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COMPARISON OF NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS BEFORE AND AFTER INDUCTION CHEMOTHERAPY

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ABSTRACT
Acute Lymphoblastic Leukemia (ALL) is the most common hematologic malignancy in children. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are simple inflammatory biomarkers that may serve as prognostic and therapeutic response indicators. The aim of this research is to evaluate the differences in NLR and PLR before and after induction chemotherapy and to determine optimal cut-off values for predicting treatment response in pediatric ALL patients. An observational analytic study with a retrospective design was conducted on 48 pediatric ALL patients at Adam Malik General Hospital, Medan. Data were obtained from medical records between January 2023 and December 2024. Consecutive sampling was applied on this study. The Wilcoxon test was applied to assess differences in NLR and PLR, while ROC analysis was used to determine cut-off values, sensitivity, and specificity. Most patients were under 10 years of age (66.7%) and male (58.3%). Following induction chemotherapy, 87.5% achieved complete remission. Significant differences in NLR and PLR were observed before and after therapy ($p<0,001$). The optimal cut-off for NLR was 2.33 (sensitivity 45.2%, specificity 83.3%), while for PLR it was 219.98 (sensitivity 42.9%, specificity 83.3%). NLR and PLR significantly changed after induction chemotherapy in pediatric ALL patients. Despite limited sensitivity, both markers may serve as simple hematological tools for evaluating treatment response.

Keywords: induction phase chemotherapy; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio

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INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a malignant proliferation of lymphoid cells characterized by maturation arrest at an early stage, affecting the bone marrow, blood, and extramedullary sites (Malard & Mohty, 2020). It is the most common childhood cancer, with an annual incidence of 3.5 cases per 100,000 children in the United States and 2.5–4.0 per 100,000 in Indonesia, accounting for approximately 2,000–3,200 new cases per year. Patients with ALL require comprehensive laboratory evaluations, including complete blood count, peripheral smear, and biochemical assessments. L-asparaginase, a key component of ALL therapy, is associated with a reduction in coagulation factors such as fibrinogen (Howlader et al., 2019; Suzanna et al., 2007).

The neutrophil-to-lymphocyte ratio (NLR) has been proposed as a prognostic marker in several solid tumors, including hepatocellular carcinoma, non–small cell lung cancer, and gastric cancer. Similarly, platelet activation during systemic inflammation promotes tumor proliferation, and the platelet-to-lymphocyte ratio (PLR) has also been studied as a prognostic factor. Combining NLR and PLR has been suggested as a useful prognostic tool in malignancies; however, evidence in ALL remains limited (Zhang et al., 2021). Therefore, this study aims to evaluate differences in NLR and

PLR before and after induction chemotherapy and to determine their optimal cut-off values for predicting treatment response in pediatric ALL patients.

METHOD

This retrospective analytic study evaluated changes in neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) before and after induction chemotherapy in children with acute lymphoblastic leukemia (ALL) at Haji Adam Malik General Hospital, Medan. Data were obtained from medical records between January 2023 and December 2024. A total of 48 patients were enrolled using consecutive sampling. Eligible subjects were 1–16 years old, diagnosed with ALL, and completed the 7-week induction protocol. Patients with incomplete records, early death, or severe comorbidities were excluded. Collected variables included demographics, ALL classification, chemotherapy protocol, blood counts, NLR, and PLR. NLR and PLR were calculated from absolute neutrophil, lymphocyte, and platelet counts. Data were collected from medical records and laboratory results. Analyses were performed using SPSS v24 with descriptive statistics, paired t-test or Wilcoxon test according to data distribution, and ROC analysis for cut-off determination. Ethical approval was granted by the Universitas Sumatera Utara Ethics Committee (No. 108/KEPK/USU/2025).

RESULT

Table 1.
Characteristics of ALL patients and response to induction chemotherapy (n = 48)

Characteristics	n (%) / Mean ± SD
Age, n (%)	
<10 years	32 (66.7)
≥10 years	16 (33.3)
Sex, f (%)	
Male	28 (58.3)
Female	20 (41.7)
Chemotherapy protocol, f (%)	
Standard-risk ALL	31 (64.6)
High-risk ALL	17 (35.4)
FAB classification, f (%)	
LLA-L1	41 (85.4)
LLA-L2	7 (14.6)
LLA-L3	0
Treatment response, f (%)	
Complete remission	42 (87.5)
Partial remission	6 (12.5)
Hemoglobin (Mean ± SD, g/dL)	
Before induction	9.57 ± 2.99
After induction	11.64 ± 1.74
Leukocyte count (Mean ± SD, /µL)	
Before induction	15,999 ± 27,150.25
After induction	9,180 ± 10,550.01
Platelet count (Mean ± SD, /µL)	
Before induction	129,267 ± 155,534.90
After induction	397,750 ± 584,560.70
NLR (Mean ± SD)	
Before induction	1.35 ± 2.15
After induction	2.38 ± 2.25
PLR (Mean ± SD)	
Before induction	69.75 ± 108.99
After induction	5,521.15 ± 34,192.03

A total of 48 pediatric ALL patients were included. Most were <10 years old (66.7%) and male (58.3%). Standard-risk ALL accounted for 64.6% of cases, and FAB classification was dominated by LLA-L1 (85.4%). Complete remission was achieved in 87.5% of patients, while 12.5% had partial remission. After induction chemotherapy, mean hemoglobin increased from 9.57 to 11.64

g/dL and platelet counts from 129,267 to 397,750/µL, while leukocyte counts decreased from 15,999 to 9,180/µL. NLR rose from a mean of 1.35 to 2.38, and PLR from 69.76 to 5,521.16. (Table 1).

Bivariate analysis using the Shapiro–Wilk test showed that data were not normally distributed (p = 0.001), thus the Wilcoxon signed-rank test was applied. Both NLR and PLR increased significantly after induction chemotherapy. Median NLR rose from 0.38 to 1.68 (p = 0.001), while PLR increased from 17.36 to 152.50 (p = 0.001). Subgroup analysis showed that pre-induction NLR was significantly higher in patients ≥10 years (p = 0.017), and post-induction NLR was higher in males (p = 0.043). No significant differences were observed in PLR by age or sex.

ROC curve analysis indicated poor discriminatory ability of both markers. For NLR, the AUC was 0.544 with a cut-off ≥2.33 (sensitivity 45.2%, specificity 83.3%, PPV 95.0%, NPV 17.9%). For PLR, the AUC was 0.579 with a cut-off ≥219.98 (sensitivity 42.9%, specificity 83.3%, PPV 94.7%, NPV 17.2%). Both markers demonstrated very high PPV (>94%), suggesting their potential utility to confirm poor response, but limited sensitivity and overall efficacy.

Table 2.
Comparison of NLR and PLR before and after induction chemotherapy

Variable	Median (Min–Max)	p-value
NLR		
Before induction	0.38 (0.02–10.25)	0.001
After induction	1.68 (0.02–12.86)	
PLR		
Before induction	17.36 (0.15–445.13)	0.001
After induction	152.50 (1.04–237,155.96)	

Table 3.
Subgroup analysis of NLR and PLR by age and sex

Variable	<10 years	≥10 years	p	Male	Female	p
NLR (before)	0.25 (0.02–5.36)	1.19 (0.07–10.25)	0.017	0.28 (0.02–10.25)	0.68 (0.07–6.22)	0.369
NLR (after)	1.82 (0.35–12.86)	1.68 (0.02–3.00)	0.115	2.50 (0.12–6.47)	1.43 (0.02–12.86)	0.043
PLR (before)	17.36 (0.15–223.19)	16.35 (0.17–445.13)	0.457	14.81 (0.22–373.78)	19.20 (0.15–445.13)	0.900
PLR (after)	159.95 (2.95–237,155.96)	144.36 (1.04–481.61)	0.457	219.98 (1.04–237,154.92)	131.76 (2.95–922.53)	0.127

Table 4.
Diagnostic performance of NLR and PLR after induction chemotherapy

Parameter	AUC	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Efficacy (%)
NLR	0.544	2.33	45.2	83.3	95.0	17.9	50.0
PLR	0.579	219.98	42.9	83.3	94.7	17.2	47.9

DISCUSSION

This study evaluated changes in neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) before and after induction chemotherapy in 48 pediatric ALL patients. Most patients were younger than 10 years, consistent with global evidence showing ALL peaks in early childhood and is the most common pediatric malignancy (Cancer Research UK, 2024; Kiem Hao et al., 2020; Ekpa et al., 2023). Male predominance was also observed, as previously reported in Indonesia and Vietnam, with genetic polymorphisms such as ARID5B, ERCC1, HLA-DRA, and IFNG linked to male-specific risk (Nagaraj et al., 2022; Chang et al., 2024). The majority of cases were standard risk and FAB L1, findings that align with favorable prognostic features in younger children and those with lower leukocyte counts (Khandelwal et al., 2023; Kakaje et al., 2020; Ur Rahman et al.,

2021). Complete remission was achieved in 87.5% of patients, which is comparable to studies from Egypt, China, and Brazil (Rahman Sayed et al., 2016; Gao et al., 2014; Lopes Araújo Oliveira et al., 2016). Hemoglobin increased after induction, reflecting bone marrow recovery, while leukocyte counts decreased, consistent with blast clearance during induction (Patologi Klinik et al., 2017; Garbim et al., 2022; Wicaksono et al., 2023; Syntia et al., 2017).

This study found that NLR increased after induction (0.38 to 1.68), differing from results in Egypt where NLR decreased in patients who achieved remission (Chen et al., 2021). Elevated NLR reflects neutrophil predominance, impaired immunity, and worse prognosis, while low NLR indicates stronger antitumor immune activity (Nagaraj et al., 2022; Chen et al., 2021). Previous studies identified cut-offs of 2.8 in India and >10 in Croatia, both associated with poorer survival (Nagaraj et al., 2022; Lucijanic et al., 2018). PLR also increased significantly (17.36 to 152.50). High PLR is associated with systemic inflammation, platelet-driven angiogenesis, and tumor protection, and has been correlated with adverse outcomes in multiple cancers (Nagaraj et al., 2022; Buergy et al., 2012).

ROC curve analysis confirmed limited prognostic ability for both markers. NLR showed an AUC of 0.544 with a cut-off of 2.33, sensitivity of 45.2%, and specificity of 83.3%. PLR had an AUC of 0.579 with a cut-off of 219.98, sensitivity of 42.9%, and specificity of 83.3%. Despite low sensitivity, both NLR and PLR demonstrated very high positive predictive values above 94 percent, suggesting their greater value lies in confirming poor response rather than excluding it. These findings are consistent with prior studies reporting low sensitivity but moderate specificity of inflammatory indices for ALL prognosis (Nagaraj et al., 2022; Lucijanic et al., 2018).

Pathophysiologically, high NLR reflects a pro-inflammatory state with relative lymphopenia that compromises antitumor immunity, while high PLR reflects platelet activation supporting angiogenesis and tumor progression. Although simple and inexpensive, NLR and PLR alone have limited prognostic value. Their clinical utility may be enhanced when combined with minimal residual disease (MRD), systemic immune-inflammation index (SII), or molecular biomarkers for more comprehensive risk stratification. (Templeton et al., 2014; Buergy et al., 2012). This study has several limitations, including its retrospective design, absence of immunophenotyping, cytogenetics, and MRD evaluation, and restriction to the induction phase. Prospective longitudinal studies are needed to confirm the prognostic role of NLR and PLR throughout the treatment course.

CONCLUSION

This study demonstrated that both neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) significantly increased after induction chemotherapy in pediatric acute lymphoblastic leukemia (ALL) patients. Although both markers showed limited sensitivity and overall prognostic performance, their high positive predictive values suggest they may be useful in confirming poor therapeutic response rather than excluding it. These findings highlight that NLR and PLR, as simple and inexpensive hematological indices, could serve as supportive parameters in treatment evaluation but should not be used as standalone predictors. Their clinical utility may be enhanced when combined with minimal residual disease (MRD) assessment, systemic immune-inflammation index (SII), or molecular biomarkers to achieve more accurate risk stratification. Prospective longitudinal studies are warranted to validate their role across all treatment phases.

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