The Relationship Between Leukocytosis and Lymphopenia and the Clinical Outcome of Pneumonia in Toddlers Aged 12-59 Months

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Abstract

Pneumonia is an acute infection of the lung parenchyma that commonly affects children under five years of age and remains a leading cause of pediatric morbidity and mortality worldwide. The inflammatory response to pneumonia is accompanied by alterations in hematological parameters, including leukocytosis and lymphopenia, which may reflect disease severity. This study aimed to evaluate the association between leukocyte and lymphocyte counts and clinical outcomes in toddlers hospitalized with pneumonia at Budhi Asih Regional Hospital. This observational analytical study employed a cross-sectional design using medical records of 117 toddlers diagnosed with pneumonia. Leukocytosis was defined as a leukocyte count of >15,500 cells/µL, while lymphopenia was defined as a lymphocyte count of <2,000 cells/µL. Clinical outcomes were categorized as improvement or deterioration. Associations between hematological parameters and clinical outcomes were analyzed using the Chi-square test, and effect sizes were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Leukocytosis was significantly associated with clinical deterioration (OR = 24.27, 95% CI: 6.97–84.52; p < 0.001). Likewise, lymphopenia was significantly associated with unfavorable clinical outcomes (OR = 3.05, 95% CI: 1.13–8.26; p = 0.024). A significant association was also observed between leukocyte and lymphocyte abnormalities (p = 0.004). Children with leukocytosis and lymphopenia were more likely to experience clinical deterioration than those without these hematological abnormalities. These findings suggest that leukocytosis and lymphopenia are significantly associated with clinical outcomes in toddlers with pneumonia and may serve as useful adjunctive laboratory markers in clinical assessment. However, because of the cross-sectional design, causal or prognostic inferences cannot be established. Prospective longitudinal studies are warranted to validate their predictive value for disease progression and clinical outcomes.

Keywords: Clinical Outcomes, Leukocytes, Lymphocytes, Toddler Pneumonia

INTRODUCTION

Pneumonia remains one of the leading causes of morbidity and mortality among children under five years of age worldwide, particularly in low- and middle-income countries. In Indonesia, pneumonia continues to pose a significant public health challenge despite improvements in immunization coverage and child health services. The disease is caused by a wide range of bacterial and viral pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and respiratory syncytial virus (RSV). Toddlers aged 12–59 months are particularly vulnerable because of their immature immune system and increased exposure to respiratory pathogens (Lokida et al., 2022; Prawidia et al., 2023; Purnama et al., 2025). Recent global estimates continue to identify pneumonia as one of the leading infectious

causes of death among children under five years of age, highlighting the importance of early identification of children at risk of poor clinical outcomes.

Clinical outcomes in pediatric pneumonia are commonly categorized as either improvement or deterioration based on indicators of clinical recovery, including resolution of fever, normalization of respiratory rate, and maintenance of adequate oxygen saturation. Children wo experience clinical deterioration are at increased risk of treatment failure, prolonged hospitalization, complications, and mortality. Therefore, the identification of simple and readily accessible laboratory markers associated with clinical outcomes may facilitate early risk stratification and support clinical decision-making in hospitalized toddlers with pneumonia (Adbela et al., 2024; Alemu et al., 2025; Anteneh et al., 2023; Jakhar et al., 2018; Qawasmeh et al., 2020; Schuh et al., 2023).

Leukocytes and lymphocytes play essential roles in the host immune response to infection. Leukocytosis reflects activation of the innate immune response through cytokine-mediated stimulation of leukopoiesis during acute inflammation, whereas lymphopenia may result from lymphocyte redistribution, apoptosis, or immune dysregulation in the setting of severe infection. Previous studies have demonstrated that elevated leukocyte counts and reduced lymphocyte counts are associated with increased disease severity and poorer outcomes among children with pneumonia. However, findings have been inconsistent across populations, and most studies have focused on disease severity or mortality rather than overall clinical outcomes (Delves et al., 2017; Dudognon et al., 2021; Elçioğlu et al., 2023; Pervin et al., 2024). Although leukocyte and lymphocyte counts are routinely measured as part of complete blood counts, evidence regarding their association with clinical outcomes among Indonesian toddlers hospitalized with pneumonia remains limited. In particular, few studies have evaluated leukocytosis using a cut-off of >15,500 cells/μL and lymphopenia using a cut-off of <2,000 cells/μL in relation to clinical improvement or deterioration. Establishing the clinical relevance of these readily available laboratory parameters could provide an inexpensive and practical adjunct for early risk assessment in resource-limited hospital settings.

Therefore, this study aimed to determine the association between leukocytosis and lymphopenia and clinical outcomes among toddlers aged 12–59 months hospitalized with pneumonia at Budhi Asih Regional Hospital. We hypothesized that leukocytosis (>15,500 cells/μL) and lymphopenia (<2,000 cells/μL) would be significantly associated with clinical deterioration among hospitalized toddlers with pneumonia.

METHODS

This observational analytical study employed a retrospective cross-sectional design using secondary data obtained from medical records. A cross-sectional approach was selected because leukocyte count, lymphocyte count, and clinical outcomes were extracted from the same hospitalization episode to evaluate their associations rather than to establish temporal or causal relationships. The study was conducted at Budhi Asih Regional General Hospital, Jakarta. Data collection, processing, and analysis were performed between August and December 2025, using medical records of patients hospitalized during January 2024–July 2025.

The study population consisted of toddlers aged 12–59 months who were hospitalized with a diagnosis of pneumonia at Budhi Asih Regional General Hospital. Total sampling was employed, whereby all eligible patients during the study period were included. A total of 117 medical records met the eligibility criteria and were included in the analysis. The inclusion criteria were: (1) toddlers aged 12–59 months with a physician diagnosis of pneumonia; (2) hospitalization at Budhi Asih Regional General Hospital between January 2024 and July 2025; and (3) complete medical records containing leukocyte count, lymphocyte count, and clinical outcome data. Patients with severe concomitant infectious diseases or incomplete medical records were excluded.

Leukocytosis was defined as a leukocyte count of >15,500 cells/µL, while lymphopenia was defined as a lymphocyte count of <2,000 cells/µL, based on pediatric reference values reported in previous studies. Clinical outcomes were classified as improved (resolution of fever, oxygen saturation ≥95%, normal respiratory rate, and discharge with clinical improvement) or deteriorated (persistent or worsening respiratory symptoms requiring escalation of treatment, prolonged hospitalization, referral to intensive care, or death).

Data were extracted from hospital medical records using a standardized data collection form by trained members of the research team. Medical records were reviewed for completeness and consistency before analysis. Records with missing information on the primary study variables were excluded to ensure data quality.

Data were analyzed using IBM SPSS Statistics version 30. Univariate analyses were performed to describe patient characteristics. Associations between leukocytosis, lymphopenia, and clinical outcomes were evaluated using the Chi-square test or Fisher's exact test as appropriate. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from 2×2 contingency tables to estimate the strength of associations. Because of the relatively small sample size and the retrospective design, multivariable logistic regression was

not performed. Consequently, potential confounding factors including age, sex, nutritional status, and comorbidities, were not adjusted for and should be considered when interpreting the findings. Statistical significance was defined as $p < 0.05$.

This study was approved by the Ethics Committee of the Institute for Research and Community Service (LPPM), Universitas Kristen Indonesia (UKI), under Ethical Clearance Number: 085/UKI.LPPM/PPM.00.00/ET.2024. Because the study used retrospective, anonymized medical record data, the requirement for informed consent was waived by the ethics committee.

RESULTS

Table 1. Characteristics of Toddler Patients with Pneumonia at Budhi Asih Regional Hospital in 2024-2025

Characteristic	Frequency	Percentage
Gender		
Male	71	60.7
Female	46	39.3
Age (Months)	31.22 ± 12.36	
Leukocytes		
Normal	100	85.5
Increase	17	14.5
Lymphocytes		
Normal	65	55.6
Decrease	52	44.4
Clinical outcomes		
Improvement	96	82.1
Deterioration	21	17.9

A total of 117 toddlers with pneumonia were included in this study. Most patients were male (71/117, 60.7%), while 46 (39.3%) were female. The mean age was 31.22 ± 12.36 months. Based on laboratory findings, 100 patients (85.5%) had normal leukocyte counts (5,500–15,500 cells/µL), whereas 17 (14.5%) had leukocytosis (>15,500 cells/µL). Regarding lymphocyte counts, 65 patients (55.6%) had normal lymphocyte counts (2,000–5,000 cells/µL) and 52 (44.4%) had lymphopenia (<2,000 cells/µL). Most patients showed clinical improvement (96/117, 82.1%), while 21 (17.9%) experienced clinical deterioration (Table 1).

Table 2. The relationship between leukocytosis and clinical outcomes in toddlers with pneumonia at Budhi Asih Regional Hospital in 2024-2025

	Improvement	Deterioration	Total	OR (95% CI)	*p value*
Leukocytes 5,500-15,500	91	9	100	Reference	0.001
Leukocytes >15.500	5	12	17	24.27 (6.97–84.52)	
Total	96	21	117		

Among patients with normal leukocyte counts, 91 (91.0%) experienced clinical improvement, and 9 (9.0%) experienced clinical deterioration. In contrast, among patients with leukocytosis, 5 (29.4%) improved, and 12 (70.6%) deteriorated. Thus, a substantially higher proportion of children with leukocytosis experienced clinical deterioration than those with normal leukocyte counts. The association was statistically significant ($p < 0.001$). Children with leukocytosis had 24.27-fold higher odds of clinical deterioration than those with normal leukocyte counts (OR = 24.27; 95% CI: 6.97–84.52) (Table 2).

Table 3. Relationship Between Lymphopenia And Clinical Outcomes Of Toddlers With Pneumonia At Budhi Asih Regional Hospital in 2024- 2025

	Improvement	**Deterioration**	**Total**	**OR (95% CI)**	***p value***
Lymphocytes 2.000-5.000	58	7	65	Reference	0.024
Lymphocytes <2.000	38	14	52	3.05 (1.13–8.26)	
Total	96	21	117		

Among patients with normal lymphocyte counts, 58 (89.2%) showed clinical improvement and 7 (10.8%) experienced clinical deterioration. Among patients with lymphopenia, 38 (73.1%) improved and 14 (26.9%) deteriorated. A higher proportion of children with lymphopenia experienced clinical deterioration than those with normal lymphocyte counts. This association was statistically significant ($p = 0.024$). Children with lymphopenia had 3.05-fold higher odds of clinical deterioration compared with those with normal lymphocyte counts (OR = 3.05; 95% CI: 1.13–8.26) (Table 3).

Table 4. Relationship Between Leukocytosis And Lymphopenia In Pneumonia In Toddlers Aged 12-59 Months At Budhi Asih Regional Hospital

		Leukocytes					
		Normal	**%**	**increase**	**%**	**Total**	***p value***
Lymphocytes	2.000-5.000	61	93.8	4	6.2	65	.004
	<2000	39	75.0	13	25.0	52	
	Total	100		17		117	

A secondary analysis evaluated the association between leukocyte and lymphocyte abnormalities. Among patients with normal leukocyte counts, 61 (61.0%) had normal lymphocyte counts, and 39 (39.0%) had lymphopenia. Among patients with leukocytosis, 4 (23.5%) had normal lymphocyte counts and 13 (76.5%) had lymphopenia. The association between leukocytosis and lymphopenia was statistically significant ($p = 0.004$) (Table 4).

DISCUSSION

The present study yielded three principal findings. First, leukocytosis was significantly associated with unfavorable clinical outcomes in hospitalized children with pneumonia ($p < 0.001$). Second, lymphopenia was also significantly associated with clinical deterioration ($p =$

0.024). Third, leukocytosis and lymphopenia were significantly associated with each other (p = 0.004), suggesting that these hematological abnormalities frequently coexist during severe inflammatory responses.

The strongest association observed in this study was between leukocytosis and unfavorable clinical outcomes. Among children who experienced clinical deterioration, 57.1% had leukocytosis (>15,500 cells/mm³), whereas 42.9% had leukocyte counts within the normal range. These findings are consistent with previous studies demonstrating that elevated leukocyte counts are associated with greater disease severity and poorer clinical outcomes in pediatric pneunomia. Ningrum et al. reported that abnormal leukocyte counts increased the likelihood of severe pneumonia by more than sevenfold, whereas Ainurfaiz et al. observed an even stronger association between leukocytosis and respiratory failure. Similarly, Liu et al. identified leukocyte counts above 14.3×10^9/L as an indicator of refractory *Mycoplasma pneumoniae* pneumonia. Although the present study did not calculate an adjusted odds ratio, the highly significant association observed suggests that leukocytosis may serve as a useful marker of disease severity and an increased risk of clinical deterioration. Nevertheless, differences in study populations, pneumonia etiology, severity classification, and laboratory cut-off values should be considered when comparing the magnitude of associations across studies (Chen et al., 2025; Liu et al., 2025).

The association between leukocytosis and unfavorable clinical outcomes is biologically plausible. Leukocytosis reflects activation of the innate immune response following pulmonary infection. Pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1β, granulocyte colony-stimulating factor (G-CSF), and tumor necrosis factor-α (TNF-α), stimulate bone marrow production and release of neutrophils into the circulation. Although this response plays a critical role in pathogen clearance, excessive systemic inflammation may contribute to endothelial dysfunction, increased vascular permeability, diffuse alveolar damage, and progression to respiratory failure or sepsis. Therefore, leukocytosis should be interpreted as a marker of an exaggerated inflammatory response rather than a direct cause of clinical deterioration.

This study also demonstrated a significant association between lymphopenia and unfavorable clinical outcomes. Previous studies have similarly reported that reduced lymphocyte counts are associated with prolonged hospitalization, increased rates of intensive care unit (ICU) admission, and higher mortality among patients with pneumonia. Cilloniz et al. found that lymphopenic patients had longer hospital stays and higher mortality, while Errington et al. reported increased risks of shock, ICU admission, and death. Therefore, the

findings of the present study reflect impaired immune competence in patients with severe pneumonia (Cilloniz et al., 2021; Elçioğlu et al., 2023).

Several biological mechanisms may explain this association. During severe infection, excessive inflammatory cytokine production can induce apoptosis of circulating lymphocytes and suppress lymphopoiesis. In addition, activated lymphocytes may migrate from the peripheral circulation to infected pulmonary tissue, contributing to reduced lymphocyte counts. Persistent lymphopenia may also reflect immune exhaustion, which can impair adaptive immune responses and reduce the efficiency of pathogen clearance. Consequently, lymphopenia is likely to represent a marker of immune dysregulation associated with severe infection rather than a direct cause of unfavorable clinical outcomes (Hamilton et al., 2020; Mert & Merdin, 2020; Putri et al., 2023).

Several previous studies cited in this discussion investigated lymphopenia among patients with coronavirus disease (COVID-19). Although viral pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) differs etiologically from community-acquired bacterial pneumonia in children, these studies remain relevant because they describe common immunopathological mechanisms, including systemic inflammation, cytokine-mediated lymphocyte apoptosis, and immune dysregulation. Nevertheless, the direct applicability of COVID-19 studiesto pediatric pneumonia in general should be interpreted with caution, as immune responses may vary according to the causative pathogen, patient age, and underlying clinical characteristics (Corica et al., 2022; Huang et al., 2020).

A significant association was also observed between leukocytosis and lymphopenia. Rather than representing independent abnormalities, these hematological findings may occur simultaneously during severe systemic inflammation. Leukocytosis reflects activation of innate immunity, whereas lymphopenia reflects suppression or redistribution of adaptive immune responses. The coexistence of these abnormalities may therefore indicate an imbalance between innate and adaptive immunity, which has been associated with more severe infection in several studies. However, because our study was cross-sectional, it cannot determine whether one abnormality precedes the other or whether both develop concurrently during disease progression. Although statistically significant associations were identified, several potential confounding factors should be considered when interpreting these findings.

Nutritional status, immunization history, exclusive breastfeeding, underlying comorbidities, pathogen type (viral, bacterial, or mixed infection), severity of pneumonia at presentation, prior antibiotic therapy, corticosteroid use, dehydration, co-infections, and the duration between symptom onset and hospital admission may all influence leukocyte and

lymphocyte counts independently of clinical outcome. Because these variables were not included in the present analysis, residual confounding cannot be excluded.

Despite these limitations, the findings have important clinical implications. Complete blood count testing is inexpensive, rapid, and routinely available even in resource-limited healthcare settings. Leukocyte and lymphocyte counts may therefore serve as practical adjunctive prognostic markers to assist clinicians in early risk stratification, identify children requiring closer monitoring, and support timely referral or escalation of care. However, these laboratory parameters should always be interpreted together with clinical assessment and other laboratory findings rather than being used as standalone prognostic indicators.

This study has several limitations. First, its retrospective design relied on medical records, which may contain incomplete or inconsistent clinical information. Second, the study was conducted in a single referral hospital, limiting the generalizability of the findings to other healthcare settings. Third, the relatively small sample size may have reduced statistical power and the precision of the observed associations. Fourth, multivariable analysis was not performed; therefore, potential confounding variables could not be adjusted. Fifth, selection bias may have occurred because only patients with complete laboratory records were included. Finally, the cross-sectional design precludes establishing temporal or causal relationships between hematological abnormalities and clinical deterioration.

Future prospective multicenter cohort studies with larger sample sizes are needed to validate these findings. Incorporating multivariable regression analyses and controlling for important clinical confounders including nutritional status, vaccination history, breastfeeding history, comorbidities, pathogen type, disease severity, prior antibiotic exposure, corticosteroid use, and time from symptom onset would provide more robust evidence regarding the prognostic value of leukocyte and lymphocyte counts in pediatric pneumonia.

CONCLUSIONS

The present study demonstrated significant associations between leukocytosis, lymphopenia, and unfavorable clinical outcomes among hospitalized toddlers with pneumonia at Budhi Asih Regional Hospital. In addition, leukocyte and lymphocyte counts were significantly associated with each other, suggesting that these hematological abnormalities frequently coexist during more severe inflammatory responses. Given the cross-sectional and retrospective nature of this study, these findings should be interpreted as associations rather than evidence of prognostic or causal relationships. Nevertheless, the observed associations suggest that leukocyte and lymphocyte counts, which are inexpensive and routinely available

laboratory parameters, may assist clinicians in identifying toddlers at higher risk of clinical deterioration when interpreted alongside clinical assessment. Larger prospective multicenter cohort studies incorporating multivariable analyses are warranted to validate these findings, evaluate their independent prognostic value, and support the development of clinically applicable risk prediction models. Early recognition of leukocytosis and lymphopenia may facilitate closer monitoring and more timely management of children with pneumonia, particularly in resource-limited healthcare settings.

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