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Unveiling Inflammation: Blood Peripheral Indices in Pulmonary Tuberculosis

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ABSTRACT

Pulmonary tuberculosis (TB) remains a global and national health challenge. Peripheral blood inflammatory indices—NLR, PLR, PNR, MLR, dNLR, SIRI, SII, and AISI—have been proposed as markers of systemic inflammation and prognosis, yet local data are scarce and findings vary. Thus, this study was aimed to describe these indices in pulmonary TB patients at Dr. Pirngadi Regional General Hospital, Medan (2019–2020). This cross-sectional study was analysed 105 inpatient medical record via total sampling technique. Demographics and eight inflammatory indices were analyzed using descriptive statistics. Median values of NLR, PLR, PNR, MLR, dNLR, SIRI, SII, and AISI in pulmonary tuberculosis patients are quite varied and tend to be higher than several previous studies. High NLR and PLR values can reflect a severe degree of inflammation, while PNR and dNLR values show less consistent results. Indices such as SIRI, SII, and AISI show potential as indicators of systemic inflammation, but still require further study. These indices have the potential to be used as markers of inflammation and prognosis in pulmonary tuberculosis, but cannot yet be used as a single reference.

Keywords: inflammation, blood, pulmonary tuberculosis

INTRODUCTION

According to data from the World Health Organization (WHO), non-communicable diseases accounted for 7 of the top 10 global causes of death in 2021, representing approximately 38% of all deaths worldwide and 68% of the top 10 leading causes. Tuberculosis (TB) remained a major cause of mortality, ranking 10th among the top global causes of death. In low- and middle-income countries, its burden was even greater, ranking 8th in low-income countries and 6th in middle-income countries. Globally, WHO estimated that 7.1 million people were infected with tuberculosis in 2021, with approximately 58% of cases occurring in males. The mortality risk of tuberculosis is further increased by certain comorbidities; notably, around 214,000 of the 1.5 million tuberculosis-related deaths in 2021 occurred in patients co-infected with HIV/AIDS [1], [2], [3], [4], [5].

Pulmonary tuberculosis also constitutes a substantial national health burden in Indonesia. Data from the Indonesian Ministry of Health, through the 2018 Basic Health Research (Riset Kesehatan Dasar/Riskesdas), reported a national prevalence of pulmonary tuberculosis of 0.42%, while the prevalence in North Sumatra was 0.30%. In addition, the same report showed that only 68.9% of pulmonary tuberculosis patients underwent sputum examination, 80.2% chest X-ray examination, and 43.8% Mantoux testing. These findings indicate that tuberculosis—particularly pulmonary tuberculosis—remains a significant public health problem in Indonesia and highlight the need for accessible and effective diagnostic approaches. Early diagnosis and appropriate management are crucial for controlling pulmonary tuberculosis. Routine blood examinations, as one of the initial diagnostic modalities, play an important role in the early clinical assessment of suspected pulmonary tuberculosis, especially prior to confirmatory tests such as Acid Fast Bacilli (AFB) staining or cartridge-based nucleic acid amplification tests (CBNAAT), including GeneXpert® [6].

In recent years, increasing attention has been directed toward routine blood-test parameters such as platelet, neutrophil, lymphocyte, and monocyte counts which can be integrated into various peripheral blood inflammation indices. These indices include the C-

reactive protein to albumin ratio (CAR), C-reactive protein to lymphocyte ratio (CLR), derived neutrophil to lymphocyte ratio (dNLR), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI). Previous studies have demonstrated that these indices are associated with unfavorable treatment outcomes in pulmonary tuberculosis [7]. Furthermore, CRP, platelet-to-lymphocyte ratio (PLR), and SIRI were found to be significantly higher in cavitary compared with non-cavitary pulmonary tuberculosis, and a combined panel of these markers improved screening accuracy and specificity for cavitary disease [7], [8]

Collectively, these findings underscore the growing interest in peripheral blood inflammation indices not only as indicators of systemic inflammation involved in the pathogenesis of pulmonary tuberculosis but also as potential prognostic markers. Despite their advantages—being inexpensive, widely available, and easily obtained—the clinical validity, consistency, and applicability of these indices remain inconclusive. Moreover, local data from Indonesian populations are limited, and previous studies often report heterogeneous or conflicting results. To address this gap, the present study aims to describe the profile of Peripheral Blood Inflammation Indices, including NLR, PLR, platelet-to-neutrophil ratio (PNR), monocyte-to-lymphocyte ratio (MLR), dNLR, SIRI, systemic immune-inflammation index (SII), and aggregate inflammation systemic index (AISI), in pulmonary tuberculosis patients treated at Dr. Pirngadi Regional General Hospital, Medan. This study provides novel local evidence by comprehensively evaluating multiple inflammation indices simultaneously in a real-world clinical setting, thereby contributing to a better understanding of their potential utility in the assessment of pulmonary tuberculosis within the Indonesian context.

RESEARCH METHODS

This observational study was used cross-sectional model and all procedure have been approved by Komite ETIK Penelitian Kesehatan (KEPK) Universitas HKBP Nommensen with letter no. 238/KEPK/FK/XII/2021. This study was selected 105 medical records of tuberculosis inpatient in Dr. Pirngadi Regional General Hospital, Medan between 2019-2020 using Total Sampling Technique, that was also act as secondary data. Thus, all medical records also act as Population. This study collected some data including demography (age, sex, and occupation) and peripheral blood inflammation Indices, which are NLR (*Neutrophile-to-Lymphocyte Ratio*), PLR (*Platelet-to-Lymphocyte Ratio*), PNR (*Platelet-to-Neutrophile Ratio*), LMR (*Lymphocyte-to-Monocyte Ratio*, dNLR (*derived Neutrophil to Lymphocyte Ratio*), SIRI (*Systemic Inflammation Response Index*), SII (*Systemic Immune-Inflammation Index*), dan AISI (*Aggregate Index of Systemic Inflammation*). These peripheral blood inflammation index's definitions were described in Table 1.

Table 1. Description of Peripheral Bloof Inflammation Index

Index	Description
NLR (*Neutrophile-to-Lymphocyte Ratio*)	The ratio of the absolute neutrophil count to the absolute lymphocyte count [9].
PLR (*Platelet-to-Lymphocyte Ratio*)	The ratio of the absolute platelet count to the absolute lymphocyte count [10].
PNR (*Platelet-to-Neutrophile Ratio*)	The ratio of the absolute platelet count to the absolute neutrophile count [10].
MLR (*Monocyte-to-Lymphocyte Ratio*)	The ratio of the absolute neutrophil count to the absolute lymphocyte count [11].
dNLR (*derived Neutrophil to Lymphocyte Ratio*)	The ratio of the absolute neutrophil count to the difference between the total leukocyte count and the absolute neutrophil count [7], [12], [13].
SIRI (*Systemic Inflammation Response Index*)	The ratio of the product of the absolute neutrophil and monocyte counts to the absolute lymphocyte count [7], [12], [13].
SII (*Systemic Immune-Inflammation Index*)	The ratio of the product of the absolute platelet and neutrophil counts to the absolute lymphocyte count [7], [12], [13].
AISI (*Aggregate Index of Systemic Inflammation*)	The ratio of the product of the absolute neutrophil, platelet, and monocyte counts to the absolute lymphocyte count [7], [12], [13].

All data were analyzed using descriptive statistics, which included measures of central tendency (median) and dispersion (interquartile range, minimum, and maximum). The results were presented in both narrative form and tables.

RESULT AND DISCUSSION

Initially, this study described the socio-demography from pulmonary tuberculosis patients treated at Dr. Pirngadi Regional General Hospital, Medan, during 2019-2020 and it was shown in Table 2.

Table 2. Distribution of Pulmonary Tuberculosis Cases by Age and Gender at Dr. Pirngadi Regional General Hospital, Medan, 2019–2020

Gender	Frequency (%)	Age (Years), Mean ± SD
Male	71 (67.62)	48.72 ± 15.10
Female	34 (32.38)	45.18 ± 17.54

Table 2 shows that most pulmonary tuberculosis patients treated at Dr. Pirngadi Regional General Hospital, Medan, during 2019–2020 were male, with a mean age of 48.72 ± 15.10 years**.** In addition to age and gender, this study also evaluated socio-demographic characteristics**,** including occupation and it was shown in Table 3.

Table 3. Frequency Distribution of Pulmonary Tuberculosis Cases by Occupation at Dr. Pirngadi Regional General Hospital, Medan, 2019–2020

Occupation	Frequency	Percentage
Self-Employed	50	47.6
Housewife	23	21.9
Civil Servant	10	9.5
Private Sector Employee	8	7.6
Unemployed	5	4.8
Farmer	4	3.8
College Student	3	2.9
School Student	1	1.0
Driver	1	1.0
Total	**105**	**100.0**

Table 3 can be seen that the majority of pulmonary tuberculosis patients treated at the dr. Pirngadi Regional General Hospital, Medan, during 2019-2020 worked as self-employed, accounting for 50 patients (47.6%). This was followed by housewives (23 patients, 21.9%), civil servants (10 patients, 9.5%), private sector employees (8 patients, 7.6%), unemployed individuals (5 patients, 4.8%), farmers (4 patients, 3.8%), and college students (3 patients, 2.9%). The smallest groups were a school student and a driver, with one patient (1%) each. Subsequently, the analysis proceeded to examine the distribution of pulmonary tuberculosis patients treated at Dr. Pirngadi Regional General Hospital, Medan, during 2019–2020 based on Peripheral Blood Inflammatory Index, as presented in the Table 4.

Table 4. Distribution of Pulmonary Tuberculosis Cases by Peripheral Blood Inflammation Index at Dr. Pirngadi Regional General Hospital, Medan, during 2019-2020 Based on Inflammatory Index

Index	Median	IQR	Min	Max
NLR	6.47	8.03	1.40	54.65
PLR	271.09	317.42	34.34	2198.74
PNR	39.61	31.61	5.31	847.92
MLR	0.73	0.59	0.06	4.17
dNLR	3.39	3.77	0.10	26.78
SIRI	5,237.92	9,063.91	86.18	57,412.20
SII ($x10^6$)	2.17	3.75	0.30	42.08
AISI ($x10^6$)	1,640.80	3,825.84	21.55	44,207.39

Table 4 presents the distribution of peripheral blood inflammation indices, including NLR, PLR, PNR, MLR, dNLR, SIRI, SII, and AISI. As the data for these indices were not normally distributed, the results are expressed as median values along with minimum, maximum, and interquartile range (IQR). This approach provides a more accurate representation of the central tendency and variability of inflammatory markers in pulmonary tuberculosis patients.

Regarding baseline characteristics, most tuberculosis patients in this study were male and belonged to the productive age group. These findings are consistent with the 2018 Basic Health Research conducted by the Indonesian Ministry of Health, which reported that the majority of pulmonary tuberculosis cases occurred in males, accounting for 510,714 cases (0.5%) [6]. Most tuberculosis patients at a tertiary care hospital were in the 41–50 year age group (38.5%) [14]. The majority of tuberculosis patients at a community health center falling into the 45–54 and 55–64 year age groups (26.5%) [15].

This study not only analyses socio-demographic characteristics, but also inflammatory index. Neutrophils, as component of NLR, were reported to play no significant role in the process of Mycobacterium tuberculosis infection due to their short lifespan, which is 6-24 hours in the bloodstream and up to 7 days in the tissue. Meanwhile, lymphocytes, as part of the adaptive immune system, also play a crucial role during Mycobacterium tuberculosis infection particularly CD4+ T cells, which secrete interferon-gamma, and CD8+ T cells, which exhibit cytotoxic activity. A decrease in lymphocyte response, especially CD8+ T cells, has been observed in drug-resistant cases [9], [16]. 55.3% of tuberculosis patients were either self-employed or worked in the private sector employee. It was inline with this result study. Environmental exposures and daily activities that may not adequately support hygiene and health are potential contributing risk factors for this group [17].

A previous study at Haji Adam Malik General Hospital reported that NLR values in patients with drug-resistant tuberculosis were lower (3.28 ± 1.44)

compared to those with drug-sensitive pulmonary TB (4.62 ± 1.44), with a statistically significant difference (P-Value < 0.05). In this study, the average age of male patients was 48.72 years and female patients 45.18 years. It was due to the tendency of NLR values to increase proportionally with age [9], [18], [19].

Platelet-to-lymphocyte ratio (PLR) has been implicated in tuberculosis (TB) pathogenesis. Elevated PLR may reflect increased platelet-associated gene expression and release of CCL17 (TARC), which recruits Th2 cells, indicating ongoing inflammation [10]. Studies have linked higher PLR to cavitary pulmonary TB, likely due to platelet accumulation in granulomas. He et al. (2024) found significantly greater PLR in patients with cavitary lesions; as a standalone marker, PLR's sensitivity and specificity were modest (66.6% and 50.2%). Combining PLR with CRP and SIRI improved sensitivity but kept specificity low (22.5%). PLR cutoff of 198.23 for cavitary TB, whereas recent study revealed median PLR of 271.09 suggests more severe disease and supports the need for inpatient management [8], [20].

Platelets, as component of PNR, are implicated in tuberculosis pathogenesis particularly in cavitary and granulomatous lesions while neutrophil counts rise during the early innate immune response. However, PNR may not reliably distinguish pulmonary tuberculosis in patients without comorbidities; Koc and Gullu (2022) reported significantly lower PNR values in TB patients compared to controls (P-Value = 0.010) [9], [16], [21]. This lower value may reflect the predominance of neutrophile activity over platelet involvement in pulmonary tuberculosis without comorbid. Several studies, however, underscore PNR's utility as an immuno-inflammatory marker. PNR value tended to be higher in pulmonary tuberculosis patients with comorbid diabetes mellitus, and Chen et al. (2022) also reported a significant PNR increase in extrapulmonary (spinal) tuberculosis [21], [22], [23].

Monocytes, as component of MLR, serve as antigen-presenting cells that bridge the innate and adaptive immune systems, while lymphocytes—particularly T cells—mediate targeted antimicrobial responses against Mycobacterium tuberculosis. Thus, MLR reflects the host's immunological response capacity to pulmonary tuberculosis infection. Suraidah et al. (2024) identified an optimal MLR cutoff of 0.205 (AUC = 0.03) for diagnosing active disease. Higher cutoff, achieving 95.1% sensitivity and 71.7% specificity [20], [24], [25].

Unlike other indices, dNLR is most often applied as a prognostic marker in pulmonary tuberculosis. Increased dNLR values were associated with a significantly higher risk of adverse outcomes [7]. A significant link between dNLR (among other leukocyte indices) and tuberculosis-associated pulmonary obstructive disease (P-Value = 0.006) [8]. In contrast, patients with tuberculosis had lower dNLR levels than those with bacterial or atypical pneumonia [7], [12], [13].

SIRI, SII, and AISI, as groups of systemic inflammation indices, have limit number of studies that investigated these indices. SIRI and SII were significantly higher in pulmonal tuberculosis patients with obstructive pulmonary disease than in those with tuberculosis alone [13], and [7] also demonstrated that SIRI, SII, and dNLR may serve as prognostic indicators. However, these indices can be confounded by other inflammatory markers and patient comorbidities; triglyceride levels, PNR, PMR, MHR, and MLR also influence tuberculosis prognosis [7], [13].

The findings suggest that systemic inflammatory markers particularly NLR and PLR may support clinical monitoring of tuberculosis progression and severity. Elevated PLR values may indicate persistent inflammation, while changes in NLR could reflect treatment response. Although PNR and MLR show limited diagnostic value in uncomplicated TB, they may help identify inflammation in cases with comorbidities or extrapulmonary involvement. Composite indices like SIRI, SII, and dNLR may offer prognostic insights but should be interpreted cautiously, especially in patients with underlying conditions. These markers could aid clinical decision-making, though further validation is needed before routine implementation. AISI as other systemic inflammation markers, still has limited data to use as either prognostic indicator or diagnostic.

CONCLUSION

Based on the findings of this study, it can be concluded that the Peripheral Blood Inflammation Indices namely NLR, PLR, PNR, MLR, dNLR, SIRI, SII, and AISI varied widely among pulmonary tuberculosis patients treated at Dr. Pirngadi Regional General Hospital, Medan, between 2019 and 2020. Notably, the median values of NLR and PLR were higher than those reported in earlier studies, which may reflect a stronger inflammatory response or more severe disease, particularly in older individuals. The PNR, MLR, and dNLR indices demonstrated potential in reflecting the immune response, although their consistency across different studies remains limited. Additionally, the wide distribution of SIRI, SII, and AISI values highlights the heterogeneity of systemic inflammation in these patients. These findings highlight the potential value of these hematologic indices in supporting clinical evaluation and management of pulmonary tuberculosis especially when interpreted alongside key factors such as patient age and the presence of comorbidities. These findings emphasize the importance of further research to identify the role and develop a prediction model of each index in evaluating the incidence and prognosis of pulmonary tuberculosis with inferential statistic approach. One of these indices, AISI, which has limited number of data as either diagnostic or prognostic function in pulmonary tuberculosis and it highlighting the require for further investigation and predictive of it.

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