	n	%	n	%
Gender						
Male	33	49.3	13	48.1	20	50.0
Female	34	50.7	14	51.9	20	50.0
Age (Years)						
<1	1	1.5	1	3.7	0	0
1–4	30	44.8	9	33.3	21	52.5
5–9	15	22.4	5	18.6	10	25.0
10–14	13	19.4	9	33.3	4	10.0
15–18	8	11.9	3	11.1	5	12.5
Diagnosis of Malignancy						
Acute Lymphoblastic Leukemia	38	56.7	16	59.3	22	55.0
Acute Myeloblastic Leukemia	19	28.3	7	25.9	12	30.0
Burkitt Lymphoma	2	3.0	2	7.4	0	0
Hodgkin Lymphoma	2	3.0	0	0	2	5.0
Non-Hodgkin Lymphoma	3	4.5	1	3.7	2	5.0
Lymphoreticular Neoplasm	2	3.0	0	0	2	5.0
Myelodysplastic Syndrome	1	1.5	1	3.7	0	0
Culture Results						
Positive	21	31.3	11	40.7	10	25.0
Negative	46	68.7	16	59.3	30	75.0

included, only 67 met the inclusion criteria. Patients characteristics, including sex, age, and type of malignancy, are presented in Table 1. Between 2021 and 2022, most of the patients were female (50.7%), belonged to the 1–4 year age group (44.8%), and were diagnosed with acute lymphoblastic leukemia (56.7%).

From culture examinations performed on 67 patients, positive cultures were identified in 21 (31.3%), as shown in Table 2. During 2021–2022, most of the patients were female (57.1%), aged 10–14 years (38.1%), and diagnosed with acute lymphoblastic leukemia (66.7%). Based on the number of bacteria causing infections, three patients experienced infections attributed to more than 1 type of bacteria in 2021, with 2 experiencing a polymicrobial infection comprising 2 types of bacteria. In 2022, 6 patients were infected with more than 1 type of bacteria, with 3 out of 6 experiencing a polymicrobial infection. These polymicrobial infections originated from isolated pathogens of urine (3) and pus (2) specimens.

Hematological parameters, including leukocyte count, hemoglobin level, and platelet count, from 21 patients are presented in Table 3. Laboratory results showed that in 2021, all patients experienced a decrease in leukocyte levels, and in 2022, the majority experienced a reduction to 64.3%. In 2021, all patients experienced a decrease in hemoglobin levels, and in 2022, most had reduced hemoglobin levels of 85.7%. In both 2021 and 2022, all patients had decreased platelet levels.

Based on culture examinations, a total of 33 bacterial isolates were obtained from blood (13 isolates), urine (9 isolates), and pus specimens (11 isolates), as shown in Table 4. During 2021–2022, Gram-negative bacteria were the most frequently found microbes (25 isolates, 75.8%), with *Escherichia coli* being the most common (13 isolates, 29.4%). Meanwhile, *Staphylococcus hominis* was the most frequently found Gram-positive bacteria (4 isolates, 12.1%), while 8 Gram-positive (24.2%) bacteria were identified.

In blood specimens, *Escherichia coli* was the

**Table 2 Characteristics of Patients Based on Bacteria Identification Results**

Variable	Total		2021		2022	
	n	%	n	%	n	%
Gender						
Male	9	42.9	7	63.6	2	20
Female	12	57.1	4	36.4	8	80
Age (years)						
<1	0	0	0	0	0	0
1–4	6	28.6	2	18.2	4	40
5–9	4	19.0	3	27.3	1	10
10–14	8	38.1	5	45.4	3	30
15–18	3	14.3	1	9.1	2	20
Diagnosis of Malignancy						
Acute lymphoblastic leukemia	14	66.7	9	75	5	55.6
Acute myeloblastic leukemia	5	23.8	2	16.7	3	33.3
Burkitt lymphoma	1	4.8	1	8.3	0	0
Lymphoreticular neoplasm	1	4.8	0	0	1	11.1
Total of bacteria						
1 isolate	12	57.1	8	72.7	4	40
>1 isolate	9	42.9	3	27.3	6	60

most frequently found in 2021, whereas in 2022, both *Escherichia coli* and *Staphylococcus homini* were predominant. In urine and pus specimens, *Escherichia coli* was the most frequently isolated organism in both 2021 and 2022.

**Table 3 Characteristics of Patients Based on Hematology Laboratory Results**

Variable	Total		2021		2022	
	n	%	n	%	n	%
Leukosit						
Decreased	22	81.5	13	100	9	64.3
Normal	2	7.4	0	0	2	14.3
Increased	3	11.1	0	0	3	21.4
Hemoglobin						
Decreased	25	92.6	13	100	12	85.7
Normal	2	7.4	0	0	2	14.3
Increased	0	0	0	0	0	0
Trombosit						
Decreased	27	100	13	100	14	100
Normal	0	0	0	0	0	0
Increased	0	0	0	0	0	0

Among 33 bacterial isolates, 23 (69.7%) were identified as multidrug-resistant organisms (MDROs). In the Gram-positive bacteria, 5 isolates (62.5%) were *methicillin-resistant coagulase negative staphylococci* (MRCoNS), consisting of 4 *Staphylococcus hominis* and 1 *Staphylococcus haemolyticus*. Furthermore, 12 isolates (48%) were extended spectrum beta lactamase (ESBL) procedure, including 10 *Escherichia coli* and two *Klebsiella pneumoniae*. In addition, six isolates (24%) were carbapenem-resistant organisms, comprising of 2 *Acinetobacter baumannii*, 1 *Klebsiella pneumoniae*, 2 *Escherichia coli*, and 1 *Providencia rettgeri*.

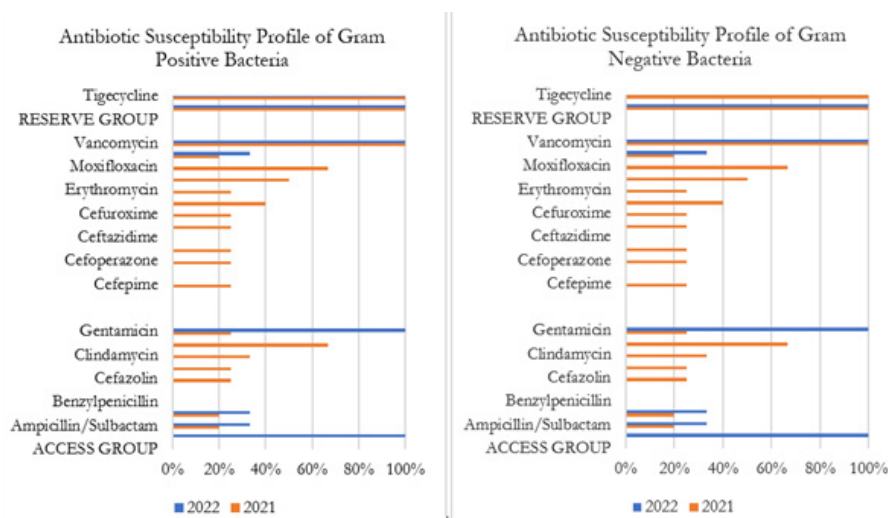
The antibiotic susceptibility profiles of Gram-positive and Gram-negative bacteria are shown in Figure 1. In 2021, Gram-positive bacteria were most susceptible to Linezolid, Tigecycline, and Vancomycin, with 100% susceptibility. In 2022, Ampicillin, Gentamicin, Linezolid, Tigecycline, and Vancomycin were the antibiotics with the highest susceptibility, also at 100%. In 2021, Amikacin, Amoxicillin/Clavulanate Acid, Imipenem, and Tetracycline were the antibiotics with the highest susceptibility, at 100%. In 2022, Tigecycline was the antibiotic with the highest susceptibility, at 85.71%.

**Table 4 Microbial Distribution by Specimen Type and Year**

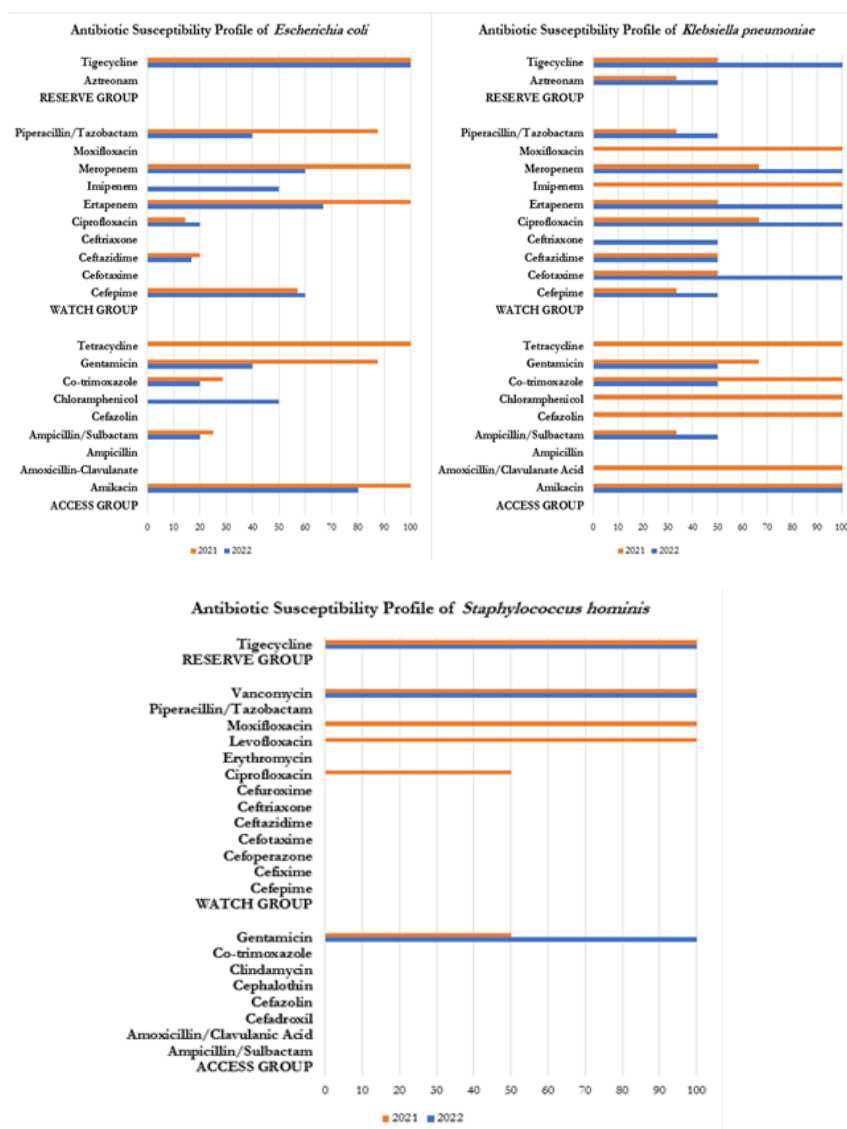
Microbes	Total	Blood n (%)		Urine n (%)		Pus n (%)	
	n (%)	2021	2022	2021	2022	2021	2022
Gram-positive bacteria	8 (24.2)						
<i>Enterococcus faecalis</i>	1 (3.0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)
<i>Enterococcus faecium</i>	1 (3.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.6)	0 (0)
<i>Staphylococcus aureus</i>	1 (3.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.6)	0 (0)
<i>Staphylococcus haemolyticus</i>	1 (3.0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)
<i>Staphylococcus hominis</i>	4 (12.1)	1 (20.0)	3 (37.5)	0 (0)	0 (0)	0 (0)	0 (0)
Gram-negative bacteria	25 (75.8)						
<i>Acinetobacter baumannii</i>	2 (6.1)	1 (20.0)	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)
<i>Acinetobacter lwoffii</i>	1 (3.0)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)
<i>Enterobacter cloacae</i>	1 (3.0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)
<i>Escherichia coli</i>	13 (39.4)	2 (40.0)	3 (37.5)	0 (0)	2 (40.0)	2 (33.3)	4 (80.0)
<i>Klebsiella pneumoniae</i>	5 (15.2)	1 (20.0)	1 (12.5)	0 (0)	1 (20.0)	1 (16.6)	1 (20.0)
<i>Providencia rettgeri</i>	1 (3.0)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)
<i>Pseudomonas aeruginosa</i>	1 (3.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.6)	0 (0)
<i>Pseudomonas putida</i>	1 (3.0)	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	0 (0)

Figure 2 shows the antibiotic susceptibility profile of *Escherichia coli* (n=13), the most frequently isolated bacteria in this study. The results showed that Amikacin, Ertapenem, Meropenem, Tetracycline, and Tigecycline had the highest susceptibility, at 100% in 2021. In 2022, Tigecycline was the antibiotic with the highest susceptibility, at 100%. Antibiotic

susceptibility of *Klebsiella pneumoniae* (n=5), the most frequently isolated Gram-negative bacteria after *Escherichia coli*. The results showed that Amikacin, Amoxicillin/Clavulanate Acid, Aztreonam, Cefazolin, Chloramphenicol, Imipenem, Moxifloxacin, and Tetracycline had 100% susceptibility in 2021. Meanwhile, in 2022, Amikacin, Cefotaxime, Ciprofloxacin,

**Figure 1 Antibiotic Susceptibility Profile of Gram-positive and Gram-negative Bacteria**





**Figure 2 Antibiotic Susceptibility Profile of *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus hominis***

Ertapenem, Meropenem, and Tigecycline had 100% susceptibility. The antibiotic susceptibility of *Staphylococcus hominis* (n=4), the most frequently isolated Gram-positive bacterium, was tested. It was found that Levofloxacin, Moxifloxacin, Tigecycline, and Vancomycin had 100% susceptibility in 2021, while in 2022, Gentamicin, Tigecycline, and Vancomycin had 100% susceptibility.

## Discussion

Infections remain a major cause of mortality and morbidity among patients with hematological

malignancies. Increased susceptibility to infections is related to the decline in immunity, which may result from disease progression and the effects of treatment received.<sup>2</sup> The main predisposing factor for infections in patients with hematological malignancies is neutropenia.<sup>10</sup> In this study, 21 out of 67 pediatric patients with hematological malignancies and neutropenia (31.3%) had infection identified in culture results. Most affected patients were female, consistent with findings from a study conducted in Zimbabwe.<sup>11</sup> The highest proportion of infections occurred in the 10–14-year age group. The most common type of malignancy among patients was Acute Lymphoblastic

Leukemia (66.7%). This result was also reported in previous studies conducted in India and Egypt.<sup>12,13</sup> Meanwhile, 2 studies conducted in India found that Acute Myeloblastic Leukemia was the most common diagnosis among patients.<sup>13</sup> All patients experienced a decrease in platelet counts, hemoglobin levels, and leukocyte counts. This decrease can be attributed to the progression of the malignancy or as an effect of the chemotherapy received by the patients.<sup>14</sup>

A total of 33 bacterial isolates were identified, consisting of 25 Gram-negative (75.8%) and 8 Gram-positive (24.2%) bacteria. Similar results were reported in studies conducted in Indonesia (57.9%), Egypt (55.5%), Poland (50.6%), and France (43%) among pediatric patients with hematological malignancies.<sup>12,15–17</sup> The vulnerability to infections caused by Gram-negative bacteria may result from exposure to broad-spectrum antibiotics, which can lead to a shift in normal flora to a pathogenic state in patients with mucosal damage caused by chemotherapy.<sup>16</sup> On the contrary, studies conducted in South Africa found that Gram-positive bacteria had a higher proportion among those with hematological malignancies.<sup>18</sup> This may be due to several factors, including a high prevalence of neutropenia, intensive chemotherapy regimens, the use of invasive medical devices (such as CVAD), mucosal damage, and antimicrobial prophylaxis.<sup>18</sup> Meanwhile, a study conducted in Zimbabwe found that the proportions of Gram-negative and Gram-positive bacteria were equal among pediatric patients with hematological malignancies.<sup>11</sup>

*Escherichia coli* was the most frequently isolated Gram-negative bacteria was, as also reported in previous studies on pediatric patients with hematological malignancies.<sup>13,17,18</sup> A different result was found in 2 other studies, where *Pseudomonas aeruginosa* was the predominant Gram-negative bacteria isolate.<sup>12,15</sup> Another study found that *Klebsiella pneumoniae* was the predominant Gram-negative bacteria in this patient population. The high prevalence of *Escherichia coli* infections may be explained by chemotherapy related disruptions of the intestinal microbiota balance and mucosal barrier injury, which increase the risk of bloodstream invasion.<sup>19</sup>

Among Gram-positive bacteria, *Staphylococcus hominis*, as also found in a previous study conducted on pediatrics with hematological malignancies.<sup>15</sup> A different result was observed in another study, where *Staphylococcus aureus* was the most frequently

isolated Gram-positive bacteria in pediatrics with hematological malignancies and solid tumors.<sup>11</sup> Other studies only mentioned that Coagulase-negative Staphylococci (CoNS) were the predominant Gram-positive bacteria.<sup>13</sup> Infections caused by *Staphylococcus hominis* may be associated with the use of invasive medical devices, mucosal damage in the gastrointestinal and genitourinary tracts.<sup>20</sup> Moreover, previous study indicates that CoNS should be considered since it can mediate resistance to *S. aureus*, particularly in immune-compromised, hospitalized, and elderly patients.<sup>21</sup>

This study found that 23 isolates (69.7%) were multidrug-resistant organisms (MDROs). Among Gram-positive isolates, 5 isolates (62.5%) were MRCoNS. Staphylococci with the *mecA* gene encode a binding protein known as PBP2a, which has a low affinity for  $\beta$ -lactam antibiotics.<sup>22</sup> Among Gram-negative bacteria, 12 isolates (48%) were ESBL-producing bacteria. ESBL-producing bacteria that could hydrolyze  $\beta$ -lactam antibiotics and inhibit  $\beta$ -lactamase inhibitors. Some common types of ESBL include TEM, SHV, and CTX.<sup>23</sup> The emergence of CTX-type ESBL is associated with the appearance of *Escherichia coli* strain ST131, which is connected to *Escherichia coli* resistant to fluoroquinolones. Additionally, 6 Gram-negative bacteria isolates (24%) were carbapenem-resistant organisms. Resistance occurs when bacteria produce enzymes that can degrade the  $\beta$ -lactam ring.<sup>15</sup>

This study found that the antibiotics with the highest sensitivity against Gram-positive bacteria during 2021–2022 include Linezolid, Tigecycline, and Vancomycin, while Amikacin had the highest sensitivity against Gram-negative bacteria. Similar results were reported in studies conducted in India. A study in India found that in pediatric patients with hematological malignancies, Linezolid, Teicoplanin, and Vancomycin showed 100% sensitivity against Gram-positive bacteria. Antibiotics from the aminoglycoside class had the highest sensitivity against Gram-negative bacteria.<sup>13</sup>

A different result was reported in a study conducted in Egypt, where the antibiotic with the highest sensitivity against Gram-positive bacteria in pediatric patients with hematological malignancies was Ampicillin/Sulbactam, while Cefepime had the highest sensitivity against Gram-negative bacteria.<sup>12</sup> A study in India found that Meropenem was the antibiotic with the highest sensitivity against Gram-negative bacteria in pediatric patients with hematological malignancies and

solid tumors.<sup>11</sup> A study in Indonesia found that Gentamicin and Chloramphenicol had the highest sensitivity against Gram-positive bacteria, while Meropenem showed the highest sensitivity (>90%) against Gram-negative bacteria in pediatrics with hematological malignancies and solid tumors.<sup>15</sup>

The most frequently identified bacteria in this study was *Escherichia coli*, which showed the highest sensitivity to Amikacin, with 100% sensitivity in 2021 and 80% in 2022. Previous studies have found that amikacin has the highest sensitivity against *Escherichia coli* in pediatric patients with hematological malignancies and solid tumors.<sup>11</sup> However, another study reported that Colistin (82%) had a higher sensitivity than Amikacin (55%).<sup>13</sup>

The most frequently identified bacteria, namely *Klebsiella pneumoniae*, showed the highest sensitivity (100%) to Amikacin in both 2021 and 2022. A similar result was reported in a study where Amikacin showed 100% sensitivity against *Klebsiella pneumoniae*.<sup>16</sup> Another study also found that Amikacin had 100% sensitivity against *Klebsiella pneumoniae*.<sup>11</sup> However, 2 other studies reported that Colistin had higher sensitivity than aminoglycosides.<sup>13</sup> Another study found that Meropenem was the antibiotic with the highest sensitivity against *Klebsiella pneumoniae* in pediatric patients with hematologic malignancies.<sup>15</sup>

After *Klebsiella pneumoniae*, the most frequently identified bacteria was *Staphylococcus hominis*. The bacteria showed the highest sensitivity (100%) to Vancomycin and Tigecycline in both 2021 and 2022. However, a different study found that Gentamicin and Chloramphenicol were the antibiotics with the highest sensitivity (100%). In this study, *Staphylococcus hominis* exhibited 100% sensitivity to Levofloxacin and Moxifloxacin in 2021; however, this sensitivity declined to 0% in 2022. For Clindamycin, Erythromycin, and Cephalosporin-class antibiotics, *Staphylococcus hominis* showed 0% sensitivity in 2021 and 2022. Another study also found that Cefepime and Cefazolin had 0% sensitivity.<sup>15</sup>

According to national guidelines, Ampicillin/Sulbactam, Gentamicin, and Cefepime are recommended for the empirical treatment of febrile neutropenia in pediatric chemotherapy patients.<sup>24</sup> In this study, Ampicillin/Sulbactam and Cefepime showed low sensitivity against both Gram-positive and negative bacteria. Gentamicin showed variable sensitivities of 25% and 100% in 2021 and 2022, respectively, against Gram-

positive bacteria, and 66.6% and 55.5% in 2021 and 2022, respectively, against Gram-negative bacteria. According to WHO recommendations, the antibiotics for pediatric neutropenic fever include Amoxicillin/Clavulanate Acid and Ciprofloxacin for low-risk patients, and Piperacillin/Tazobactam, Meropenem, Amikacin, and Vancomycin for high-risk patients.<sup>9</sup> Among these antibiotics, Amoxicillin/Clavulanate Acid, Ciprofloxacin, and Piperacillin/Tazobactam showed low sensitivity, while Vancomycin had the highest sensitivity at 100% in both 2021 and 2022.

Antibiotic resistance has become a significant global health issue. In response, the WHO has developed a classification system to help countries evaluate and monitor antibiotic use. This classification divides antibiotics into 3 groups namely Access, Watch, and Reserve.<sup>9</sup> The first-line therapy antibiotics for pediatrics oncology patients experiencing neutropenia at Dr. Hasan Sadikin General Hospital Bandung include Ampicillin/Sulbactam, Gentamicin, Cefepime, and Ceftazidime for high-risk patients. Among these antibiotics, Ampicillin/Sulbactam and Gentamicin belong to the Access group. Compared to these 2 antibiotics, Amikacin, which is also in the same group, showed higher sensitivity. Meanwhile, Cefepime and Ceftazidime belong to the Watch group. Vancomycin, which is in the same group, showed higher sensitivity against Gram-positive bacteria, while Meropenem and Ertapenem had higher sensitivity against Gram-negative bacteria. Antibiotics with 100% sensitivity, namely Vancomycin and Linezolid, belong to the Watch and Reserve groups, respectively.

In conclusion, Gram-negative bacteria are the predominant pathogens among pediatrics patients with hematological malignancies and neutropenia, with *Escherichia coli* as the most frequently isolated organism. Antibiotic susceptibility varied between 2021 and 2022, with a general trend of declining susceptibility. These results highlight the importance of regular, institution-based surveillance in monitoring microbial profiles and resistance trends. Continuous evaluation of empirical antibiotic therapy based on local data is crucial to ensure effective treatment and reduce the risk of multidrug-resistant infections. Strengthening antibiotic stewardship programs and infection control measures in pediatric oncology wards is crucial to optimize antibiotic use, prevent antimicrobial resistance, and enhance patient outcomes.



This study has limitations, including its retrospective design, incomplete medical records, and relatively small sample size, which may limit generalizability.

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