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White Blood Cell Count and Neutrophil-Lymphocyte Ratio in Children with Complicated and Uncomplicated Pneumonia

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Abstract:
Purpose: Community-acquired pneumonia (CAP) remains one of the leading causes of morbidity and mortality among children, particularly those under the age of five. This study aimed to compare white blood cell (WBC) count and neutrophil-lymphocyte ratio (NLR) between children with complicated and uncomplicated pneumonia hospitalized at Dr. Soetomo Hospital Surabaya.
Research methodology: This retrospective study evaluated 49 children hospitalized with CAP from January to October 2021. Pneumonia was diagnosed based on symptoms (fever, cough, dyspnea) and physical findings (tachypnea, chest indrawing, rales). The comparison of WBC count and NLR of children with and without pneumonia complications was made using the Mann-Whitney U test.
Results: Of the 49 patients, 28 (57.1%) were male and 40 (81.6%) were under five years old. The median hospital stay was 7 (Interquartile Range [IQR] 4.5 – 9) days. Nine patients (18.4%) had complications, including pneumothorax (33%) and sepsis (22%). Patients with complications had higher median WBC counts (19.5 [IQR 7.2 – 25.1] vs. 12.7 [IQR 10.7 – 15.7] x103/mm3, p=0.224). Similarly, the median NLR was found higher in the complicated pneumonia group (2.9 [IQR 1.5 – 10.8]) than uncomplicated group (1.7 [IQR 0.9 – 4.4], p=0.178).
Limitations: The few sample size and retrospective nature of the study limits the generalizability of the findings. Future studies with larger sample sizes and the inclusion of additional biomarkers are warranted to confirm our findings.
Contribution: These trends suggest potential utility of WBC count and NLR as biomarkers for pneumonia severity, warranting further research with larger cohorts.
Keywords: *children, pneumonia, WBC count, NLR*
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1. Introduction

Community-acquired pneumonia (CAP) poses a major public health concern, particularly among pediatric populations. CAP is one of the primary causes of illness and mortality globally, particularly affecting children under five years of age (Kapoor, Awasthi, & Kumar Yadav, 2022). The rate of hospitalizations due to CAP remains high, reflecting the ongoing need for effective diagnostic and therapeutic strategies. Pneumonia is responsible for about 15% of all deaths in children under five globally, with the greatest impact seen in low- and middle-income countries (Organization, 2017).

Blood parameters, including white blood cell (WBC) count and neutrophil-lymphocyte ratio (NLR), have been increasingly recognized as potential biomarkers for assessing the severity and prognosis of pneumonia (Okay, Okay, Hatipoglu, Akkoc, & Sahin, 2024; Visuddho Visuddho, Subagjo, Setyoningrum, & Rosyid, 2021; Yildiz, Cigri, Dincer, Narsat, & Calisir, 2021). Elevated WBC counts and NLRs have been associated with poorer outcomes. The WBC count is component of the body's immune response to infection, and an elevated WBC count often indicates an ongoing inflammatory process. This makes it a commonly used parameter in clinical settings to assess the body's response to infectious diseases, including pneumonia (Kourilovitch & Galarza–Maldonado, 2023; Zhang, Peng, & Zheng, 2024).

The identification and utilization of reliable biomarkers are crucial for improving the quality of care in pediatric pneumonia (Kapoor, Awasthi, & Kumar Yadav, 2022). By differentiating between complicated and uncomplicated cases, healthcare providers can tailor treatment strategies more effectively, potentially reducing the duration of hospital stays (Le Saux, Robinson, Society, Diseases, & Committee, 2015). However, the evidence on the ability of WBC and NLR to differentiate between complicated and uncomplicated pneumonia still varied. Addressing this gap is critical to conclude the usefulness of these markers that offer guidance into more precise therapeutic interventions. This study aims to compare the WBC count and NLR between children with complicated and uncomplicated pneumonia who were hospitalized at Dr. Soetomo Hospital Surabaya. This study provide valuable data that could answer are the common blood diagnostic marker could inform the likelihood to complicated pneumonia.

2. Literature Review

The WBC count has long been recognized as a standard marker for detecting bacterial infections, including pneumonia in children. When a pathogen invades the respiratory tract, the immune response is initiated, leading to an increase in circulating leukocytes, particularly neutrophils, which are responsible for phagocytosis (Grudzinska et al., 2020). Studies have consistently shown that children with complicated pneumonia, such as those with pleural effusion or empyema, tend to have higher WBC counts compared to those with uncomplicated cases (Gayretli-Aydın et al., 2016). However, WBC is a non-specific marker, and its elevation can be influenced by various factors, such as underlying chronic conditions or concurrent viral infections, which may limit its diagnostic specificity for predicting complications (Cetın, Kocaturk, Tufan, Kıraz, & Alatas, 2023) A systematic review also revealed poor evidence on leukocytosis alone as predictor of pneumonia severity (Dean & Florin, 2018).

Despite its widespread use, the role of WBC in predicting the severity or complications of pneumonia in children remains controversial. While elevated WBC levels indicate a good immune response, they do not necessarily correlate with the degree of lung involvement or the risk of severe outcomes, such as pleural effusion or empyema (Florin et al., 2020). Additionally, there is difference between bacterial and viral pneumonia in terms of WBC count. Elevated WBC counts are more commonly observed in bacterial infections, while viral causes typically present with normal or only slightly elevated WBC counts (Don, Valent, Korppi, & Canciani, 2009). This variability complicates the interpretation of WBC counts as a reliable prognostic marker in pediatric pneumonia and underscores the need for additional markers to improve diagnostic accuracy.

The NLR has emerged as a potentially more sensitive biomarker for evaluating the systemic inflammatory response in pediatric pneumonia (Russell et al., 2019). NLR reflects the balance between the innate immune response, dominated by neutrophils, and the adaptive immune response, primarily represented by lymphocytes. In case of bacterial pneumonia, an increased neutrophil count and decreased lymphocyte count are typically observed, leading to a higher NLR (Omran et al., 2022). This shift in immune cell populations reflects an acute inflammatory state, with neutrophils playing a key role in the early response to bacterial pathogens. Elevated NLR has been associated with more severe cases of pneumonia and an increased risk of complications, such as empyema or sepsis, in both adult and pediatric populations (Li et al., 2023; Wu et al., 2021). Recent studies suggest that NLR is a better predictor of disease severity and outcomes than WBC alone, making it a promising tool for clinicians to measure the risk of complications in children with pneumonia (Omran et al., 2022; Zhang et al., 2024).

The pathophysiology of NLR in pediatric pneumonia lies in its ability to capture the dynamic interplay between neutrophils and lymphocytes during infection. Neutrophils are the first responders to bacterial invasion, releasing reactive oxygen species and enzymes to destroy pathogens, but this response can also lead to tissue damage and increased inflammation if left unchecked (Craig, Mai, Cai, & Jeyaseelan, 2009; Grudzinska et al., 2020). A reduction in lymphocytes, which are crucial for resolving the infection and regulating the immune response, indicates an overwhelming inflammatory response. Thus, NLR not only reflects the acute inflammatory process but also provides insights into the imbalance of immune regulation during pneumonia, offering clinicians a more nuanced understanding of disease severity and prognosis (Kourilovitch & Galarza–Maldonado, 2023).

3. Methodology

3.1 Study Design and Participants

This study was retrospective cohort study conducted at Dr. Soetomo Hospital Surabaya, a tertiary care center, and included pediatric patients hospitalized with CAP between January and October 2021. The protocol was approved by the hospital's Ethical Review Board (Reference Number 1206/LOE/301.4.2/I/2023). Informed consent was obtained from the parents or guardians of all participants. Inclusion criteria encompassed children diagnosed with pneumonia based on clinical symptoms such as cough, fever, and dyspnea, supported by physical examination findings including tachypnea, chest indrawing, and rales. The exclusion criteria were children with pre-existing chronic conditions such as congenital heart disease, chronic lung disease, immunodeficiency, or malignancy.

3.2 Data Collection

Data were collected from medical records. The data collected including demographic information, clinical presentation, laboratory results, and clinical outcomes. The primary laboratory parameters of interest were the WBC count and NLR, which were obtained from peripheral blood samples at the time of admission. The NLR was calculated from the result of complete blood count by dividing the absolute neutrophil count to the absolute lymphocyte count. Additional data on comorbidities, previous antibiotic use, and vaccination status were also recorded to control for potential confounders.

3.3 Definition

The complicated pneumonia was defined as additional pathological conditions that following the primary disease in the lung parenchyma. The complications considered in this study included pleural effusion, empyema, pneumothorax, atelectasis, sepsis, and respiratory failure. Pleural effusion and pneumothorax was diagnosed through clinical examination and confirmed by chest X-rays and thoracocentesis. Atelectasis was defined as the collapse of lung tissue, confirmed through chest X-rays. Sepsis was diagnosed using systemic inflammatory response syndrome (SIRS) criteria. Respiratory failure was indicated by clinical sign (severe hypoxia, hypercapnia, or respiratory distress), blood gas analysis, and requirement of mechanical ventilation due to inadequate oxygenation or ventilation.

3.4 Statistical Analysis

Patients were categorized into two groups; first group was patients with uncomplicated pneumonia and the other was patients with complicated pneumonia. Continuous variables were presented by median (interquartile range [IQR]), while categorical variables were presened by count (percentage). The Fisher Exact test was used to compare between groups characteristics. The Mann-Whitney U test was used to compare the WBC count and NLR between the two groups, with a significance level set at 0.05. The IBM SPSS version 23.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analysis.

4. Result and discussion

The study cohort consisted of 49 children with CAP (Table 1). Total 28 (57.1%) participants were male and 40 (81.6%) were under the age of five. The median length of hospitalization was 7 (IQR 4.5 – 9) days. The median peripheral WBC count and NLR for the entire cohort was 12.7 (IQR 10.6 – 18.3) $x10^3/mm^3$ and 1.9 (IQR 1.0 – 4.7), respectively.

Table 1. Baseline characteristic of study participants

Variable	Total (49)	Complicated Pneumonia(9)	Uncomplicated Pneumonia(40)	*p* value
Gender				0.714
- Male	28 (57.1)	6 (66.7)	22 (55.0)	
- Female	21 (42.9)	3 (33.3)	18 (45.0)	
Age				0.336
- < 5 years old	40 (81.6)	6 (66.7)	34 (85.0)	
- ≥ 5 years old	9 (18.4)	3 (33.3)	6 (15.0)	
Hospitalization (day	7 (4.5 – 9)	14 (9 – 18.5)	6 (4 – 8)	<0.001*
WBC ($x10^3/mm^3$)	12.7 (10.6 – 18.3)	19.5 (7.2 – 25.1)	12.7 (10.7 – 15.7)	0.224
NLR	1.9 (1.0 – 4.7)	2.9 (1.5 – 10.8)	1.7 (0.9 – 4.4)	0.178

Note: The categorical data was presented as count (percent). The numerical data was presented as median (interquartile range). *significant p-value < 0.05

The median WBC count were higher in the group with complicated pneumonia (19.5 [IQR 7.2 – 25.1] $x10^3/mm^3$) compared to the group uncomplicated pneumonia (12.7 [IQR 10.7 – 15.7] $x10^3/mm^3$). Similarly, the median NLR was found higher in the complicated pneumonia group (2.9 [IQR 1.5 – 10.8]) than uncomplicated group (1.7 [IQR 0.9 – 4.4]). However, both differences did not reach statistical significance (p=0.224, p=0.178 respectively). Nine patients (18.4%) developed complications during their hospital stay (Table 2). Among these, three patients (33.3%) had pneumothorax, and two patients (22.2%) developed sepsis.

Table 2. Pneumonia with complications

Pneumonia with	Total 9
Pneumothorax	3 (33.3)
Sepsis	2 (22.2)
Atelectasis	2 (11.1)
Pleural Effusion	1 (11.1)
Respiratory Failure	1 (22.2)

Note: The categorical data was presented as count (percent).

4.1 Discussion

The findings of this study indicate that children with complicated pneumonia tend to have higher WBC counts and NLRs compared to those with uncomplicated pneumonia. Although this study did not find significant difference between groups, the trend suggests that these hematologic parameters could potentially serve as indicators of disease severity. The insignificant result may because of the limitation on sample size and the individual variability in immune responses to infection (Magee & Miller, 1970). Elevated WBC counts and NLRs have been reported in various studies as markers of systemic inflammation and immune response to infection (V Visuddho, Subagjo, Setyoningrum, & Rosyid, 2022; Zhang et al., 2024). These findings are consistent with other research in pediatric populations, which has demonstrated that high WBC counts are associated with more severe cases of pneumonia (Xie et al., 2024). Study on pediatric population in Makassar also reveal higher NLR in severe pneumonia compared to moderate pneumonia, but this difference was not statistically significant (Afiah, Handayani, & Kadir, 2023).

Cytokines, such as IL-6 and TNF-α, are released in response to bacterial infections and stimulate the production of neutrophils in the bone marrow (Esa et al., 2023). This cytokine-driven response results in an increased WBC count, predominantly due to neutrophilia, which reflects the body's attempt to combat the infection. The trends observed in this study may be explained by the fact that more severe infections trigger a stronger inflammatory response, resulting in higher WBC counts and NLRs (Farkas, 2020).

The clinical applicability of WBC count and NLR as prognostic markers in pediatric pneumonia warrants further investigation (Titova, Christensen, Henriksen, Steinshamn, & Åsberg, 2018). These markers could still be valuable in helping clinicians identify children at higher risk for complications, especially when combined with other diagnostic information. The ability to differentiate between complicated and uncomplicated pneumonia at the time of admission could facilitate more targeted and efficient management strategies (Xu et al., 2023). Children identified as having a higher risk of complications might benefit from closer monitoring, more aggressive treatment, or early interventions (Florin et al., 2020). Early interventions, including the prevention of malnutrition and support with active metabolites, may modulate the immune system in patients (Afifa, 2022; Heryandi, Susanti, & Samsuni, 2024; Khalidah, 2022; Nugraheni et al., 2024; Pereiz, Oksal, Chuchita, Sylvani, & Komara, 2024).

The variability results in WBC count and NLR among children with pneumonia underscores the complexity of the host immune response to infection. Factors such as the type of pathogen, host immune status, and comorbidity can all influence this parameter. Domnicu et al. (2023) Moreover, viral pneumonias, which are common in pediatric populations, may not elicit the same degree of neutrophil response as bacterial infections, further complicating the use of WBC and NLR as standalone prognostic tools. (Farida et al., 2023; Omran et al., 2022) Therefore, while these biomarkers provide valuable insights into the immune response, they should be used in conjunction with other diagnostic tools, such as radiographic imaging, microbiological cultures, or clinical scoring systems, to improve the accuracy of diagnosis.

5. Conclusion

This study highlights the role of WBC count and NLR as blood biomarkers for assessing the complication of pneumonia in children. Despite the lack of statistically significant differences, the observed trends underscore the need for further research to elucidate the clinical relevance of these parameters. Early identification of children at risk for complications could improve outcomes through timely and targeted interventions.

The strengths of this study lie in its focus on a well-defined pediatric population within a single tertiary care center, ensuring a high level of clinical and diagnostic consistency. However, several limitations exist in our study. The limited sample size restricts the generalizability of the findings. The reliance on medical records for data collection and restropective design cannot give best evidence for study result. Additionally, the study did not differentiate between viral and bacterial pneumonia, which can lead to different inflammatory responses and influenced the WBC count and NLR. Moreover, the lack of specific culture-proven cases limits the ability to conclusively determine pathogen-driven variations. Finally, the study did not include certain key parameters or biomarkers that could further enhance the understanding of pneumonia severity and etiology.

Future research should aim to include larger, multicenter cohort designs to validate these findings and exploring the utility of other biomarkers (e.g., C-reactive protein, procalcitonin) in conjunction with WBC count and NLR. Include a control group of healthy children or those with non-pneumonia respiratory infections for comparison may also enriched the results. WBC count and NLR could be incorporated with clinical parameters into predictive models for predicting the complicated pneumonia in children.

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