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RESEARCH

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Treatment Duration and Its Impact on the Number of Polymorphonuclear, Mononuclear and Neutrophil Lymphocyte Ratio as Indicators of Recovery Rate in Tuberculosis Patients

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Abstract

The calculation of leukocyte types can be used to assess the level of infection or inflammation, particularly through the neutrophil-lymphocyte ratio (NLR). The NLR has been established as a useful biomarker for predicting bacteremia. Although differential leukocyte count and the neutrophil-lymphocyte ratio (NLR) have been widely proposed as indicators of infection and inflammation, their clinical interpretation remains unclear across disease states, particularly in tuberculosis. Current evidence is limited regarding how leukocyte profiles and NLR change during standard anti tuberculosis treatment (ATT), especially in the early and intermediate phases of therapy. Furthermore, it is not well established whether changes in leukocyte subtypes reflect treatment response or disease recovery in tuberculosis patients. Therefore, there is a need to quantify changes in leukocytes and NLR during TB treatment and to determine their potential role as readily accessible biomarkers for monitoring therapy outcomes. The goal of this study was to determine the effect of treatment duration on the number of polymorphonuclear cells, mononuclear cells, and the neutrophil-lymphocyte ratio as indicators of recovery in TB patients. This study employed a cross-sectional design with an analytical observational approach, involving 26 TB patients undergoing treatment for 1 to 6 months. The results showed the following average cell counts (per microliter) over the treatment period: basophils at 0.04, eosinophils at 0.30, neutrophils at 4.10, lymphocytes at 2.36, monocytes at 1.84, and a neutrophil-lymphocyte ratio of 0.53. One-way ANOVA analysis revealed a positive correlation between basophils, neutrophils, lymphocytes, monocytes, and the neutrophil-lymphocyte ratio with TB recovery. In conclusion, treatment of TB patients during the fourth to sixth month, or in the advanced phase of treatment showed differences in the number of polymorphonuclear cells, mononuclear cells and the NLR ratio compared to intensive phase treatment in TB patients at the Karang Taliwang and akranegara Health Centers.

Keywords: Tuberculosis, Neutrophil Lymphocyte Ratio, Polymorphonuclear, Mononuclear, Anti-tuberculosis Drugs.

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1. INTRODUCTION

Transmission of tuberculosis (TB) infection occurs through sputum or droplets from TB patients containing *Mycobacterium tuberculosis* bacteria (Coleman et al., 2022). This disease is the second deadliest infectious disease in the world, after COVID-19, and ranks thirteenth as the leading cause of death globally (Stefanescu et al., 2021). The incidence rate of tuberculosis increased by 3.6% in 2021 compared to 2020. Despite the high incidence and mortality of tuberculosis worldwide, reliable and easily accessible indicators to monitor treatment response and recovery are still limited. Hematological parameters such as polymorphonuclear cells, mononuclear cells, and the neutrophil-lymphocyte ratio have therefore gained attention as potential markers during TB treatment (Babu, 2019).

Previous studies in Indonesia have reported significant changes in leukocyte counts before and after the intensive phase of TB treatment (Permana, 2020). However, these studies did not specifically map the monthly dynamics of PMN, MN, and NLR during the complete six-month treatment period. Nabilah (2020), also identified the relationship between lymphocyte and monocyte levels with TB severity but did not assess their role as recovery indicators. Thus, there remains a gap in comprehensively evaluating the hematological parameters monthly throughout TB treatment to identify critical phases of immunological recovery and to strengthen the scientific basis for monitoring therapy using hematological biomarkers.

The problem addressed in this study is how the duration of treatment affects the number of polymorphonuclear cells (PMN), mononuclear cells (MN), and neutrophil-lymphocyte ratio (NLR) values, which can serve as indicators of the recovery rate in TB patients. The aim is to understand how the length of treatment influences these values as markers of recovery in TB patients (Reta et al., 2023; Aini et al., 2024). This study was conducted through an observational analytic design with a cross-sectional approach, focusing on TB patients undergoing treatment for one to six months. The selection of PMN, MN, and NLR as hematological parameters is based on their relevance to the host immune response and their potential utility as cost-effective markers in clinical settings. The selection of PMN, MN, and NLR is based on their specific roles in tuberculosis-related immune responses, with PMN indicating acute inflammation, MN reflecting adaptive immunity, and NLR serving as an integrated marker of systemic inflammatory balance, while remaining cost-effective and routinely measurable in clinical practice.

However, the current monitoring of TB treatment response still heavily relies on sputum conversion status or clinical improvement, which may not fully reflect the underlying immunological changes. According to Bohrer et al. (2021), NLR has emerged as a potential prognostic marker for TB severity and response to treatment, yet limited studies have directly linked treatment duration with dynamic changes in PMN, MN, and NLR during therapy. Moreover, according to a study by Khalid et al. (2022), patients with delayed NLR normalization showed slower clinical improvement, suggesting the need for better hematological monitoring parameters.

The hypothesis of this study is that treatment duration affects changes in the number of PMN, MN, and NLR values, which in turn indicate the recovery rate of TB patients. Previous studies have examined changes in leukocyte counts during treatment, but no research has focused on measuring the effect of treatment duration as an indicator of recovery during the treatment period. However, no studies have focused on measuring the effect of treatment duration as an indicator of recovery during the treatment period. Previous studies have mostly focused on single-time measurements, and the influence of treatment duration on leukocyte profiles and NLR as indicators of recovery during the treatment period has not been adequately explored. Therefore, this study aims to explore the effect of treatment duration on the number of polymorphonuclear (PMN), mononuclear (MN), and neutrophil-lymphocyte ratio (NLR) values as indicators of TB patients' recovery from *Mycobacterium tuberculosis* infection.

2. RESEARCH METHOD

This study uses an observational analytic method with a cross-sectional approach to determine differences in PMN, MN, and NLR values in TB patients undergoing treatment for 1, 2, 3, 4, 5, and 6 months (Azmi et al., 2023). The sample size was determined using total sampling (saturated sampling), with a non-probability sampling technique and a purposive sampling method. The examination was carried out at the Hepatika Mataram Laboratory in December 2023 - April 2024. The population in this study were TB patients in the working area of Karang Taliwang and Cakranegara Health Centers.

The study population consisted of all tuberculosis (TB) patients within the working areas of the Karang Taliwang and Cakranegara Health Centers. The total sample was determined through a saturated sampling technique, encompassing all eligible TB patients who met the study criteria and had been undergoing anti-TB treatment for 1 to 6 months. Inclusion criteria were patients who willingly agreed to participate and were currently in their 1st, 2nd, 3rd, 4th, 5th, or 6th month of TB treatment. Patients were excluded if they were newly diagnosed TB cases with comorbid Diabetes Mellitus, or if they had other significant complications such as HIV, chronic kidney failure, severe pulmonary disease, or pneumonia. Based on these criteria, the final sample size included TB patients who fulfilled both the inclusion and exclusion requirements.

This study uses an observational analytic method with a cross-sectional approach to determine differences in PMN, MN, and NLR values in TB patients undergoing treatment for 1 to 6 months. The population consisted of TB patients at Karang Taliwang and Cakranegara Health Centers, Mataram City, Indonesia, with a total sample of 26 patients selected by total sampling. Inclusion criteria included patients aged 18-65 years, diagnosed with pulmonary TB, undergoing treatment for 1-6 months, and willing to provide informed consent, while patients with diabetes, HIV/AIDS, autoimmune diseases, or other infections were excluded. Ethical approval for this study was obtained from the Research Ethics Committee of the Health Polytechnic of Mataram, Indonesia. The study was approved under ethical clearance certificate number DP.04.03/F.XLVIII.14/219/2024.

3. RESULTS AND DISCUSSION

Anti-TB treatment using OAT (antituberculosis therapy) is given in two phases: the first phase, known as the initial or intensive phase, and the second phase, known as the continuation phase (Buonacera et al., 2022). In the administration of OAT, monitoring occurs in two stages: Treatment monitoring is performed through microscopic examination at the end of the second month, aiming to assess the treatment response, potential side effects, and complications (Anggreani et al., 2023; Paton et al., 2023). Additionally, treatment monitoring at the end of the fifth month is conducted to evaluate any increase in drug side effects resulting from continued therapy (Bohrer et al., 2021). In terms of NRL values, TB patients generally exhibit higher NRL values compared to healthy individuals, as calculated by dividing the absolute neutrophil count by the absolute lymphocyte count (Darwin & Yolanda 2023).

When examining the length of treatment in relation to PMN, MN, and NLR values (Table 1), several trends were observed across the treatment period. At one month of treatment, most patients exhibited normal basophil, eosinophil, and neutrophil levels, with a small proportion showing increased values, while lymphocyte and monocyte levels were generally elevated and NLR values were within the normal range. At two months, basophil and eosinophil levels remained normal, neutrophil and monocyte levels increased, lymphocyte levels increased, and NLR values decreased. After three months of treatment, basophil levels were largely normal, eosinophil and monocyte levels increased, neutrophil and lymphocyte levels returned to normal, and NLR values also normalized. By the fourth and fifth months, basophil, eosinophil,

neutrophil, and lymphocyte levels were predominantly within normal ranges, monocyte levels remained increased, and NLR values largely stayed normal. After six months of treatment, basophil and neutrophil levels were mostly normal, eosinophil levels showed both normal and increased values, lymphocyte levels remained normal, monocyte levels continued to increase, and NLR values were within the normal range. The transient increase in neutrophil levels during the first month of treatment may reflect their role in the early immune response to bacterial infection.

During months 1 and 2, basophils and eosinophils were typically normal, with neutrophils also normal in the third month, although basophils and eosinophils showed an increase (Bohrer et al. 2021). The elevated neutrophil count in months 1 and 2 may be associated with defensins, small peptides with antimicrobial properties that inhibit or kill microorganisms, including bacteria. A decrease in neutrophil PMNs by month 4 could indicate a reduction in bacterial infection and antimicrobial protein production. However, the initial increase in neutrophils reflects the immune system's early response to infection, while normal neutrophil levels may signify a new TB infection in its initial phase, where leukocyte types have not yet undergone significant changes (Bloom, 2023).

The results of this study indicate that TB treatment for up to six months shows gradual healing as seen in PMN, MN, and NLR values. Maximum results are obtained after the fourth month. The increase in neutrophils at the beginning of treatment reflects an acute immune response, while their decrease indicates clinical improvement. These results are in line with Omair et al. (2024), who noted a decrease in NLR, MLR, and NMR in the first two months of treatment. Kissling et al. (2023) also confirmed the role of NLR and MLR in the diagnosis of childhood TB. Meanwhile, the increase in monocytes during therapy is in line with the report of (Shima et al. 2024) regarding monocyte activation as an immune response. Monitoring for up to six months in this study complements previous evidence by confirming the role of PMN, MN, and NLR as dynamic biomarkers for TB recovery.

Table 1. Duration of therapy to number of Polymorphonuclear cell in TB patients at Karang Taliwang and Cakranegara Community Health Centers in 2024.

Treatment Duration (Months)	Percentage of Basophil cells		Percentage of Eosinophil cells		Percentage of Neutrophil cells				
	Normal	Total	Normal	Hight	Total	Normal	Low	Hight	Total
1 Months	11.5%	11.5%	11.5%	0.0%	11.5%	7.7%	0.0%	3.8%	11.5%
2 Months	3.8%	3.8%	3.8%	0.0%	3.8%	0.0%	0.0%	3.8%	3.8%
3 Months	7.7%	7.7%	0.0%	7.7%	7.7%	7.7%	0.0%	0.0%	7.7%
4 Months	34.6%	34.6%	19.2%	15.4%	34.6%	30.8%	3.8%	0.0%	34.6%
5 Months	34.6%	34.6%	26.9%	7.7%	34.6%	30.8%	3.8%	0.0%	34.6%
6 Months	7.8%	7.8%	3.8%	3.8%	7.7%	7.7%	0.0%	0.0%	7.7%
Total		100%	65.4%	34.6%	100%	84.8%	7.6%	7.6%	100%

Table 2. Cross Distribution of Duration of therapy with Mononuclear Values in patients with tuberculosis at Karang Taliwang and Cakranegara Community Health Centers in 2024.

Treatment Duration (Months)	Percentage of Lymphocytes			Total	Percentage of Monocytes		Total
	Normal	Low	Hight		Normal	Hight	
1 Months	0%	0%	11.5%	11.5%	3.8%	7.7%	11.5%
2 Months	0%	0%	3.8%	3.8%	0%	3.8%	3.8%
3 Months	3.8%	3.8%	0%	7.7%	0%	7.7%	7.7%
4 Months	30.8%	0%	3.8%	34.6%	0%	34.6%	34.6%
5 Months	23.1%	7.7%	3.8%	34.6%	0%	34.6%	34.6%

6 Months	7.7%	0%	0%	7.7%	0%	7.7%	7.7%
Total	65.4%	11.5%	23.1%	100%	3.8%	96.2%	100%

In the overall assessment of TB patients, all patients (100%) had normal basophil levels. Among these patients, as many as 17 TB patients (65.4%) had normal eosinophil levels, while 9 TB patients (34.6%) showed an increase in eosinophils. Neutrophils were normal in 22 patients (84.6%), with 2 patients (7.7%) experiencing a decrease and another TB patients (7.7%) showing an increase Click or tap here to enter text.. The observed decrease in eosinophils could be due to side effects of OAT (Algifari et al., 2021). Normal basophil and eosinophil levels were maintained throughout the 6-month treatment period, which may be attributed to the effects of tuberculosis drugs like rifampicin and isoniazid on blood cells (Nabilah, 2020; Mancuso et al., 2023). Rifampicin, in particular, can cause hematologic. reactions by binding to macromolecular plasma proteins, which leads to the formation of antigen-antibody complexes (Shojaan et al., 2023). These complexes are absorbed by leukocytes, leading to leukocyte lysis and a subsequent decrease in leukocyte count (Sugiyono. 2023).

In mononuclear lymphocytes, 6 TB patients (23.1%) showed an increase, 3 patients (11.5%) showed a decrease, and 17 patients (65.4%) had normal levels. For monocytes, an increase was observed in 25 patients (96.2%), with only 1 patient (3.8%) showing normal levels. At Public Hospital Paru Medan, leukocyte cell counts increased by 25%, eosinophils by 5%, neutrophils decreased by 10%, lymphocytes increased by 5%, and monocytes by 3% (Lubis, 2021). These changes may be due to the response of monocytes and lymphocytes to TB infection in patients taking OAT. During TB infection, the immune system increases the production of white blood cells, such as monocytes and lymphocytes, to help combat the infection and support recovery (Shojaan et al., 2023).

Table 3. Cross distribution of duration of therapy with neutrophil lymphocyte ratio in patients with tuberculosis at Karang Taliwang and Cakranegara Health Centers in 2024.

Treatment Duration (Months)	Percentage of Neutrophil Lymphocyte Ratio (NLR)		Total
	Normal	Low	
1 Month	3.8%	7.7%	11.5%
2 Month	3.8%	0.0%	3.8%
3 Month	0.0%	7.7%	7.7%
4 Month	3.8%	30.8%	34.6%
5 Month	0.0%	34,6%	34.6%
6 Month	0.0%	7.7%	7.7%
Total	11.5%	88.5%	100.0%

Table 4. The results of the Anova test based on the duration of treatment against the number of polymorphonuclear cells, mononuclear cells and neutrophil lymphocyte ratio in TB patients.

		Sum of Squares	Df	Mean Square	F	Sig.
PMN Basophil	Between Groups	.004	5	.001	2.934	.038
	Within Groups	.006	20	.000		
	Total	.010	25			
PMN Neutrofil	Between Groups	31.907	5	6.381	3.170	.029
	Within Groups	40.266	20	2.013		
	Total	72.173	25			

MN Lymposit	Between Groups	39.872	5	7.974	10.099	.000
	Within Groups	15.792	20	.790		
	Total	55.664	25			
MN Monosit	Between Groups	3.790	5	.758	1.362	.280
	Within Groups	11.133	20	.557		
	Total	14.923	25			
NRL	Between Groups	.637	5	.127	4.053	.011
	Within Groups	.629	20	.031		
	Total	1.265	25			

Based on Table 4 data analysis, the results indicated that the data was normally distributed ($P > 0.05$). Following this, statistical tests using One-way ANOVA revealed that PMN cells (basophils and neutrophils) and MN cells (lymphocytes and monocytes) showed a value of $P < 0.05$. This suggests a positive relationship between PMN cells (basophils and neutrophils), MN cells (lymphocytes and monocytes), and NRL, with an indication of the recovery rate of TB patients at Karang Taliwang and Cakranegara Community Health Centers in 2024.

Table 5. Results of the Kruskal-Wallis Test on the sample length of treatment on the number of Eosinophils of the cure rate of tuberculosis patients at Karang Taliwang and Cakranegara Community Health Centers.

	PMN Eosinophil
Kruskal-Wallis H	7.889
Df	5
Asymp. Sig.	.162

Based on Table 5, eosinophil PMN cells, which showed a non-normal distribution, were tested using the Kruskal-Wallis non-parametric test. The results indicated that eosinophils do not have a positive relationship with the cure rate of TB patients at the Karang Taliwang and Cakranegara health centers in 2024 (Permana, 2020). In several studies, eosinophils have been seen as an indicator of OAT side effects rather than an indicator of TB cure. Therefore, eosinophils do not significantly impact TB recovery (Yu et al., 2022). Adherence to OAT is crucial for improving TB patient recovery (Kim et al., 2021). Indications of cure can be observed through clinical symptoms, such as a decrease in NRL values and normalisation of lymphocyte counts in TB patients. Neutrophil counts have also been used as a marker of the healing phase in TB patients. In the intensive phase, TB patients typically show increased lymphocytes and normal NRL due to infection. In the advanced phase, all TB patients have normal lymphocyte levels and decreased NRL values. These results suggest that lymphocytes and NRL can serve as indicators of the cure rate in TB patients, as successful TB treatment is expected to restore cell counts to normal (Levy et al., 2023).

4. CONCLUSION

Treatment of TB patients during fourth month to sixth month or in the advanced phase of treatment showed differences in the number of polymorphonuclear cells, mononuclear cells and the NLR ratio compared to intensive phase treatment in TB patients at the Karang Taliwang and Cakranegara Health Centers as an indication of patient recovery.

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