

# Clinical and Hematological Characteristics of Pediatric Acute Lymphoblastic Leukemia at Tertiary Care General Hospital, Surabaya: A Descriptive Review from 2022–2024

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## ABSTRACT

**Background.** Pediatric acute lymphoblastic leukemia (ALL) outcomes in low- and middle-income countries remain substantially worse than in high-income settings. This study describes the demographic, nutritional, and hematological profiles of pediatric ALL at a tertiary referral center in East Java, Indonesia (2022–2024), and highlights low-cost hematological ratios with potential clinical utility.

**Methods.** We conducted a retrospective descriptive analysis of 385 consecutive pediatric ALL cases diagnosed between 1 January 2022 and 31 December 2024 using electronic medical records and the Indonesian Pediatric Cancer Registry. Key variables included age, sex, nutritional status, full blood count at presentation, and derived indices: neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), hemoglobin-to-platelet ratio (HPR), and monocyte-to-neutrophil ratio (MNR). Vital status at last follow-up was recorded.

**Results.** Median age at diagnosis was 5.5 years (range 0.4–17.9); male patients comprised 64.2% (n=247). Underweight or severely underweight status affected 25.7% of the cohort. Median hemoglobin and platelet counts were 7.6 g/dL and  $25 \times 10^3/\mu\text{L}$ , respectively, indicating severe marrow failure at presentation. Median WBC was  $7.7 \times 10^3/\mu\text{L}$  (range up to  $750.3 \times 10^3/\mu\text{L}$ ). Derived indices showed a median NLR of 0.1 and median HPR of 0.3. Overall mortality during the observation period was 48.1% (n=185).

**Conclusion.** Pediatric ALL in this tertiary Indonesian center presents with profound cytopenias, a high prevalence of undernutrition, and high mortality. Low-cost CBC-derived ratios (e.g., NLR, HPR) reflect severe marrow compromise and warrant further evaluation as early risk markers where advanced diagnostics are limited. Interventions targeting earlier diagnosis, nutritional optimization, and sepsis prevention are priorities to narrow the survival gap.

**Keywords:** Pediatric ALL, Hematology, Neutrophil-to-lymphocyte ratio, Hemoglobin-to-platelet ratio, Indonesia.

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## Introduction

### Background

Pediatric Acute Lymphoblastic Leukemia (ALL) is a heterogeneous hematological malignancy characterized by the uncontrolled proliferation of

lymphoid progenitor cells in the bone marrow, blood, and extramedullary sites.<sup>1</sup> It represents approximately 75% to 80% of all pediatric leukemia cases worldwide.<sup>1</sup> Over the last five decades, the landscape of pediatric ALL has been transformed from a

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uniformly fatal disease to one of the most successful examples of modern oncology, with five-year overall survival (OS) rates exceeding 90% in high-income countries (HICs).<sup>3</sup> This remarkable progress is attributed to highly refined risk-adapted chemotherapy protocols, advanced supportive care, and the integration of molecular and cytogenetic profiling into standard diagnostic algorithms.<sup>6</sup>

However, this success story is not uniform across the globe. In low- and middle-income countries (LMICs), including Indonesia, the survival rates for childhood ALL remain significantly lower, often ranging from 20% to 70%.<sup>3</sup> Indonesia, the world's largest archipelago with a population of over 270 million, faces unique geographic and socioeconomic challenges that result in inequalities in health service delivery.<sup>10</sup> With an estimated 4.32 new cases per 100,000 children annually, ALL is the most common childhood cancer in Indonesia, leading to a substantial public health burden.<sup>8</sup>

Dr. Soetomo General Hospital in Surabaya serves as the primary tertiary referral center for East Java and the eastern regions of Indonesia. This institution manages a high volume of pediatric oncology cases, operating within the framework of the Indonesian National Health Insurance (BPJS) and following national treatment guidelines issued by the Indonesian Pediatric Society (IDAI).<sup>3</sup> The period from 2022 to 2024 is particularly critical as it follows the major disruptions caused by the COVID-19 pandemic, which saw delayed diagnoses, increased treatment abandonment, and higher mortality among pediatric cancer patients due to concurrent infections and resource reallocations.<sup>10</sup>

### Clinical Significance of Hematological Parameters

The initial hematological presentation of a child with ALL provides a window into the biological aggressiveness of the disease and the extent of bone marrow replacement. Classic features include anemia, thrombocytopenia, and a variable white blood cell (WBC) count.<sup>15</sup> Anemia, often presenting as pallor and fatigue, is a hallmark of ineffective erythropoiesis as leukemic blasts crowd the marrow.<sup>17</sup> Thrombocytopenia results in bleeding manifestations like petechiae, purpura, and epistaxis, which are frequent presenting symptoms in Indonesian cohorts.<sup>15</sup> Beyond these traditional parameters, recent research has highlighted the prognostic and diagnostic utility of derived hematological ratios. Ratios such as the

Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Lymphocyte-to-Monocyte Ratio (LMR) are thought to reflect the systemic inflammatory response and the tumor microenvironment.<sup>20</sup> In solid tumors and some adult hematological malignancies, a high NLR is typically associated with a poor prognosis.<sup>21</sup> Conversely, in acute leukemia at the time of diagnosis, the NLR is often extremely low because the malignant lymphoblasts suppress normal granulopoiesis, leading to absolute neutropenia.<sup>17</sup>

Emerging biomarkers like the Hemoglobin-to-Platelet Ratio (HPR) and Monocyte-to-Neutrophil Ratio (MNR) are being investigated for their roles in predicting mortality, clinical severity, and therapy response in various conditions, ranging from Immune Thrombocytopenic Purpura (ITP) to Acute Myeloid Leukemia (AML) and COVID-19.<sup>25</sup> Their accessibility and cost-effectiveness make them highly relevant for clinical practice in resource-constrained environments like Surabaya.<sup>28</sup>

### Objectives

- (1) Describe demographic and nutritional characteristics;
- (2) quantify hematological derangements and derived ratios at presentation;
- (3) report vital status within the study period;
- (4) propose potential clinical roles for CBC-derived indices in resource-limited settings.

### Benefit of the Research

The findings of this study offer several benefits. For clinicians at Dr. Soetomo and similar tertiary centers, the data clarifies the "baseline" patient who presents with ALL in East Java, emphasizing the high prevalence of malnutrition and severe cytopenias. This awareness is vital for early complications management, such as sepsis prevention and Tumor Lysis Syndrome (TLS) prophylaxis.<sup>30</sup> For researchers, the study establishes the descriptive ranges for novel ratios like HPR and MNR in a large pediatric ALL cohort, paving the way for future analytic studies on their prognostic significance. For public health officials, the documented mortality rate serves as a performance metric for the national cancer protocol and the efficacy of the referral system.<sup>12</sup>

### Research Hypothesis

It is hypothesized that:

1. Pediatric ALL in Surabaya exhibits a significant male predominance and a classic age peak in the

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- 2- to 5-year range.
2. A substantial portion of the population (exceeding 20%) presents with malnutrition.
  3. The median NLR at diagnosis is significantly lower than normal physiological ranges due to marrow failure.
  4. The mortality rate remains high (approaching 50%) due to late presentation and environmental comorbidities.

## Research Gap and Novelty

While several studies have described ALL in Indonesia, most recent high-volume data from Surabaya comes from before the 2020s or focuses on specific complications like COVID-19 or TLS.<sup>13</sup> There is a lack of comprehensive baseline descriptive data covering the post-pandemic recovery years (2022–2024). Furthermore, this study is among the first in Indonesia to integrate a full battery of derived hematological ratios—NLR, LMR, PLR, HPR, and MNR—into a single large-scale descriptive report for pediatric ALL. This multidimensional approach provides a more nuanced understanding of the leukemic state than traditional CBC parameters alone.

## Methods

### Study Design

Retrospective descriptive study at the Department of Pediatrics, Dr. Soetomo General Academic Hospital (Surabaya), a tertiary referral center. Study period: 1 January 2022–31 December 2024. The study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

### Setting and Period

The study was conducted at the Department of Pediatrics, Dr. Soetomo General Academic Hospital,

Surabaya, East Java, Indonesia. Dr. Soetomo is a 1,500-bed Class A teaching hospital and the primary tertiary referral center for the eastern half of the island of Java and much of Eastern Indonesia. The study period was January 1, 2022, to December 31, 2024.

### Population and Sampling

All pediatric patients (age 0–18 years) with a new diagnosis of ALL, confirmed by bone marrow aspiration showing  $\geq 20\%$  lymphoblasts, and with a baseline complete blood count (CBC) at admission were included.

**Exclusions:** AML, chronic leukemias, L3 morphology (Burkitt-type), incomplete records, or transfer before therapy initiation.

### Data Sources

Data extracted from the hospital electronic medical record, Laboratory Information System, and the Indonesian Pediatric Cancer Registry.

**Variables:** age, sex, weight/height (nutritional status categorized by WHO/CDC growth charts), Hb, WBC, platelet count, differential counts, and vital status at last follow-up.

Derived ratios calculated as:  $NLR = ANC/ALC$ ;  $LMR = ALC/AMC$ ;  $PLR = \text{platelet}/ALC$ ;  $HPR = Hb/\text{platelet}$  (g/dL per  $10^3/\mu\text{L}$ );  $MNR = AMC/ANC$ .

- **Outcome Data:** Vital status (Alive or Death) as of the final follow-up date within the 2022–2024 timeframe.

### Risk of Bias Assessment

A rigorous assessment of potential biases was conducted based on the Cochrane Handbook's principles for observational research.<sup>37</sup> Although typically used for trials, these domains were adapted to evaluate the quality of this retrospective cohort study.

**Table 1. Risk of Bias (RoB) Assessments**

Domain	Assessment	Rationale
<b>Selection Bias</b>	Low Risk	The study used consecutive enrollment from a comprehensive national registry (IPCAR) and hospital record system, ensuring that almost all cases diagnosed at the facility were captured.
<b>Information / Detection Bias</b>	Low Risk	Laboratory outcomes (CBC) are objective measures performed using standardized automated analyzers (Sysmex) with regular quality control. This eliminates the risk of assessor judgment bias.
<b>Performance Bias</b>	Not Applicable	As a descriptive study of baseline characteristics, no intervention was under investigation.
<b>Attrition Bias</b>	Moderate Risk	Retrospective data often suffer from loss to follow-up,

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		particularly in Indonesia where treatment abandonment (dropping out) is a recognized issue. This may slightly underestimate the true mortality rate.
<b>Reporting Bias</b>	Low Risk	The study reports all pre-specified outcomes, including novel hematological ratios, regardless of the direction of the results.
<b>Confounding Bias</b>	Moderate Risk	As a descriptive study, the analysis does not adjust for every potential confounder (e.g., socioeconomic status, parental education) that might influence the severity of presentation.

### Ethical Considerations

This study received ethical clearance from the Health Research Ethics Committee of Dr. Soetomo General Hospital (Certificate Number: [As per institutional record]). Patient data were anonymized using unique identification codes to ensure confidentiality. Since the study was retrospective and used secondary data, individual patient consent was waived.

### Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0. Normality of the data was tested using the Kolmogorov-Smirnov test. Given the extreme outliers common in hematological malignancies (e.g., hyperleukocytosis), continuous data were described using medians and ranges (minimum-maximum) rather than means and standard

deviations.<sup>40</sup> Categorical variables were summarized as frequencies and percentages. Survival data were presented as point-prevalence vital status at the study conclusion.

### Results

The study population comprised 385 pediatric patients who met the inclusion criteria during the 2022–2024 period. This represents a substantial volume for a single-center experience in Indonesia.

### Patient Demographics

The median age of the cohort at diagnosis was 5.5 years, with a wide range from infancy (0.4 years) to late adolescence (17.9 years). The gender distribution was markedly unbalanced, with a clear male predominance.

Parameters	Patients (n=385)	n (%) or Median (Min-Max)
<b>Age (Years)</b>	385	5.5 (0.4-17.9)
<b>Genders</b>		
Male	247	64.2%
Female	138	35.8%
<b>Nutritional Status</b>		
Severely Underweight	48	12.5%
Underweight	51	13.2%
Normal Weight	234	60.8%
Overweight	32	8.3%
Obesity	20	5.2%
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	385	14.8 (7.2-28.7)
<b>Vital Status</b>		
Alive	200	51.9%
Death	185	48.1%

As shown in the table above, more than one-quarter of the patients (25.7%) presented with some degree of weight deficiency (severely underweight or underweight) at the time of their first leukemia diagnosis. Conversely, a combined 13.5% of the children were either overweight or obese.

### Hematological Characteristics

The laboratory parameters at presentation revealed significant bone marrow failure across the cohort. Median hemoglobin levels indicated moderate-to-severe anemia (7.6 g/dL), and median platelet counts were critically low (25.0 X 10<sup>3</sup> µL), placing most

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patients at high risk for spontaneous hemorrhage. The median total WBC count was  $7.7 \times 10^3 \mu\text{L}$ , but the maximum value of  $750.3 \times 10^3 \mu\text{L}$  highlights the

subgroup of patients with extreme hyperleukocytosis, a major clinical risk factor.

Laboratory Test Results	Median	Min - Max
Hemoglobin (g/dL)	7.6	0.9 - 12.0
WBC ( $\times 10^3 \mu\text{L}$ )	7.7	0.3 - 750.3
Platelets ( $\times 10^3 \mu\text{L}$ )	25.0	0.3 - 391.0
Lymphocytes (%)	75.5	1.9 - 97.2
Neutrophils (%)	7.6	0.01 - 88.5
Monocytes (%)	9.6	0.1 - 81.5
ANC ( $\times 10^3 \mu\text{L}$ )	0.7	0.0 - 123.5
ALC ( $\times 10^3 \mu\text{L}$ )	4.9	0.05 - 626.5

The differential counts showed a median lymphocyte percentage of 75.5%, whereas neutrophils (7.6%) and monocytes (9.6%) were suppressed. The median Absolute Neutrophil Count (ANC) was  $0.7 \times 10^3 \mu\text{L}$ , which is below the threshold for clinical neutropenia ( $< 1.5 \times 10^3 \mu\text{L}$ ).

Analysis of derived inflammatory and prognostic ratios provided more nuanced clinical information. The median Neutrophil-to-Lymphocyte Ratio (NLR) was 0.1, indicating that for most patients, lymphocytes (primarily malignant blasts) overwhelmingly outnumbered normal neutrophils.

### Derived Hematological Ratios

Derived Indices	Median	Min - Max
NLR	0.1	0.0 - 18.8
LMR	7.6	0.09 - 194.4
PLR	3.5	0.01 - 422.6
HPR	0.3	0.01 - 32.0
MNR	1.3	0.01 - 7660.0

The median Hemoglobin-to-Platelet Ratio (HPR) was 0.3, while the median Monocyte-to-Neutrophil Ratio (MNR) was 1.3. These ratios demonstrate extreme variability, particularly the MNR, which reached a maximum value of 7660.0 in a patient with profound neutropenia combined with some monocyte preservation.

### burden, and vulnerability to infection and treatment-related complications.

The descriptive analysis of 385 pediatric ALL cases at Dr. Soetomo General Hospital from 2022 to 2024 paints a detailed picture of a high-burden clinical environment. The core findings—significant male predominance, a high rate of malnutrition, severe hematological derangements at diagnosis, and a high mortality rate—provide critical insights for the Indonesian oncology community.

### Survival Outcomes

The vital status as of the study's conclusion revealed a survival rate of 51.9% (n=200). A high mortality rate of 48.1% (n=185) was recorded. This mortality includes deaths occurring during the induction phase, consolidation phase, or as a result of treatment abandonment and subsequent progression.

### Demographic Trends and Gender Disparity

The median age of 5.5 years is perfectly aligned with the standard epidemiological peak for ALL worldwide, which occurs between the ages of 2 and 5.<sup>1</sup> This peak corresponds to the developmental phase where the immune system is rapidly evolving, and early childhood exposure to common infectious agents might trigger leukemogenic transformations in genetically predisposed individuals.<sup>8</sup>

### Discussion

**Key findings.** In this large single-center pediatric ALL cohort, presentations were marked by **severe anemia** and **thrombocytopenia**, a **low median NLR (0.1)**, **substantial undernutrition (25.7%)**, and a **high crude mortality rate (48.1%)**. These findings suggest **late presentation**, **substantial disease**

However, the male predominance (64.2%) is higher than the typical 1.2:1 ratio seen in HICs. This finding

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is consistent with other Indonesian epidemiological studies.<sup>11</sup> While biological factors like the role of sex hormones in leukemogenesis have been suggested, there is currently no definitive evidence explaining why males are more frequently affected.<sup>15</sup> In some LMIC contexts, gender differences in healthcare-seeking behavior can also influence diagnostic rates, though acute conditions like leukemia usually necessitate care regardless of gender.

### Nutritional Status and Its Implications

One of the most alarming findings is the nutritional status of the cohort. Over 25% of patients presented as underweight or severely underweight. In the context of leukemia, malnutrition acts as both a predictor and a consequence of disease severity. The malignant cells have extremely high metabolic demands, leading to the breakdown of endogenous protein and fat stores.<sup>34</sup> Previous studies in Indonesia have shown that malnutrition at the time of diagnosis is an independent risk factor for death (Relative Risk of 2.34).<sup>43</sup> Malnourished patients are significantly more susceptible to prolonged neutropenia following chemotherapy, increasing the risk of life-threatening infectious complications like sepsis and pneumonia—the leading causes of induction-phase mortality in Indonesia.<sup>34</sup> Furthermore, malnutrition can lead to treatment delays and reduced protocol compliance because these children are often "too sick" to receive their scheduled intensive therapy.<sup>3</sup> Conversely, a small portion of the cohort (5.2%) was obese, which international literature has linked to higher relapse rates and toxicity, though this effect is less studied in the Indonesian population.<sup>34</sup>

### Hematological Profile: The Evidence of Late Diagnosis

The median hemoglobin of 7.6 g/dL and platelet count of  $25.0 \times 10^3 \mu\text{L}$  are remarkably low compared to baseline values typically reported in HICs. In the United States or Europe, earlier diagnosis often occurs when children present with bruising or pallor while hemoglobin is still in the 9–10 g/dL range. The severe values observed in Surabaya suggest a long "diagnostic lag"—the time between the first symptom and the formal diagnosis.<sup>12</sup>

Hyperleukocytosis was present in a subset of the cohort, with WBC counts reaching as high as 750,000 cells  $\mu\text{L}$ . This feature is a primary determinant of high-risk (HR) stratification under the Indonesian ALL Protocol.<sup>3</sup> These patients are at immediate risk for

leukostasis and Tumor Lysis Syndrome (TLS).<sup>30</sup> In Dr. Soetomo hospital, TLS has been identified in approximately 33% of ALL patients, with decreased renal function and high leukocyte counts being the most significant predictors.<sup>30</sup>

### The Biological Insight of Hematological Ratios

The use of derived ratios provided an innovative layer to this descriptive study.

#### Neutrophil-to-Lymphocyte Ratio (NLR)

The median NLR of 0.1 is drastically lower than the normal range of 1.0 to 3.0 seen in healthy children.<sup>46</sup> In solid tumors, a high NLR reflects a state of systemic inflammation that promotes tumor growth and metastasis.<sup>21</sup> However, in acute leukemia at diagnosis, the biological context is different. The malignant lymphoblasts crowd the bone marrow, specifically suppressing the production of mature neutrophils.<sup>17</sup> Therefore, a low NLR at diagnosis is a marker of severe bone marrow failure.

Recent studies have explored whether NLR can predict mortality or remission. In some adult contexts, an NLR > 3.28 was found to be a predictor of mortality, likely reflecting secondary infections or physiologic stress in patients who have already begun treatment.<sup>20</sup> In our cohort, the extremely low median ratio at diagnosis emphasizes that the "leukemic signature" in Surabaya is one of profound marrow replacement.

#### Hemoglobin-to-Platelet Ratio (HPR)

The median HPR of 0.3 is a relatively new parameter in pediatric oncology. In Immune Thrombocytopenic Purpura (ITP), a *high* HPR is associated with bleeding symptoms because it indicates a relative preservation of hemoglobin despite low platelets.<sup>25</sup> In our ALL cohort, the HPR is low, indicating that both lineages are suppressed simultaneously. This ratio could potentially serve as a simplified metric for bone marrow "shutdown" that is more sensitive than either Hb or Platelets alone.<sup>28</sup>

#### Monocyte-to-Neutrophil Ratio (MNR)

The median MNR of 1.3, with a maximum of 7660.0, is significant. In conditions like COVID-19 or AML, MNR has been investigated as an independent risk factor for mortality or therapy failure.<sup>26</sup> In ALL, a high MNR may indicate a "stress response" where the monocyte lineage is relatively preserved while neutrophils are severely depleted. This ratio provides an accessible marker of immune dysregulation in children who present with sepsis during induction.<sup>45</sup>

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## Analysis of the 48.1% Mortality Rate

The mortality rate of 48.1% is the most critical finding and requires contextualization. While this rate is significantly higher than the 10% seen in HICs, it is consistent with other reports from Indonesian tertiary centers. For example, a study at Hasan Sadikin Hospital in Bandung reported a mortality rate of 60.5%.<sup>3</sup>

Several factors likely contribute to this outcome in the Surabaya cohort:

- 1. Late-Stage Presentation:** As discussed, the severe anemia and high tumor burden indicators suggest many children arrive at the hospital with advanced disease.<sup>12</sup>
- 2. Infection-Related Mortality:** In LMICs, up to 35% of ALL deaths are caused by infections such as *Pseudomonas aeruginosa* or *Aspergillus fumigatus*, which often occur during the neutropenic phase of induction.<sup>45</sup>
- 3. Treatment Abandonment:** Socioeconomic burdens often lead parents to stop therapy before completion. Abandonment rates in Indonesia have historically been recorded as high as 10% to 25%.<sup>8</sup>
- 4. Tumor Lysis Syndrome:** Fatal metabolic derangements during the first two weeks of chemotherapy contribute to early mortality.<sup>30</sup>
- 5. Post-Pandemic Effects:** The period of 2022–2024 likely includes patients whose initial symptoms occurred during pandemic lockdowns when access to primary care was restricted.<sup>13</sup>

## Protocol Challenges and Healthcare Delivery

All patients in this cohort were treated based on the Indonesian Protocol ALL-2018. While this protocol has improved survival compared to previous versions, its success depends on meticulous adherence.<sup>32</sup> Research has indicated that Indonesian health-care providers sometimes fail to document all high-risk criteria, such as lymphoblast count on day 8 of chemotherapy, which can lead to inadequate treatment intensification for high-risk patients.<sup>3</sup>

Moreover, the lack of advanced diagnostics—such as flow cytometry for Minimal Residual Disease (MRD) or molecular testing for Philadelphia chromosome translocation t(9;22)—means that some patients may be under-stratified and receive less intensive therapy than they biologically require.<sup>9</sup> In HICs, molecular features like the *ETV6::RUNX1* fusion gene are used

to identify favorable outcomes, but in Surabaya, risk grouping still relies heavily on age and leukocyte count.<sup>6</sup>

## Limitations and Strengths of the Study

This study has inherent limitations that warrant careful interpretation. First, the retrospective design limits causal inference and is vulnerable to missing or incomplete records (e.g., some nutritional or socioeconomic variables). Second, outcome ascertainment may be incomplete because treatment abandonment and external transfers can obscure true survival status, possibly biasing mortality estimates upward or downward. Third, lack of molecular/cytogenetic and MRD data prevents correlation of hematological indices with established biological risk markers. Fourth, no multivariable modeling was performed to adjust for potential confounders (e.g., age, WBC, nutritional status) — future analytic studies should evaluate independent predictive value of NLR/HPR/MNR. Despite these limitations, the cohort is large and contemporaneous (2022–2024), providing a valuable snapshot of current clinical realities at a major Indonesian tertiary center.

**Strengths.** Large single-center sample size, comprehensive inclusion of derived hematological ratios, and relevance in a post-pandemic recovery period add practical value for clinicians in similar settings.

## Conclusion

The clinical and hematological characterization of 385 pediatric ALL patients at Dr. Soetomo General Hospital between 2022 and 2024 reveals a challenging landscape for pediatric oncology in East Java. The demographic profile confirms a male-skewed population with a peak incidence at 5.5 years. The hematological presentation is severe, characterized by profound anemia, critical thrombocytopenia, and a very low median NLR (0.1). Nearly half of the patients (48.1%) died during the study period, highlighting the persistent survival gap in Indonesian tertiary care.

## Recommendations

### Clinical Practice

- 1. Immediate Nutritional Intervention:** Every child diagnosed with ALL should undergo immediate nutritional screening and receive aggressive dietary support, as more than 25% of patients present with significant weight deficits.

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- 2. Sepsis Vigilance:** Given the profound neutropenia evidenced by the low NLR and ANC, clinicians must maintain a low threshold for starting broad-spectrum antibiotics and antifungal prophylaxis during the induction phase.
- 3. Biomarker Recording:** Simple ratios like HPR and MNR should be routinely calculated and entered into the patient's record to assist in preliminary severity assessment where molecular testing is unavailable.

## Public Health and Policy

- 1. Early Detection Education:** Regional healthcare networks must train primary care physicians and nurses on the "red flags" of childhood cancer to reduce the diagnostic lag that leads to severe presentation.
- 2. Strengthening IPCAR Registry:** Continued support for the national cancer registry is vital for identifying geographic clusters of late-stage presentation and targeting resources effectively.
- 3. Molecular Diagnostic Expansion:** Efforts should be made through the BPJS system to provide centralized access to cytogenetic and molecular testing, as morphology-based risk stratification is no longer sufficient to achieve 90% survival goals.

## Future Research

- 1. Analytic Cohort Studies:** Future research should evaluate the specific prognostic cut-off values for NLR, PLR, and HPR in pediatric ALL to determine if they can effectively supplement the current stratification markers.
- 2. Qualitative Barriers:** Studies investigating the reasons for treatment abandonment and late presentation in the Surabaya region are necessary to design culturally appropriate interventions.

By addressing the clinical and systemic vulnerabilities identified in this 2022–2024 cohort, Indonesia can move closer to achieving the survival standards enjoyed by developed nations and ensure that every child with ALL has the best possible chance for a cure.

## Author Contribution

Study conception and design: PAN, AC; Data collection: MCSL, MRA; Analysis: IDGU, RPA;

Manuscript drafting: PAN, AC; All authors reviewed and approved the final manuscript.

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The authors declare the study received no funding.

## Conflict of Interest

The authors declare that there is no conflict of interest.

## Ethical Approval

The study was conducted in accordance with the ethical standards of the Helsinki Declaration. Ethical approval and informed consent were not required for this study as it was based on secondary analysis of publicly available, aggregated data that did not contain any personal identifiers.

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