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Monocyte, Lymphocyte, and Monocyte–Lymphocyte Ratio Responses to Treatment Phases in Pulmonary Tuberculosis Patients

Nurul Hidayathul Mahpudinah Restu[1], *Leka Lutpiatina[2], Ahmad Muhlisin[2], Ratih Dewi Dwiyanti[2]

[1]Puskesmas Jonggon Jaya, Loa Kulu, Kutai Kartanegara, Kalimantan Timur, [2]Medical Laboratory Technology Poltekkes Kemenkes Banjarmasin, Mistar Cokrokusumo Street 4A Banjarbaru Indonesia**.** *Email: leka.zns@gmail.com

Abstract: Pulmonary tuberculosis is a chronic infectious disease that affects the balance of innate and adaptive immune responses, reflected in changes in hematological parameters, particularly monocyte and lymphocyte counts, and the monocyte-lymphocyte ratio (MLR). This study aimed to analyze differences in lymphocyte and monocyte counts and MLR values in pulmonary tuberculosis patients based on treatment phase. This cross-sectional analytical survey study involved 60 pulmonary tuberculosis patients divided into 0-month treatment groups, the intensive phase, and the continuation phase in Loa Kulu District from January to April 2025. Peripheral blood smears were stained with Giemsa to determine the percentage of lymphocytes and monocytes, and then the MLR value was calculated. Statistical analysis using one-way ANOVA showed significant differences in lymphocyte and monocyte counts between treatment groups ($p<0.05$). The mean lymphocyte count increased with treatment duration, while the mean monocyte count decreased, resulting in a decrease in the MLR value from 0.64 in the pre-treatment group to 0.29 in the intensive phase and 0.22 in the continuation phase. The decrease in MLR reflects an improved immune response balance and decreased systemic inflammation during tuberculosis therapy. The results of this study indicate that MLR demonstrated variation across treatment phases, suggesting its potential relevance in the clinical assessment of TB patients.
Keywords: Lymphocytes; monocyte-lymphocyte ratio; monocytes; pulmonary tuberculosis; tuberculosis treatment.

INTRODUCTION

Tuberculosis (TB) is a chronic respiratory infection caused by Mycobacterium tuberculosis (MTB) and remains a global health problem, with an estimated 1–3% of the world's population affected[1]. TB diagnosis is generally made through bacteriological examination of sputum, such as Acid Fast Bacilli (AFB) staining, molecular testing using Gene Xpert, and culture as the gold standard. Once the diagnosis is established, the next important step is evaluating the response to treatment[2].

Conventionally, evaluating the success of TB treatment is based on sputum smear conversion or culture as objective parameters. However, these tests are relatively time-consuming and not always easy to perform. Meanwhile, clinical evaluation and chest radiographic imaging are frequently used in practice, but they are subjective and

Corresponding Author: Leka Lutpiatina
Medical Laboratory Technology Poltekkes Kemenkes Banjarmasin.
Mistar Cokrokusumo Street 4A Banjarbaru Indonesia.
Email: leka.zns@gmail.com

influenced by variations in patient symptoms, differences in reader interpretation, and the quality of the radiological examination, so they do not always accurately reflect the patient's immunological condition[2].

Immunopathologically, TB is the result of a complex interaction between the innate and adaptive immune responses aimed at eliminating the pathogen. Monocytes serve as the primary target cells for Mycobacterium tuberculosis, while lymphocytes are the primary effectors in the protective immune response against TB[3]. Various studies have shown that patients with active pulmonary TB exhibit changes in hematological parameters, including increased leukocytes, monocytes, lymphocytes, and neutrophils compared to the healthy population[4]. Furthermore, MTB infection is known to affect the differentiation of hematopoietic stem cells and cause changes in the profile of peripheral immune cells, including monocytes and lymphocytes[5,6].

Monocytes are professional phagocytes that play a crucial role in defense against MTB through phagocytosis and antigen presentation. These cells can differentiate into macrophages and dendritic cells, linking the innate and adaptive immune responses[7-9]. Conversely, lymphoid cells, particularly lymphocytes, are the primary effector cells that determine the effectiveness of the immune response to TB infection[9]. Therefore, changes in the proportions of monocytes and lymphocytes can reflect the dynamics of a patient's immune status throughout the course of the disease and treatment.

Standard TB treatment consists of a two-month intensive phase and a four-month continuation phase. Anti-tuberculosis drug (OTD) therapy is known to reduce the number and proportion of leukocytes that were previously elevated due to the infection process, allowing hematological parameters to gradually return to normal after several months of treatment[10]. Previous research has shown that active TB patients with positive AFB smear results have a high monocyte-lymphocyte ratio (MLR), which decreases after the intensive phase as AFB smears convert to negative, an indicator of therapy success[11]. However, research findings regarding changes in monocytes during the treatment phase vary. Nabila et al. (2023) reported that during the intensive phase, some patients still experienced monocytosis, which is thought to be related to the early phase of the immune response before optimal infection control is achieved. In the continuation phase, the proportion of patients with normal monocyte counts increased, although monocytosis was still found in some cases[12]. This indicates that immune cell dynamics during TB treatment are complex and influenced by the duration of therapy.

According to the 2023 Indonesian Health Survey (SKI 2023), the prevalence of pulmonary tuberculosis in East Kalimantan Province was 0.20% (95% CI: 0.12–0.34) based on a doctor's diagnosis[13]. A preliminary study in Loa Kulu District, Kutai Kartanegara Regency, recorded 51 cases of pulmonary TB, indicating that this region has a significant disease burden and requires further study, particularly regarding patient immune responses during treatment.

Against this background, evaluating simple hematological parameters, such as monocyte and lymphocyte counts, and the monocyte-lymphocyte ratio (MLR), has the potential to provide additional insight into the balance of the immune response and the dynamics of immunological repair during TB therapy. Therefore, this study aims to determine differences in lymphocyte and monocyte counts, and MLR values in pulmonary TB patients across the intensive and continuation phases of treatment in Loa Kulu District.

MATERIALS AND METHODS

This study was an analytical survey with a cross-sectional design. The aim was to analyze differences in lymphocyte and monocyte counts in pulmonary tuberculosis (TB) patients based on three treatment duration groups: 0-month TB patients, the intensive phase, and the continuation phase. Lymphocyte and monocyte counts were measured once for each respondent, depending on the treatment group they were in.

The study was conducted at the Jonggon Jaya Community Health Center and the Loa Kulu Community Health Center, in Loa Kulu District, from January to April 2025. The study population consisted of all registered pulmonary TB patients undergoing treatment in the area. A sample of 60 respondents was selected using purposive sampling based on the following inclusion criteria: patients who were willing to participate and signed informed consent, pulmonary TB patients who had not yet received treatment (0 months), patients in the intensive phase (2–3 months), and patients in the continuation phase (4–6 months). Patients who were unwilling to participate, patients with treatment durations of less than 1 month, or more than 6 months were excluded from the study.

The independent variable in this study was the duration of TB treatment, while the dependent variable was the number of lymphocytes and monocytes expressed as a percentage. Primary data was obtained through laboratory examination of the patient's peripheral blood smears, while secondary data came from medical records related to patient identity and treatment duration.

Prior to conducting the study, researchers obtained ethical approval from the Health Research Ethics Committee of the Banjarmasin Ministry of Health Polytechnic and a permit from the relevant community health center. All equipment and materials were prepared and kept clean, sterile, and ready for use. Capillary blood sampling was performed by laboratory personnel following standard procedures: personnel wore personal protective equipment, prepared equipment, disinfected fingertips with 70% alcohol, and then performed a 3 mm puncture using an autoclicker for adults. The first drop of blood was discarded, while subsequent drops were used to prepare a peripheral blood smear.

Blood smear preparation was performed by placing a drop of blood on the side of a glass slide and then shifting the slide at a 45° angle until a thin, even smear was formed. The slide was dried at room temperature and fixed with absolute methanol for two minutes. Staining was performed using Giemsa solution for 30 minutes. The slides were then rinsed with water and dried. The dried slides were observed under a light microscope at 1000x magnification with oil immersion. For each slide, 100 types of leukocytes were counted in the monolayer area, and the percentage of lymphocytes and monocytes was determined. The leukocyte differential count is interpreted according to the standard adult reference range. A lymphocyte count of 20–40% is considered normal, with values <20% classified as low and >40% as high. A monocyte count of 2–8% is considered normal, with values <2% classified as low and >8% as high.

Data analysis was performed using univariate analysis to examine the distribution of respondent characteristics and lymphocyte and monocyte counts. Bivariate analysis was used to test for differences in values between the three treatment groups. The Shapiro-Wilk normality test and the homogeneity of variance test were used to determine the choice of further tests. If the data were normally distributed and homogeneous,

differences in lymphocyte and monocyte counts between groups were analyzed using one-way ANOVA. The research ethics commission of the Poltekkes Kemenkes Banjarmasin approved this research with certificate number 281/KEPK-PKB/2025.

RESULTS AND DISCUSSION

Respondent Characteristics

This study involved 60 pulmonary tuberculosis patients divided into three groups based on treatment duration: the 0-month treatment group, the intensive phase, and the continuation phase, each with 20 respondents. Respondent characteristics included age, gender, lymphocyte count, and monocyte count, as presented in Table 1.

Table 1. Distribution of Respondent Characteristics of Pulmonary TB Patients by Treatment Group in Loa Kulu District (n=60)

Characteristics	0 Months (n=20)	Intensive Phase (n=20)	Continuation Phase (n=20)
Age, n (%)			
Early adolescence (12–16)	1 (5.0)	0 (0.0)	0 (0.0)
Late adolescence (17–25)	5 (25.0)	7 (35.0)	3 (15.0)
Early adulthood (26–35)	0 (0.0)	7 (35.0)	4 (20.0)
Middle adulthood (36–45)	10 (50.0)	3 (15.0)	3 (15.0)
Early elderly (46–55)	3 (15.0)	1 (5.0)	6 (30.0)
Late elderly (56–65)	1 (5.0)	2 (10.0)	4 (20.0)
Sex, n (%)			
Male	13 (65.0)	13 (65.0)	15 (75.0)
Female	7 (35.0)	7 (35.0)	5 (25.0)
Lymphocyte Count, n (%)			
Low	15 (75.0)	2 (10.0)	1 (5.0)
Normal	5 (25.0)	18 (90.0)	19 (95.0)
High	0 (0.0)	0 (0.0)	0 (0.0)
Monocyte Count, n (%)			
Low	0 (0.0)	1 (5.0)	0 (0.0)
Normal	7 (35.0)	16 (80.0)	17 (85.0)
High	13 (65.0)	3 (15.0)	3 (15.0)

Based on Table 1, the majority of TB patients in the 0-month treatment group were in late adulthood (36–45 years), representing 10 individuals (50%). In the intensive phase, the largest proportions were in late adolescence (17–25 years) and early adulthood (26–35 years), representing 7 individuals (35%) each. Meanwhile, in the continuation phase, the largest age group was in early elderly (46–55 years), representing 6 individuals (30%). In terms of gender, the majority of respondents in all three treatment groups were male, representing 65% in the 0-month and intensive phase groups, and 75% in the continuation phase.

The distribution of lymphocyte counts showed that in the 0-month treatment group, most respondents had low lymphocyte counts (75%). Conversely, in the intensive and continuation phases, the majority of respondents had normal lymphocyte counts, representing 90% and 95%, respectively. The average lymphocyte count increased with

increasing treatment duration, from 15.70±6.57 in the 0-month group to 22.60±5.67 in the intensive phase and 29.25±7.65 in the continuation phase.

In terms of monocyte count distribution, the 0-month treatment group was dominated by high monocyte counts (65%), while in the intensive and continuation phases, the majority of respondents were in the normal category, at 80% and 85%, respectively. The average monocyte count decreased from 10.00±4.72 in the 0-month group to 6.45±4.22 in the intensive phase and 6.35±3.21 in the continuation phase.

Differences in Lymphocyte Counts Between Treatment Groups

Before conducting the analysis, the lymphocyte count data were first tested for normality using the Shapiro–Wilk test. The data across all groups were normally distributed ($p>0.05$), thus meeting the requirements for a parametric One-Way ANOVA test.

The results of the One-Way ANOVA test (Table 2) indicated a significant difference in lymphocyte counts between the pulmonary TB treatment groups. The average lymphocyte count in the 0-month treatment group was 15.70±6.57, increasing to 22.60±5.67 in the intensive phase and reaching 29.25±7.65 in the continuation phase. A p-value of 0.001 ($p<0.05$) indicates that the difference in lymphocyte counts between the three groups is statistically significant.

Table 2. Differences in Mean Lymphocyte Counts (One-Way ANOVA)

Group	Mean ± SD	p-value
0 Months	15.70 ± 6.57	0.001
Intensive Phase	22.60 ± 5.67	—
Continuation Phase	29.25 ± 7.65	—

Differences in Monocyte Counts Between Treatment Groups

A normality test for monocyte count data showed that all groups were normally distributed ($p>0.05$), so the analysis of differences was continued using a One-Way ANOVA test.

Based on the One-Way ANOVA results (Table 3), there were significant differences in monocyte counts between the pulmonary TB treatment groups. The average monocyte count in the 0-month treatment group was 10.00±4.72, then decreased to 6.45±4.22 in the intensive phase and 6.35±3.21 in the continuation phase. A p-value of 0.009 ($p<0.05$) indicates that the differences in monocyte counts between the three treatment groups were statistically significant.

Table 3. Differences in Mean Monocyte Counts (One-Way ANOVA Test)

Group	Mean ± SD	p-value
0 Months	10.00 ± 4.72	0.009
Intensive Phase	6.45 ± 4.22	—
Continuation Phase	6.35 ± 3.21	—

Monocyte–Lymphocyte Ratio (MLR)

In addition to analyzing lymphocyte and monocyte counts separately, this study also evaluated the monocyte–lymphocyte ratio (MLR) as an indicator of immune response balance in pulmonary TB patients. The MLR value was calculated based on the average

percentage of monocytes and lymphocytes in each treatment group. MLR = Percentage of monocytes (%) / Percentage of lymphocytes (%)

Table 4. Estimated Monocyte–Lymphocyte Ratio (MLR) Based on Pulmonary TB Treatment Group in Loa Kulu District

Treatment Phase	Mean Monocyte (%)	Mean Lymphocyte (%)	MLR (≈)	Category
0 Months	10.00	15.70	0.64	High
Intensive Phase	6.45	22.60	0.29	Normal
Continuation Phase	6.35	29.25	0.22	Normal

Based on Table 4, the highest estimated MLR value was found in the pulmonary TB patient group before treatment (0 months), with an MLR of 0.64. This value then decreased significantly in the intensive phase to 0.29 and continued to decrease in the continuation phase to 0.22. The decrease in MLR values with treatment duration indicates a change in the balance of the immune response, characterized by a decrease in the proportion of monocytes and an increase in the proportion of lymphocytes during TB therapy.

Changes in Lymphocyte Cell Count During TB Treatment

The results showed a significant increase in lymphocyte cell count with the duration of pulmonary TB treatment (Table 2). The mean lymphocyte cell count in the 0-month group was 15.70±6.57, increasing significantly in the intensive phase (22.60±5.67) and reaching its highest value in the continuation phase (29.25±7.65), with a one-way ANOVA test showing a significant difference (p=0.001).

This increase in lymphocyte count reflects an improvement in the adaptive immune response during therapy. Immunopathologically, T lymphocytes are the primary effectors of TB immunity, primarily through the activity of CD4+ and CD8+ cells mediated by cytokines such as IFN-γ to optimize macrophage function in destroying Mycobacterium tuberculosis[14]. Active TB infection is known to cause lymphocyte depletion due to migration to the site of infection, altered hematopoiesis, or increased apoptosis (11b). Therefore, the increase in lymphocyte counts during the intensive and continuation phases in this study indicates the recovery of adaptive immune function following successful treatment.

This finding is consistent with the study by Handoko et al. (2025), which reported a significant increase in lymphocyte counts after the intensive phase of pulmonary TB treatment, contributing to a significant decrease in MLR values[15].

Changes in Monocyte Counts During TB Treatment

Conversely, the results of this study showed a significant decrease in monocyte counts along with the duration of pulmonary TB treatment (Table 5). The mean monocyte count in the 0-month group was 10.00±4.72, decreasing to 6.45±4.22 in the intensive phase and remaining relatively stable in the continuation phase (6.35±3.21), with a statistically significant difference (p=0.009).

Monocytes are the primary target cells of M. tuberculosis and play a role as phagocytes and antigen-presenting cells in the innate and adaptive immune responses[14]. In the early phase of active TB infection, immune activation leads to increased release of monocytes from the bone marrow into the peripheral circulation. The decrease in

monocyte count during treatment in this study reflects a reduction in the inflammatory burden and infectious activity, consistent with reduced innate immune stimulation.

These results align with the findings of Shima et al. (2024), who demonstrated that longitudinal changes in monocytes are associated with TB prognosis[16], and with the report of Nabila et al. (2023), who noted that some patients still experience monocytosis in the early phase of treatment, but monocyte counts tend to decrease in the continuation phase[12].

Monocyte-Lymphocyte Ratio (MLR) Dynamics During Treatment

In addition to analyzing monocytes and lymphocytes separately, this study evaluated the monocyte-lymphocyte ratio (MLR) as an indicator of immune response balance. Based on Table 4, the highest estimated MLR value was found in the TB patient group before treatment (0 months), at 0.64, then decreased to 0.29 in the intensive phase and 0.22 in the continuation phase.

The increase in MLR in active TB reflects the relative dominance of monocytes as M. tuberculosis target cells and the relative decline of lymphocytes as the primary effectors of adaptive immunity. This condition has been widely reported in various studies, which show that MLR increases in chronic inflammatory diseases, including TB, and decreases after anti-TB treatment[17,18]. The decrease in MLR in this study is consistent with the reduction in systemic inflammation and the restoration of the adaptive immune response during therapy.

These results are consistent with the findings of Wang et al. (2019), who reported a significant decrease in MLR after TB treatment[9], as well as a meta-analysis by Adane et al. (2022) showed that MLR decreased significantly after anti-TB therapy and has potential as a biomarker for monitoring treatment effectiveness[19]. Furthermore, research by Naranbhai et al. showed that MLR reflects not only the number of immune cells but also the functional and transcriptional differences of monocytes, making MLR more representative than monocyte count alone[20].

The decrease in MLR during the intensive and continuation phases in this study indicates a shift in the immune balance from a dominant innate immune response to a more effective adaptive immune response. This supports the use of MLR as a simple and potential indicator for monitoring response to pulmonary TB treatment, particularly in areas with limited advanced diagnostic facilities.

Overall, the results of this study indicate that changes in lymphocyte and monocyte counts and MLR values align with the course of pulmonary TB treatment. Increased lymphocytes, decreased monocytes, and decreased MLR reflect an improved immune response and reduced systemic inflammation during therapy. These findings strengthen the evidence that simple hematological parameters, particularly MLR, can be used as additional indicators in evaluating TB treatment response, as reported in various previous studies[18,19].

This study used a cross-sectional design; therefore, it is not possible to describe changes in lymphocyte and monocyte counts longitudinally in the same individual. The limited sample size and its origin from a single region also limit the generalizability of the results. Furthermore, confounding factors such as nutritional status, comorbidities, and treatment adherence have not been thoroughly analyzed.

CONCLUSION

There are significant differences in lymphocyte and monocyte counts in pulmonary TB patients based on treatment duration, with lymphocytes increasing and monocytes decreasing as therapy progresses. Monocyte-to-lymphocyte ratios (MLR) consistently decreased from pre-treatment to the intensive and continuation phases, reflecting an improved immune response balance. These findings suggest that MLR may serve as a supportive hematological marker associated with the treatment phase in pulmonary TB patients, particularly in healthcare settings with limited access to advanced diagnostic tools.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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