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(RESEARCH ARTICLE)

Antibiotic Use in Pediatric Patients with Acute Lymphoblastic Leukemia and Febrile Neutropenia at Dr. Soetomo General Hospital, Surabaya: A Point Prevalence Study

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Abstract

Background: Febrile neutropenia is a serious and potentially life-threatening complication in pediatric patients with acute lymphoblastic leukemia (ALL) undergoing chemotherapy. Profound neutropenia increases susceptibility to bacterial infections, making early empirical antibiotic therapy essential. However, inappropriate antibiotic use may contribute to antimicrobial resistance. Data regarding antibiotic utilization patterns in pediatric ALL patients with febrile neutropenia in Indonesia remain limited.

Methods: This study was a descriptive point prevalence survey conducted among pediatric patients aged 0–17 years diagnosed with ALL and febrile neutropenia at Dr. Soetomo General Hospital, Surabaya. Data were collected retrospectively from medical records of hospitalized patients between January and June 2025. Variables analyzed included patient demographics, severity of neutropenia, empirical antibiotic regimens, routes of administration, and microbiological culture results.

Results: total of 104 pediatric patients were included, with a predominance of males and school-aged children. More than half of the patients experienced severe neutropenia. Ampicillin–sulbactam was the most frequently prescribed empirical antibiotic, administered intravenously in the majority of cases. Positive blood culture results were predominantly Gram-positive bacteria, with Staphylococcus hemolytic as the most common isolate, followed by Gram-negative bacteria such as Pseudomonas aeruginosa.

Conclusion: Ampicillin–sulbactam was the main empirical antibiotic used in pediatric ALL patients with febrile neutropenia at Dr. Soetomo General Hospital and was generally consistent with recommended treatment guidelines. Continuous evaluation of local microbiological patterns and antibiotic prescribing practices is necessary to optimize therapy and support antimicrobial stewardship programs.

Keywords: Acute Lymphoblastic Leukemia; Febrile Neutropenia; Antibiotics; Point Prevalence Study; Pediatric Oncology

1. Introduction

Acute lymphoblastic leukemia (ALL) is the most common hematological malignancy in children and accounts for the majority of pediatric leukemia cases worldwide [1]. Advances in chemotherapy protocols have significantly improved survival rates; however, treatment-related complications remain a major cause of morbidity and mortality in pediatric

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patients [2]. One of the most serious and frequently encountered complications in children with ALL is febrile neutropenia, which is associated with a high risk of severe infection and death [3].

Febrile neutropenia occurs as a result of chemotherapy-induced myelosuppression, leading to a marked decrease in absolute neutrophil count and impaired host immune defense [4]. Clinically, febrile neutropenia is defined by the presence of fever in patients with neutropenia and is considered a medical emergency requiring immediate evaluation and treatment [5]. If not managed promptly and appropriately, febrile neutropenia may progress rapidly to sepsis, prolonged hospitalization, increased healthcare costs, and unfavorable clinical outcomes [6].

Early initiation of empirical antibiotic therapy is the cornerstone of febrile neutropenia management. International guidelines recommend the use of broad-spectrum antibiotics to cover both Gram-positive and Gram-negative pathogens, particularly Pseudomonas aeruginosa, which is associated with high mortality rates in neutropenic patients [7]. Timely and appropriate antibiotic administration has been shown to significantly reduce infection-related complications and improve survival in pediatric oncology patients [8].

Despite established clinical guidelines, antibiotic prescribing practices for febrile neutropenia vary across healthcare institutions. Variations in local bacterial epidemiology, antimicrobial resistance patterns, drug availability, and institutional protocols may influence antibiotic selection [9]. Inappropriate antibiotic use, including delayed initiation, suboptimal dosing, or unnecessary use of broad-spectrum agents, may lead to treatment failure and contribute to the emergence of antimicrobial resistance [10].

In Indonesia, data regarding antibiotic utilization patterns in pediatric patients with ALL and febrile neutropenia are still limited, particularly in tertiary referral hospitals. Understanding local patterns of antibiotic use is essential to evaluate adherence to treatment guidelines and to strengthen antimicrobial stewardship programs. Therefore, this study aimed to describe the pattern of antibiotic use in pediatric patients with acute lymphoblastic leukemia who developed febrile neutropenia at Dr. Soetomo General Hospital, Surabaya, using a point prevalence study design.

2. Material And Methods

This study employed a descriptive observational design with a cross-sectional approach. Data were collected retrospectively from medical records of pediatric patients diagnosed with acute lymphoblastic leukemia (ALL) who experienced febrile neutropenia and were hospitalized at Dr. Soetomo General Hospital, Surabaya. The study was conducted in the pediatric ward of the hospital during the period from January to June 2025.The study population consisted of all pediatric patients aged 0–17 years with a confirmed diagnosis of ALL and febrile neutropenia during the study period. A total sampling technique was applied, and all eligible patients who met the inclusion criteria were included in the study. Patients with incomplete medical records were excluded from the analysis. A total of 104 patients fulfilled the study criteria and were included as research subjects.Data collected included demographic characteristics, clinical parameters, laboratory findings (absolute neutrophil count), types of empirical antibiotics prescribed, dosage, route of administration, and microbiological culture results. All data were recorded using a standardized data collection form and analyzed descriptively.This study was approved by the Health Research Ethics Committee of Dr. Soetomo General Hospital, Surabaya. Patient identities were not disclosed to ensure confidentiality. All data obtained were used solely for research purposes, and patient privacy was strictly maintained throughout the study.

3. Result And Discussion

A total of 104 pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia at Dr. Soetomo General Hospital were included in this study. Most patients were male and of school age, with more than half experiencing severe neutropenia. These findings reflect the significant myelosuppressive effects of chemotherapy in pediatric ALL patients. Ampicillin–sulbactam was the most frequently prescribed empirical antibiotic and was predominantly administered intravenously. This prescribing pattern suggests adherence to empirical treatment guidelines and antimicrobial stewardship principles. Blood culture results showed a predominance of Gram-positive bacteria, with Staphylococcus hemolytic as the most common isolate, followed by Gram-negative pathogens such as Pseudomonas aeruginosa. These results indicate the importance of maintaining adequate Gram-negative coverage in empirical therapy.

Tabel 1 Characteristics of pediatric ALL Patients with Neutropenic Fever

Characteristics	Categories	Frequencies(n)	Percentage(%)
Gender	Male	60	57.69
	Female	44	42.3
Age Group	<1 Year	4	3.85
	1-5 Years	40	3.46
	6-12 Years	45	43.27
	13-17 Years	15	14.42
Nutritional status	Good Nutrition	68	65.38
	Malnutrition	36	34.62

Table 1 presents the demographic characteristics of pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia at Dr. Soetomo General Hospital. Based on sex distribution, the majority of patients were male, accounting for 60 patients (57.7%), while female patients comprised 44 patients (42.3%). This finding indicates a higher prevalence of male patients compared to female patients. Similar results were reported in a previous study conducted at Universitas Airlangga Hospital, which found that infections in pediatric patients were more frequent in males (56.8%) than in females (43.2%) [23]. This difference may be attributed to hormonal and anatomical factors, as male children are suggested to have relatively lower innate immune responses to certain infections. In addition, genetic predisposition and androgen hormones may influence lymphoblastic proliferation through their effects on gene expression [24]. These findings are consistent with previous studies reporting that approximately 59% of Indonesian pediatric ALL patients are male [25].

Regarding age distribution, the largest proportion of patients was found in the 6–12 years age group, with 45 patients (43.27%), followed by the 1–5 years age group with 40 patients (38.46%). Patients aged 12–17 years accounted for 15 cases (14.43%), while those under 12 months constituted the smallest group, with 4 patients (3.84%). These results indicate that most patients were of school age to early adolescence. This finding is consistent with global epidemiological data showing that the peak incidence of ALL occurs between the ages of 2 and 10 years [26]. Moreover, children aged 5–12 years have been reported to have an increased risk of infection due to the ongoing maturation of the adaptive immune system, which may increase susceptibility to novel pathogens [27].

Regarding nutritional status, most pediatric patients had normal nutritional status, accounting for 68 patients (65.38%), while 36 patients (34.62%) were classified as having poor nutritional status. Although the majority of patients were well nourished, a substantial proportion exhibited malnutrition, which may adversely affect disease progression and response to therapy, including antibiotic treatment. In the context of febrile neutropenia, nutritional status plays a crucial role in immune function and infection recovery. Malnourished patients are more susceptible to severe infections, experience delayed neutrophil recovery, and may require broader-spectrum or combination antibiotic therapy [28]. Therefore, nutritional assessment should be an integral component of routine evaluation in pediatric ALL patients with febrile neutropenia.

Tabel 2 Distribution of Laboratory Examination Results

Laboratory Parameters	Categories	Frequencies(n)	Percentage(%)
Leukocytes (x10^3/uL)	Normal	12	11.54
	Leukopenia	72	69.23
	Leukocytosis	20	19.23
Hemotocrit	Normal	24	23.08
	Low	80	76.92
Platelets(x10^3/uL)	Normal	20	19.23
	Trombocytopenia	82	78.85
	Thrombocytosis	2	1.92

Absolute Neutrophil Count (ANC)	Normal	5	4.81
	Mild neutropenia	18	17.31
	Severe neutropenia	55	52.88
	Very severe neutropenia	26	25.00

Table 2 shows the laboratory profiles of pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia. Most patients exhibited leukopenia (69.23%), followed by leukocytosis (19.23%), while only a small proportion had normal leukocyte counts. This finding reflects chemotherapy-induced bone marrow suppression, which increases susceptibility to infection and is a key contributor to febrile neutropenia [32,33]. Low hematocrit levels were observed in 76.92% of patients, indicating anemia commonly associated with leukemic bone marrow infiltration and chemotherapy-related suppression of erythropoiesis. Anemia in pediatric ALL patients has been linked to increased transfusion requirements and prolonged hospitalization [34,35].

Thrombocytopenia was present in the majority of patients (78.85%), whereas thrombocytosis was rare. This condition results from impaired megakaryopoiesis and chemotherapy-induced myelotoxicity, increasing the risk of bleeding complications and necessitating close laboratory monitoring [36]. Assessment of absolute neutrophil count (ANC) revealed that more than three-quarters of patients (77.88%) experienced severe to very severe neutropenia. Severe neutropenia is the main determinant for initiating empirical antibiotic therapy and is strongly associated with a high risk of serious bacterial infections during chemotherapy in pediatric ALL patients [37,38].

Tabel 3 Distribution of Vital Signs Examination Results

Vital Signs	**Categories**	**Frequencies(n)**	**Percentage(%)**
Temperature (C^0)	Moderete Fever	90	86.54
	High Fever	11	10.58
	Hyperthermia	3	2.88
Blood Pressure (mmhg)	Normal	92	88.46
	Hypotension	8	7.69
	Hypertension	4	3.85
Heart Rate (x/menit)	Normal	76	73.08
	Low	18	17.31
	High	10	9.62
Respiratory Rate (x/menit)	Normal	85	81.73
	Tachypnea	14	13.46
	Bradipnea	5	4.81

Table 3 presents the vital signs of pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia at Dr. Soetomo General Hospital. Most patients presented with moderate fever, accounting for 90 patients (86.54%), while high fever was observed in 11 patients (10.58%) and hyperthermia in only 3 patients (2.88%). Fever in febrile neutropenia reflects the underlying pathophysiology of chemotherapy-induced neutropenia, which increases susceptibility to bacterial and fungal infections and triggers a systemic inflammatory response [41]. In pediatric ALL patients, fever often represents the earliest clinical sign of opportunistic infection and requires prompt initiation of empirical broad-spectrum antibiotic therapy [42].

Regarding blood pressure, the majority of patients had normal values (88.46%), while hypotension was observed in 7.69% of patients and hypertension in 3.85%. These findings suggest that most patients were hemodynamically stable at presentation. Hypotension in a small proportion of patients may indicate severe systemic infection or sepsis, a known complication in patients with severe neutropenia [43]. Conversely, mild hypertension may be associated with corticosteroid therapy or certain chemotherapeutic agents used in ALL treatment protocols [44].

Assessment of heart rate showed that most patients had normal values (73.08%), whereas bradycardia and tachycardia were observed in 17.31% and 9.62% of patients, respectively. Tachycardia may occur as a physiological response to

fever, anemia, or systemic stress, highlighting the importance of continuous monitoring to detect early clinical deterioration [45].

Respiratory rate evaluation revealed that 81.73% of patients had normal breathing rates, while tachypnea and bradypnea were identified in 13.46% and 4.81% of patients, respectively. Tachypnea may reflect fever, mild hypoxia, or early metabolic stress and can serve as an early indicator of sepsis in neutropenic patients [46]. Therefore, close monitoring of respiratory parameters remains an essential component of clinical management in pediatric ALL patients with febrile neutropenia.

Tabel 4 Distribution of Antibiotic Type Use

Types of Antibiotics	Frequencies(n)	Percentage (%)
Ampicillin Sulbactam	101	97.12
Gentamicin	2	1.92
Amikasin	1	0.96

Table 4 shows the empirical antibiotic use among pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia at Dr. Soetomo General Hospital. Ampicillin–sulbactam was the most frequently prescribed antibiotic, administered to 101 patients (97.12%), followed by gentamicin in 2 patients (1.92%) and amikacin in 1 patient (0.96%). These findings indicate that ampicillin–sulbactam was the primary empirical antibiotic used in this population.

The predominant use of ampicillin–sulbactam is consistent with international guidelines, including those from the Infectious Diseases Society of America and the European Society for Medical Oncology, which recommend β-lactam/β-lactamase inhibitor combinations as first-line empirical therapy for febrile neutropenia in clinically stable pediatric patients [47,48]. This regimen provides broad coverage against common Gram-positive and Gram-negative pathogens while supporting antimicrobial stewardship.

In pediatric ALL patients with neutropenia, early administration of broad-spectrum empirical antibiotics is crucial to prevent progression to sepsis or septic shock. The limited use of gentamicin and amikacin in this study likely reflects their role as adjunctive therapy in patients with severe neutropenia or suspected infections caused by resistant Gram-negative organisms, such as Pseudomonas aeruginosa or Klebsiella pneumoniae [49,50]. Overall, the findings support the rational and guideline-concordant use of ampicillin–sulbactam as the main empirical antibiotic in this clinical setting.

Tabel 5 distribution of antibiotic administration patterns

Types of Antibiotics	Dosage (mg/kgbb/hari)	Route of Administration	Frequencies(n)	Percentage (%)
Ampicillin-Sulbactam	~100	IV	94	90.38
Ampicillin-Sulbactam	~200	IV	7	6.73
Gentamicin	~7,5	IV	2	1.92
Amikasin	~15	IV	1	0.96

Table 5 presents the dosage and route of empirical antibiotic therapy in pediatric patients with acute lymphoblastic leukemia (ALL) and febrile neutropenia. All patients (100%) received antibiotics via the intravenous route, in accordance with international guidelines recommending intravenous administration to ensure rapid onset of action and optimal bioavailability in patients with severe neutropenia [51,52].Ampicillin–sulbactam was the most frequently administered antibiotic, predominantly at a dose of approximately 100 mg/kg/day in 94 patients (90.38%), while a higher dose of approximately 200 mg/kg/day was used in 7 patients (6.73%). The use of higher doses in a limited number of patients likely reflects more severe clinical conditions or suspected resistant infections. Ampicillin–sulbactam provides broad-spectrum coverage against common Gram-positive and Gram-negative pathogens in immunocompromised patients [53].

Gentamicin (7.5 mg/kg/day) and amikacin (15 mg/kg/day) were used in a small proportion of patients as adjunctive therapy. These aminoglycosides are typically reserved for high-risk cases with suspected resistant Gram-negative infections, including Pseudomonas aeruginosa, due to their potential nephrotoxic and ototoxic effects, particularly in pediatric patients receiving chemotherapy [54].

Tabel 6 Distribution of Culture Examination Results

Gram Staining Result	Frequencies(n)	Percentage (%)
Gram Negative Rods	11	10.58
Gram Positive Rods	3	2.88
Gram Positive Coccus	8	7.69
Yeast	1	0.96
No bacterial/germ formations were found	74	71.15
No culture	7	6.73

Based on Table 6 most culture specimens showed negative Gram staining results, with no bacterial or microbial forms detected in 74 patients (71.15%). Positive findings were identified in a smaller proportion of samples, including Gram-negative bacilli in 11 patients (10.58%), Gram-positive cocci in 8 patients (7.69%), Gram-positive bacilli in 3 patients (2.88%), and yeast in 1 patient (0.96%). Culture examination was not performed in 7 patients (6.73%).

The predominance of negative culture results may be associated with prior empirical antibiotic administration and low bacterial load in patients with febrile neutropenia. Nevertheless, the presence of Gram-positive and Gram-negative organisms highlights the heterogeneity of infectious pathogens in immunocompromised pediatric patients. These findings are consistent with previous studies reporting Gram-positive bacteria as the most common pathogens in febrile neutropenia, followed by Gram-negative bacteria and fungal infections [55].

Tabel 7 Classification of bacteria based on grams

Specimen	Gram Classification	Types of Bacteria	Frequencies(n)
Blood	Positive	*S.dysgalactaie*	1 (4.3)
		Streptococcus agalactiae	1 (4.3)
		Staphylococcus kloosi	1 (4.3)
		S. haemolyticus	2 (8.7)
		Staphylococcus aureus	1 (4.3)
		Corynebacterium spp	1 (4.3)
		C. matruchoti	1 (4.3)
Blood	Negative	*Escherichia coli*	2 (8.7)
		E. coli ESBL	2 (8.7)
		Klebsiella pneumoniae ESBL	2 (8.7)
		P. aeruginosa	2 (8.7)
		Salmonella enterica spp	1 (4.3)
		Enterica sv paratyphi B	1 (4.3)
		Serratia marcescens	1 (4.3)
Pus	Positive	*S.epidermidis*	1 (4.3)
		S.hominis	1 (4.3)
		S.Coagulase-negative	1 (4.3)

Urine	Positive	*Enterococcus faecium*	1 (4.3)
Total			23 (100)

From 104 pediatric patients with acute lymphoblastic leukemia (ALL), a total of 23 positive cultures (23.7%) were identified during the study period. Most isolates originated from blood specimens, followed by pus and urine. Gram-positive bacteria predominated, accounting for 13 isolates (56.5%), while Gram-negative bacteria comprised 10 isolates (43.5%).

The most frequently isolated Gram-positive organism was Staphylococcus hemolytic, followed by Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus hominis, Streptococcus spp., and Corynebacterium spp. These findings suggest that infections commonly arise from skin and mucosal flora that become opportunistic pathogens in neutropenic and immunocompromised patients, particularly those with prolonged intravascular device use. Similar patterns have been reported in pediatric ALL patients, where coagulase-negative staphylococci and Staphylococcus aureus were the most prevalent Gram-positive isolates [56]. Among Gram-negative bacteria, Pseudomonas aeruginosa was the most frequently isolated pathogen, followed by Escherichia coli (including ESBL-producing strains), Klebsiella pneumoniae ESBL, Salmonella enterica, and Serratia marcescens. Gram-negative infections remain clinically significant due to their association with severe sepsis and antimicrobial resistance, particularly in febrile neutropenia [57].

In this study, blood culture positivity was 20.4%, which is consistent with previous reports indicating that only 20–30% of febrile neutropenia episodes yield positive blood cultures. The higher positivity rates in pus and urine specimens underscore the importance of collecting cultures from suspected infection sites to improve diagnostic yield [58].

Interpretation of culture results, especially coagulase-negative staphylococci, should consider clinical correlation, number of positive culture sets, and the presence of invasive devices, as these organisms may represent either contamination or true infection in neutropenic patients. Overall, these findings highlight the diverse microbiological profil0065

4. Conclusion

Ampicillin–sulbactam was the main empirical antibiotic used in pediatric ALL patients with febrile neutropenia at Dr. Soetomo General Hospital. Antibiotic use was generally consistent with recommended treatment guidelines. Continuous monitoring is required to support antimicrobial stewardship.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

This study was approved by the Ethics Committee of Dr.Soetomo General Academic Hospital/Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (Ethical approval number: Ref No:1856/LOE/301 4.2/XII/2024).

Statement of informed consent

The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study using medical record data.

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