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Analysis of NLR and MLR Values in Patients with Pulmonary Tuberculosis and Pulmonary Tuberculosis with Diabetes Mellitus

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ABSTRACT

Tuberculosis (TB) infection can cause changes in hematological parameters such as neutrophils, monocytes, and lymphocytes. The neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) are used as indicators of inflammation and immune response in infectious diseases, including TB. Diabetes mellitus (DM) as a comorbidity can exacerbate inflammation, potentially affecting NLR and MLR values in TB patients. This study aimed to determine the NLR and MLR values in patients with pulmonary TB and pulmonary TB with DM. This research used a quantitative observational design with a cross-sectional approach, involving 72 respondents from several primary health centers (Puskesmas) in Semarang City, divided into two groups of 36 individuals each. The sampling technique used was purposive sampling. The results showed that the mean NLR value in pulmonary TB patients was 2.20, and in pulmonary TB with DM patients was 2.89, with a significant difference (p=0.002). Meanwhile, the mean MLR value in pulmonary TB patients was 0.34 and in pulmonary TB with DM patients was 0.33, with no significant difference (p=0.752). These findings indicate that NLR is more sensitive than MLR in reflecting the inflammatory status and DM complications in TB patients. NLR can be used as an additional marker in the clinical monitoring of TB patients, especially those with DM comorbidity.

INTRODUCTION

Tuberculosis (TB) remains one of the deadliest infectious diseases in the world, with an estimated 10.8 million new cases in 2023, equivalent to 134 cases per 100,000 population. Indonesia ranks second globally in the number of TB cases, with an estimated 969,000 new cases reported in 2023. Data from the Central Java Provincial Health Office recorded 51,363 new cases by the third quarter of 2023, indicating that TB remains a significant burden on both regional and national healthcare systems (World Health Organization, 2024).

TB is caused by infection with the bacterium Mycobacterium tuberculosis, which primarily targets the lungs. After entering through the respiratory tract, the bacteria reach the alveoli and begin to proliferate. The body's immune response to TB infection is often characterized by changes in white blood cell counts, including neutrophils, lymphocytes, and monocytes. The neutrophil-to-lymphocyte ratio (NLR) is now widely used as a simple hematological indicator to assess the inflammatory status in various infectious diseases, including TB. Both the NLR and monocyte-to-lymphocyte ratio (MLR) are considered potential biomarkers for evaluating the

severity and prognosis of chronic infectious diseases, such as TB (Omair et al., 2024; Sulistyasmi et al., 2021).

An elevated NLR value in TB patients reflects the activation of the immune system and systemic inflammation. Neutrophils act as the first line of defense and increase significantly during the acute phase of infection, while lymphocytes decrease as a physiological response to systemic stress. On the other hand, monocytes become active in forming granulomas to contain the spread of M. tuberculosis. The NLR can reflect the dynamic inflammatory processes in TB patients and may serve as a rapid, cost-effective, and accessible clinical predictor in primary healthcare settings (Bakshi et al., 2024; Omair et al., 2024).

In addition to NLR, the monocyte-to-lymphocyte ratio (MLR) has also gained attention as a hematological biomarker in the diagnosis and monitoring of TB. Monocytes play a crucial role in phagocytosis and granuloma formation, which limits the spread of TB bacilli, while lymphocytes are involved in regulating the adaptive immune response. An elevated MLR has been associated with chronic inflammation and disease progression, and it may also help distinguish active TB from latent infection (Bakshi et al., 2024; Buttle et al., 2021; La Manna et al., 2017). Several studies have shown that MLR has diagnostic value comparable to, or even greater than, NLR in specific contexts. Moreover, the combination of both ratios may enhance diagnostic accuracy (Bakshi et al., 2024; Buttle et al., 2021; Choudhary et al., 2019).

Diabetes mellitus (DM) is a common comorbidity found in TB patients and is known to worsen the clinical course of the disease. DM impairs the body's immune response through chronic hyperglycemia, which induces oxidative stress, reduces the function of macrophages and lymphocytes, and increases the production of pro-inflammatory cytokines such as TNF-α and IL-6. Recent studies have shown that TB patients with DM have higher NLR and MLR values compared to TB patients without DM, indicating a more severe systemic inflammation due to the negative synergism between the two diseases (Boadu et al., 2024; Foe-Essomba et al., 2021; Zhou et al., 2023).

Previous studies have demonstrated that both NLR and MLR undergo significant changes in patients with TB and TB-DM. These two ratios serve as important indicators of complications or more severe infections. As simple and accessible measurements, they can be valuable tools for supporting diagnosis and monitoring treatment, particularly in populations with limited access to advanced laboratory facilities (Buttle et al., 2021). Based on the above background, it is important to conduct a comparative analysis of NLR and MLR values between patients with pulmonary tuberculosis and those with pulmonary tuberculosis accompanied by diabetes mellitus.

METHOD

This study is a quantitative research using a descriptive observational approach with a cross-sectional design. This approach was applied to assess and compare the neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) values between two subject groups: patients with pulmonary tuberculosis (TB) without diabetes mellitus (DM) and those with pulmonary TB accompanied by DM. The study was conducted from July to December 2024 at several primary healthcare centers (Puskesmas) in Semarang City, which have a high prevalence of TB and TB-DM cases.

The study population consisted of all registered pulmonary TB patients at the selected Puskesmas. Sampling was performed using purposive sampling. The site selection was based on the high number of TB-DM cases. Subject selection employed quota sampling to equalize the number of respondents in each group, with 36 subjects per group, resulting in a total sample of 72 participants.

The independent variable in this study is the type of patient group (pulmonary TB without DM and pulmonary TB with DM). In contrast, the dependent variables are the NLR and MLR values. Complete blood count (CBC) testing was performed using an automatic hematology analyzer (Sysmex XN-Series), and the obtained data were used to calculate NLR and MLR for each subject.

The instruments used in this study included informed consent forms, identity forms, and blood collection tools such as sterile syringes, EDTA tubes, 70% alcohol swabs, and tourniquets. The collected blood samples were stored in an ice box and analyzed in the laboratory using a

hematology analyzer. Data collection was conducted through several stages: obtaining ethical clearance, obtaining written consent from patients, reviewing medical records, collecting venous blood, performing complete blood count testing, and recording the results.

The data in this study consisted of primary data (from blood test results) and secondary data (from medical records). All collected data were analyzed using statistical software. Kolmogorov-Smirnov and Shapiro-Wilk tests were employed to assess data normality. As the data were not normally distributed, the Mann-Whitney U test—a non-parametric bivariate analysis—was used to determine differences in NLR and MLR values between the two groups.

This study was approved by the Ethics Committee of Poltekkes Kemenkes Semarang (Ethical Clearance No. 1066/EA/KEPK/2024). The researcher ensured adherence to all ethical principles of biomedical research, including obtaining informed consent and maintaining confidentiality throughout the study, ensuring the confidentiality of participant identity, and respecting participants' rights to withdraw from the study at any time without consequences, in accordance with prevailing ethical standards.

RESULTS

Based on the normality test, the NLR and MLR values in patients with pulmonary TB and pulmonary TB with DM were not normally distributed ($p<0.05$). Therefore, the comparison between the two groups was carried out using the non-parametric Mann-Whitney U test for both parameters.

Table 1. NLR Values in pulmonary TB and pulmonary TB with Diabetes Mellitus

Parameter	Pulmonary TB	Pulmonary TB + DM
Mean NLR	2.01	2.94
SD	1.0062	1.6370
Minimun	0.55	0,64
Maximum	4.38	8.20
Normal (%)	27 (75%)	29(81%)
Abnormal (%)	9(25%)	7(19%)
Total Subjects	36	36

The results showed that among patients with pulmonary TB, 75% had NLR values within the normal range, while 25% were in the abnormal category. Meanwhile, in patients with TB and DM, 78% had normal NLR values and 22% were abnormal. The average NLR in the pulmonary TB group was 2.01, whereas in the TB with DM group, it was 2.94. This difference is illustrated in the figure 1 below:

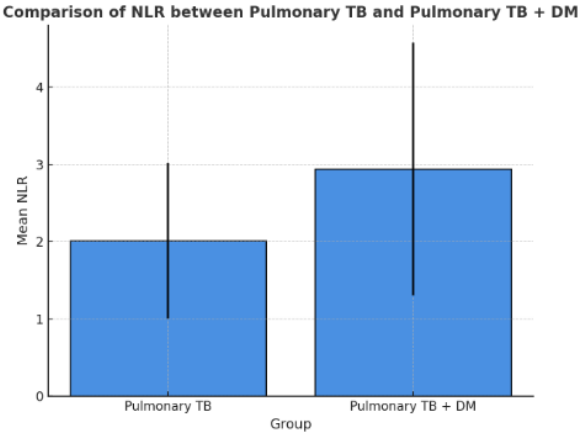

Figure 1. Mean NLR values in pulmonary TB and pulmonary TB with Diabetes Mellitus patients

Table 2. MLR values in pulmonary TB and pulmonary TB with Diabetes Mellitus

Parameter	Pulmonary TB	Pulmonary TB + DM
Mean MLR	0.34	0.33
SD	0.2065	0.2038
Minimun	0.15	0,11
Maximum	1.00	1.06
Normal (%)	27 (75%)	28(78%)
Abnormal (%)	9(25%)	8(22%)
Total Subjects	36	36

The study results showed that among patients with pulmonary TB, 75% had MLR values within the normal range, while 25% were categorized as abnormal. In the group with TB and DM, 78% had normal MLR values and 22% were abnormal. The average MLR in the pulmonary TB group was 0.34, while in the TB with DM group, it was 0.33. These results indicate that there is no significant difference in MLR values between the two groups. This difference is illustrated in the graph below:

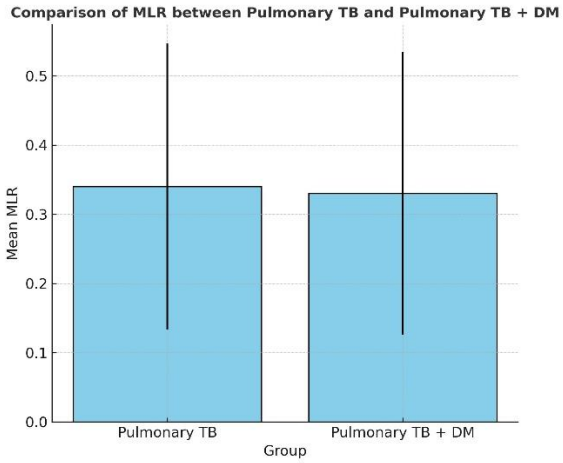

Figure 2. Mean MLR values in pulmonary TB and pulmonary TB with Diabetes Mellitus patients

Table 3. Comparative analysis of NLR and MLR values in pulmonary TB patients with and without Diabetes Mellitus

Variabels	Group	p-value
NLR	Pulmonary TB	0.002
	Pulmonary TB + DM	
MLR	Pulmonary TB	0.752
	Pulmonary TB + DM	

DISCUSSION

The present study demonstrated differences in the mean values of the Neutrophil-to-Lymphocyte Ratio (NLR) between tuberculosis (TB) patients with diabetes mellitus (DM) and those without DM. This finding is consistent with the study by Nursyahbani et al. (2024), who reported that the mean NLR in TB-DM patients (2.59) was significantly higher compared to TB patients without DM (1.60) ($p = 0.006$). This supports the hypothesis that DM as a comorbidity enhances systemic inflammatory responses in TB patients.

Similarly, Nanlohy et al. (2025) found that more than half of TB-DM patients (57.1%) had elevated NLR values above the cut-off (>3.53), whereas the proportion was lower in TB patients without DM. This indicates that chronic hyperglycemia in DM may aggravate immune dysregulation and heighten systemic inflammation, which is reflected by increased NLR levels.

Although in a different context, Sormin et al. (2018) also demonstrated the usefulness of NLR as an indicator of inflammation and disease severity in TB and multidrug-resistant TB (MDR-TB). Their study showed that the mean NLR was higher in drug-sensitive TB patients (4.62±2.37)

compared to MDR-TB patients (3.28±1.44), with values <2.91 considered suggestive of MDR-TB. These findings suggest that NLR variation is not only influenced by DM but also by infection status and drug resistance patterns.

Taken together, the findings of the present study align with previous research, highlighting that DM contributes to elevated NLR levels in patients with TB. Elevated NLR in TB-DM patients likely reflects a higher degree of systemic inflammation caused by the interaction between *Mycobacterium tuberculosis* infection and chronic hyperglycemia in DM. Therefore, NLR may serve as a simple, cost-effective biomarker for monitoring inflammatory status, prognosis, and potential complications in TB patients with DM comorbidity.

This finding indicates that patients with comorbid DM experience a higher degree of systemic inflammation compared to those with pulmonary TB without DM (Fu et al., 2025; Shan et al., 2025). This is consistent with the findings of Fadillah, who reported that TB patients with DM tend to exhibit more severe inflammation compared to TB patients without DM. This is attributed to chronic hyperglycemia, which triggers oxidative stress and impairs immune response, as indicated by an elevated NLR (Fadillah et al., 2021).

Physiologically, NLR is a simple and efficient hematological parameter used to assess inflammation, derived directly from a complete blood count. An increase in neutrophils and a decrease in lymphocytes reflect the adaptive immune response to inflammatory stress and immunosuppression (Jiang et al., 2019; Liu et al., 2022; Roldgaard et al., 2024; Yoon et al., 2013).

In diabetic patients, hyperglycemia triggers the formation of advanced glycation end-products (AGEs) and reactive oxygen species (ROS), thereby exacerbating tissue damage and stimulating the release of pro-inflammatory cytokines such as IL-6 and TNF-α (Istiqomah et al., 2024; Maria et al., 2016; Volpe et al., 2018).

The activation of the AGEs-RAGE pathway subsequently stimulates pro-inflammatory signaling cascades such as NF-κB, MAPK, and PKC, reinforcing the inflammatory loop and contributing to increased NLR levels (Smith et al., 2025; Wilkinson, 2021). This condition further clarifies why patients with pulmonary TB and DM exhibit higher NLR values. The exacerbated inflammatory state delays the response to anti-tuberculosis treatment and increases the risk of complications and mortality (Wu et al., 2021; Zhou et al., 2024).

In addition, meta-analysis studies have shown that NLR serves as a biomarker of subclinical inflammation and systemic stress in patients with both DM and TB (Han et al., 2018; Pătrîntaşu et al., 2023; Zhang et al., 2025). NLR is also superior in predicting bacteremia and sepsis compared to using neutrophil or lymphocyte counts alone (Agnello et al., 2021; de Jager et al., 2010; Huang et al., 2020). Therefore, TB patients—especially those with DM as a comorbidity—exhibit a higher degree of chronic inflammation due to hyperglycemia and immune dysfunction, which consistently results in higher NLR values compared to TB patients without DM (Istiqomah et al., 2024; Kumar Nathella & Babu, 2017; Ye et al., 2024).

Overall, NLR not only reflects the degree of acute and chronic inflammation but also serves as a practical and cost-effective prognostic marker. Monitoring NLR during TB treatment, especially in TB-DM patients, may help track therapeutic response and guide clinical decision-making to improve patient outcomes.

The results of this study showed that the average Monocyte-to-Lymphocyte Ratio (MLR) in patients with pulmonary tuberculosis (TB) was 0.34, while in those with pulmonary TB and diabetes mellitus (DM), it was 0.33. Both groups exhibited mean MLR values within the normal range, and statistical analysis using the Mann-Whitney test yielded a p-value of 0.752. This indicates that there is no significant difference in MLR values between pulmonary TB patients with and without DM.

MLR is one of the hematological ratios used as an indicator of chronic inflammation, particularly in systemic infectious diseases such as TB. This ratio represents the balance between monocytes, which are phagocytic toward pathogens, and lymphocytes, which are part of the body's adaptive immune response. Elevated MLR has been associated with the progression of active TB and immune system dysfunction in patients with comorbid conditions, including DM (Adane et al., 2022; Choudhary et al., 2019; La Manna et al., 2017).

However, in this study, although there was a slight difference in the mean MLR values between the two groups, no statistical significance was found. This finding is consistent with the study by Buttle et al., which stated that MLR values may vary across populations and are

influenced by various factors such as disease stage, the patient's immune status, and the presence of other comorbidities (Foe-Essomba et al., 2021). The study by Naranbhai et al. also noted that although MLR increases in active TB, its significance as an independent biomarker still requires further investigation, particularly in patients with diabetes mellitus (Naranbhai et al., 2014).

In patients with diabetes mellitus (DM), the immune response to TB infection is impaired due to chronic hyperglycemia, leading to macrophage and lymphocyte dysfunction, as well as increased levels of inflammatory cytokines, such as TNF-α and IL-6. Although this theory supports the possibility of elevated MLR in TB-DM cases, the results of this study showed that MLR values remained within the normal range and did not differ significantly between groups. This may suggest that MLR is less sensitive in detecting chronic inflammation in certain populations, particularly when compared to parameters such as NLR.

Nevertheless, MLR still holds potential as an additional marker in monitoring inflammation in both TB and TB-DM. The combination of MLR and NLR may provide a more comprehensive picture of a patient's immune and inflammatory status. The use of hematological ratios, such as the MLR, can serve as a practical alternative in primary healthcare settings where access to advanced immunological testing is limited.

CONCLUSION

This study concludes that the NLR values were significantly higher in pulmonary TB patients with DM compared to those without DM, suggesting that comorbid diabetes may contribute to a heightened inflammatory response. In contrast, MLR values did not show significant differences between the two groups, indicating that NLR may serve as a more sensitive marker than MLR in reflecting the inflammatory burden in pulmonary TB patients with DM.

AUTHOR'S DECLARATION

Authors' contributions and responsibilities

RBK: Conceptualization and title formulation; **PGS:** Conducting research and writing undergraduate thesis; **AS:** Primary supervisor and methodology supervision; **NQ:** Primary supervisor and validation of results.; other author**; WS:** Manuscript editing and preparation for publication**.**

Availability of data and materials

All data are available from the authors.

Competing interests

The authors affirm that there were no conflicts of interest in this research.

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