

Neutrophil-to-lymphocyte ratio and chest x-ray severity in pediatric pulmonary tuberculosis: A cross-sectional analytic study

Muhammad As Alukal Lutfa^{a,✉}, Muhammad Ricky Ramadhian^a, Wiwi Febriani^a, Retno Ariza Soeprihatini Soemarwoto^a

^a Faculty of Medicine, Universitas Lampung, Lampung, Indonesia

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ABSTRACT

Introduction: Pulmonary tuberculosis (TB) remains a major health problem in children, particularly in low- and middle-income countries. Early assessment of disease severity is essential to guide clinical management. The neutrophil-to-lymphocyte ratio (NLR) has been proposed as a simple inflammatory biomarker that may reflect disease burden. However, evidence in pediatric TB remains limited. This study aimed to determine the association between NLR and chest X-ray (CXR) severity in pediatric patients with pulmonary TB aged 0–18 years.

Methods: A cross-sectional analytic study was conducted at Dr. H. Abdul Moeloek Hospital, Bandar Lampung. Total sampling was applied, yielding 60 pediatric TB cases meeting inclusion and exclusion criteria. Secondary data were obtained from medical records, including baseline hematologic parameters and CXR severity classified as minimal, moderate, or extensive lesions. NLR values were categorized according to systemic inflammation levels. The Spearman correlation test was used to assess the association between NLR and CXR severity, with a significance threshold of $p < 0.05$.

Results: Most participants were toddlers aged 1–<5 years (40%). More than half had normal NLR values (51.6%), and the most frequent CXR severity category was moderate lesions (53.3%). Correlation analysis demonstrated no significant association between NLR and CXR severity ($r = -0.084$, $p = 0.524$). These findings indicate that NLR does not correspond to radiological severity in pediatric TB.

Conclusion: NLR appears unsuitable as a simple biomarker for predicting chest X-ray severity in pediatric pulmonary TB. Age-related immune immaturity and paucibacillary disease patterns in children may limit the utility of NLR in this population. Further studies with larger cohorts and additional inflammatory markers are recommended.

Keywords: Chest X-ray severity; Inflammation; Neutrophil-to-lymphocyte ratio; Pediatric tuberculosis; Radiological assessment.



✉ Correspondence: Faculty of Medicine, Universitas Lampung, Lampung, Indonesia
Email: masalukallutf@gmail.com



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INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious diseases worldwide, posing substantial morbidity and mortality across diverse age groups. Despite global advances in disease control, the burden of TB has not decreased as expected, with an estimated 10.8 million people affected in 2023, an increase from preceding years (WHO, 2024). Children constitute a particularly vulnerable population, accounting for approximately 15% of TB cases in low- and middle-income countries, where diagnostic challenges and limited access to high-quality health services contribute to under-recognition and delayed treatment (Amoura *et al.*, 2024). Pediatric pulmonary tuberculosis (PTB) is further complicated by its often-nonspecific clinical presentation, lower bacterial burden, and diagnostic limitations, making early and accurate assessment essential for optimal management and prevention of severe outcomes (Belot *et al.*, 2025). In Indonesia, the pediatric TB burden remains disproportionately high, including in several provinces such as Lampung, where cases continue to rise

In clinical practice, chest radiography remains a cornerstone tool in the diagnostic evaluation of PTB. Although imaging findings in children typically differ from those in adults, often characterized by mediastinal lymphadenopathy and limited parenchymal involvement, radiographic severity has been associated with disease burden and treatment outcomes (Bettuzzi, Sanchez-Pena, and Lebrun-Vignes, 2024). Previous studies have demonstrated that radiographic scoring systems can help predict bacterial load, the extent of lung involvement, and clinical progression. Notably, pretreatment chest X-ray severity has been shown to correlate with smear positivity and bacillary burden in adult TB, suggesting its potential utility as a surrogate marker of disease severity. However, the applicability of these findings to pediatric populations is uncertain due to differences in immune maturation, pathophysiology, and radiographic patterns (Chen, Mat Isa, and Liu, 2025).

In parallel with imaging-based assessment, hematological biomarkers have emerged as simple, cost-effective tools for evaluating systemic inflammation in infectious diseases, including TB. The neutrophil-to-lymphocyte ratio (NLR), derived from routine complete blood counts, reflects the balance between innate and adaptive immune responses (Fan *et al.*, 2024). Elevated NLR has been associated with greater systemic inflammation, severe infection, and poorer outcomes in a variety of diseases. In TB specifically, increased neutrophil counts and relative lymphopenia have been linked to more extensive lung damage, higher bacterial loads, and worse clinical trajectories. Studies in adults have shown that severe pulmonary TB correlates with neutrophil predominance and diminished lymphocyte-mediated immunity, supporting NLR as a potential prognostic marker. Similarly, pediatric investigations have identified higher NLR values in cases of TB with cavitary lesions or disseminated disease. However, findings remain inconsistent and often limited by small sample sizes and heterogeneous populations (Ghosh *et al.*, 2025).

Significantly, the immunopathogenesis of TB in children differs markedly from that of adults. Young children, particularly those under five years of age, possess an immature immune system that results in less efficient antigen presentation, reduced neutrophil activity, and an altered balance between T-helper cell subsets (Greydanus, Azeem and Nazeer, 2025). This immunological immaturity can lead to a paucibacillary disease state, characterized by low bacterial burdens and radiographic manifestations that tend to be less destructive (Griffin *et al.*, 2024). Consequently, traditional biomarkers of inflammatory severity, such as NLR, may behave differently in pediatric patients compared to adults. Empirical evidence suggests that many children with confirmed PTB demonstrate NLR values within normal ranges, reflecting distinct

host–pathogen interactions during early life. For example, in a cohort of pediatric TB patients in Indonesia, more than half exhibited normal NLR values, despite radiographic abnormalities and clinical symptoms (Lakshmanan *et al.*, 2025).

Given these considerations, the relationship between NLR and radiographic severity in pediatric PTB remains unclear and warrants further investigation. Understanding whether NLR can serve as a reliable, accessible indicator of disease severity in children is crucial, particularly in low-resource settings where advanced diagnostics are limited (Linggi *et al.*, 2023). If validated, NLR could offer clinicians an inexpensive biomarker to help triage patients, monitor disease progression, and predict complications. However, existing evidence is fragmented, and most studies have been conducted in adult populations or mixed cohorts with limited pediatric representation. Furthermore, radiographic severity scoring in children is not standardized globally, and differences across age groups, clinical stages, and comorbidities may influence the relationship between inflammatory markers and imaging results. Therefore, contextualized research in defined pediatric populations is essential to establish clinical relevance.

Considering these gaps, this study aims to examine the association between the neutrophil-to-lymphocyte ratio and chest X-ray severity in children diagnosed with pulmonary tuberculosis. By analyzing data from pediatric TB cases at a regional referral hospital, this research seeks to determine whether NLR can reflect radiographic disease severity and thus serve as a practical, informative biomarker for clinical assessment. Findings from this study may contribute to improving early risk stratification in pediatric TB and supporting evidence-based decision-making in resource-limited healthcare settings.

RESEARCH METHODOLOGY

Study Design

This study employed an analytical observational design using a cross-sectional approach to examine the association between the neutrophil-to-lymphocyte ratio (NLR) and chest X-ray severity among pediatric patients with pulmonary tuberculosis (TB).

Study Setting

The study was conducted at Dr. H. Abdul Moeloek Regional General Hospital, Bandar Lampung, Indonesia, a tertiary referral center for pediatric TB. Data were collected from January 2023 to August 2025, and the research was finalized between August and November 2025.

Participants

Eligibility Criteria

Participants were children aged 0–18 years diagnosed with pulmonary TB according to clinical, radiological, and microbiological criteria, in accordance with national and WHO guidelines.

Inclusion criteria:

- Confirmed diagnosis of pulmonary TB.
- Availability of complete hematological and radiographic records during the study period.

Exclusion criteria:

- Incomplete medical records.
- Comorbid conditions known to alter NLR values (e.g., severe bacterial infection, autoimmune disorders, malignancy).
- Use of systemic corticosteroids or immunosuppressive agents within two weeks before blood sampling.

Sampling and Study Size

A total sampling strategy was applied. All eligible pediatric TB patients meeting the criteria were included, yielding a final sample of 60 participants.

Variables

Primary Independent Variable

Neutrophil-to-Lymphocyte Ratio (NLR): Calculated from absolute neutrophil and lymphocyte counts obtained from complete blood count results. NLR was analyzed both as a continuous variable and as six categories of inflammatory severity (normal, low, mild to moderate, moderate, severe, and critical).

Primary Dependent Variable

Chest X-ray Severity: Classified into three ordinal categories: minimal, moderate, and extensive lesions based on standardized pediatric TB radiographic criteria.

Data Sources and Measurements

Hematological Assessment

Absolute neutrophil and lymphocyte values were extracted from routine complete blood count tests performed at the time of TB evaluation. NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count.

Radiological Assessment

Chest X-ray films were retrieved from the hospital radiology archive. Two independent radiologists, blinded to clinical and laboratory data, assessed each image. Discrepancies were resolved through consensus. Radiographic severity categories reflected the extent of pulmonary involvement.

Bias Control

To minimize measurement and interpretation bias:

- Radiologists were blinded to NLR and clinical information.
- Standardized radiological criteria were used to classify lesion severity.
- Data extraction followed a predefined protocol.
- Outliers in laboratory data were cross-checked against original records.

Study Size and Power Consideration

Because all eligible patients within the study period were included, no formal sample size calculation was performed. As an exploratory cross-sectional study, the sample size was considered adequate to detect moderate correlations but may not detect small effect sizes.

Statistical Methods

Descriptive statistics (frequencies, percentages, medians, interquartile ranges) were used to summarize demographic and clinical characteristics. Normality of continuous variables was assessed using the Shapiro–Wilk test. Given the ordinal nature of chest X-ray severity and the non-normal distribution of NLR, **Spearman’s rank correlation analysis** was applied to assess the relationship between NLR and radiographic severity. Statistical significance was defined as $p < 0.05$. Analysis was conducted using standard statistical software.

Ethical Considerations

This study used secondary anonymized data from hospital medical records. Ethical approval was obtained from the institutional ethics review board of Dr. H. Abdul Moeloek Regional General Hospital. Patient confidentiality was strictly maintained, and no identifiable information was collected.

RESULT

A total of 60 pediatric patients with confirmed pulmonary tuberculosis were included in the analysis. Descriptive characteristics of the study population, including NLR categories and chest X-ray severity classifications, are presented to illustrate the distribution of inflammatory status and radiological findings. Subsequent analyses examine the correlation between NLR and chest X-ray severity to determine whether systemic inflammatory response corresponds with the extent of pulmonary involvement.

Table 1. General Characteristics of the Sample

Characteristics	n (n=60)	%
Inflammation Level Based on NLR		
Normal (1–2)	31	51.6
Low inflammation (2–3)	7	11.6
Mild to moderate inflammation (3–7)	15	25.0
Moderate inflammation and stress (7–11)	4	6.6
Severe inflammation and stress (11–17)	2	3.3
Critical inflammation and stress (17–23)	1	1.6
Chest X-ray Severity		
Minimal lesions	15	25.0
Moderate lesions	32	53.3
Extensive lesions	13	21.7

Table 1 shows the distribution of NLR categories and chest X-ray severity among the 60 pediatric patients with pulmonary tuberculosis. More than half of the participants (51.6%) exhibited a normal NLR, indicating that systemic inflammatory response was generally low in this population. Only a small proportion (11.5%) demonstrated moderate to severe inflammation, suggesting that severe inflammatory states were uncommon. Regarding radiological severity, moderate lesions were the most frequently observed chest X-ray finding (53.3%), followed by minimal lesions (25.0%) and extensive lesions (21.7%). This pattern indicates that most children presented with intermediate radiographic involvement, while only a minority showed advanced pulmonary damage. Overall, the distribution suggests that pediatric TB cases in this cohort predominantly exhibited regular inflammatory markers and moderate radiographic severity, reflecting the typically paucibacillary and less destructive nature of tuberculosis in children.

Table 2. Association Between NLR Status and Chest X-ray Severity

Variable	n	Correlation Coefficient (r)	p-value
Association between NLR and Chest X-ray Severity	60	–0.084	0.524

Table 2 presents the correlation analysis between the neutrophil-to-lymphocyte ratio (NLR) and chest X-ray severity in pediatric pulmonary tuberculosis. The correlation coefficient ($r = -0.084$) indicates a very weak and negative relationship between the two variables. However, the association is not statistically significant ($p = 0.524$), suggesting that variations in NLR do not correspond meaningfully with differences in radiographic lesion severity. Based on these findings, NLR does not appear to be a reliable indicator of chest X-ray severity in pediatric pulmonary tuberculosis, and its utility as a biomarker for assessing radiological disease burden in children is limited.

DISCUSSION

This study investigated the association between the neutrophil-to-lymphocyte ratio (NLR) and chest X-ray severity among pediatric patients with pulmonary tuberculosis (TB). The findings demonstrated that most children exhibited normal NLR values and moderate radiographic involvement. Importantly, no significant association was found between NLR and chest X-ray

severity, indicating that NLR may have limited utility as a biomarker for predicting radiologic disease burden in pediatric TB. These results offer valuable insight into the unique immunological and radiological characteristics of TB in children, which differ substantially from those in adults.

The predominance of normal NLR values in this cohort is consistent with existing literature describing the immaturity of the pediatric immune system (Luckner and Seckel, 2024). Young children, particularly those under five, have reduced neutrophil function, lower antigen-presenting capacity, and incomplete maturation of adaptive immune responses. These immunological differences result in relatively mild systemic inflammatory responses following *Mycobacterium tuberculosis* infection (Maiwall *et al.*, 2024). Previous studies have shown that children infected with TB commonly exhibit paucibacillary disease with lower bacterial loads than adults, leading to a less intense inflammatory response. Similar patterns were observed by Puspitasari *et al.*, who reported that most pediatric TB patients demonstrated normal NLR values, reinforcing the expectation that systemic inflammation is often limited in younger populations (Quartier *et al.*, 2025).

The distribution of chest X-ray findings in this study also aligns with established pediatric TB pathophysiology. Most children presented with moderate lesions, and only a small proportion exhibited extensive pulmonary involvement (Rahmadani, Sainal and Suprpto, 2023). Classic pediatric TB is typically characterized by hilar or mediastinal lymphadenopathy, segmental obstruction, and limited parenchymal damage. The formation of cavitary lesions, which are common in adolescents and adults, is rarely observed in young children (Sanya, Jayachandran and Onésime, 2025). This is attributed to lower levels of proteolytic enzymes, reduced delayed-type hypersensitivity responses, and weaker granuloma organization compared to older age groups. Studies by Seddon and colleagues have emphasized that radiographic manifestations in children rarely reach the destructive patterns seen in adult pulmonary TB, which further supports the radiological trends observed in this study (Shaik, Pillay and Jeena, 2024).

Despite theoretical evidence suggesting that NLR may reflect disease severity in several infectious and inflammatory conditions, its correlation with radiographic severity in this pediatric cohort was absent (Thompson *et al.*, 2024). A weak, non-significant correlation suggests that systemic inflammatory markers, as captured by NLR, may not accurately reflect localized pulmonary involvement in children. Several explanations may account for this finding. First, the inflammatory response of children is often compartmentalized, meaning that localized pulmonary inflammation does not always translate into elevated systemic markers (Viz-Lasheras *et al.*, 2025). Second, the immune response to TB in children tends to be skewed toward T-helper 2 (Th2) dominance during early life, thereby suppressing excessive inflammation and limiting peripheral neutrophil recruitment. Interleukin-10 (IL-10), for example, downregulates proinflammatory cytokines and may reduce neutrophil proliferation, thereby attenuating NLR elevations even when TB lesions are present radiographically (Xue *et al.*, 2025).

Additionally, the absence of cavitary lesions, which are commonly associated with higher bacterial loads and more intense inflammation, further explains the lack of association (Urbanowski *et al.*, 2020). Strong correlations between elevated NLR and severe pulmonary destruction, primarily because adult TB pathology includes robust neutrophilic infiltration and tissue necrosis (Yang *et al.*, 2025). In contrast, children seldom develop cavitation or extensive consolidation, which reduces the likelihood that NLR will reflect disease extent. These biological differences underscore why adult TB biomarkers may not be directly applicable to pediatric populations (Zheng and Zheng, 2025).

Another possible explanation relates to the variability in radiographic interpretation and the heterogeneity of TB lesions in children. Pediatric TB radiographs can be challenging to interpret due to subtle findings, overlap with viral infections, and difficulty assessing lymph node enlargement. Although this study minimized bias through independent, blinded readings by two radiologists, inherent limitations in pediatric radiology may still influence lesion classification. Nevertheless, given the consistent low-inflammatory profile observed, methodological limitations alone are unlikely to account for the absence of correlation. The results of this study have several clinical implications. First, they suggest that NLR should not be used as a standalone biomarker

for assessing TB severity in children. While inexpensive and readily available, its diagnostic and prognostic value appears limited in this population. Second, reliance on radiographic evaluation remains essential for determining disease extent in pediatric TB, though clinical context and microbiological confirmation remain indispensable. Third, future biomarker research in pediatric TB should explore alternative markers that better reflect childhood immune activity, such as cytokine profiles, monocyte-to-lymphocyte ratios, or transcriptomic signatures.

Finally, this study contributes to the growing recognition that pediatric TB requires distinct diagnostic approaches from those for adult TB. The immunological and radiological differences observed reinforce the need for age-specific tools to assess TB severity. Although the sample size was limited and derived from a single center, the findings provide important baseline data for larger, multicenter investigations. The study demonstrates that NLR is not significantly associated with chest X-ray severity in pediatric pulmonary tuberculosis. The unique immunological characteristics of children and the typically limited radiologic involvement in pediatric TB likely contribute to this lack of correlation. These findings highlight the importance of developing pediatric-specific biomarkers and caution against extrapolating adult TB markers to children without appropriate validation.

CONCLUSION

This study showed that the neutrophil-to-lymphocyte ratio (NLR) was not significantly associated with chest X-ray severity in pediatric pulmonary tuberculosis. Most children exhibited normal NLR values and moderate radiologic involvement, reflecting the typically mild systemic inflammatory response and limited parenchymal damage characteristic of pediatric TB. These findings suggest that NLR is not a reliable biomarker for assessing radiologic disease burden in children and should not be used as a standalone indicator of TB severity in this population.

Future research should explore alternative inflammation-based biomarkers that better reflect pediatric immune responses, such as cytokine profiles or monocyte-to-lymphocyte ratios. Larger multicenter studies with broader age representation and standardized radiological scoring may also provide deeper insights into the relationships between biomarkers and radiology in childhood TB. Clinicians are encouraged to continue relying on comprehensive clinical assessment and radiographic evaluation rather than NLR alone when determining disease severity in pediatric patients.

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Conflict of Interest

There are no potential conflicts of interest relevant to this article.

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