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Evaluation of the Duration of Anti-Tuberculosis Drug Administration on Leukocyte Profiles in Tuberculosis Patients

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Abstract: Tuberculosis (TB) is a global health problem that requires monitoring the immune response during treatment. Leukocyte profile is an important indicator in assessing the body's response to anti-tuberculosis drug therapy. The purpose of the study was to determine the difference in leukocyte profiles in pulmonary TB patients after 0 months and 2 months of anti-tuberculosis drug treatment—analytical research method with cross-sectional design on 60 pulmonary TB patients in Sungai Malang and Karias Health Center. Samples were selected purposively. Leukocyte examination was performed using Hematology Analyzer, and data were analyzed by independent t-test and Mann-Whitney. The results showed a significant decrease in the number of leukocytes (9,877/mm³ to 6,678/mm³, $p<0.05$), segment neutrophils (68.73% to 51.33%, $p<0.05$), and a significant increase in lymphocytes (21.07% to 37.33%, $p<0.05$). Basophils, eosinophils, rod neutrophils, and monocytes showed no significant difference ($p>0.05$). Conclusion A 2-month anti-tuberculosis drug treatment duration decreased leukocytes and segment neutrophils and significantly increased lymphocytes. Leukocyte monitoring is recommended as an indicator of therapy response.
Keywords: Anti-tuberculosis drugs; leukocyte profile; tuberculosis

INTRODUCTION

Tuberculosis (TB) is the most common infectious disease caused by Mycobacterium tuberculosis. Despite the development of new diagnostic methods and treatment techniques, the disease remains a major public health problem globally[1]. It is estimated that 10.6 million people worldwide will fall ill with TB by 2022. This equates to 133 incident cases per 100,000 population. Most TB cases in 2022 will occur in regions in Southeast Asia (46%), Africa (23%), and the Western Pacific (18%)[2]. TB treatment is carried out in two phases: intensive and continuation. Anti-tuberculosis drugs include isoniazid, ethambutol, rifampicin, pyrazinamide, and streptomycin. Anti-tuberculosis drugs can reduce the elevated leukocyte count due to infection and return it to normal levels after a few months[3]. However, the combination of drugs may trigger side effects such as eosinophilia (increase in eosinophils) and lymphopenia (decrease in lymphocytes)[4].

Previous studies, such as the Fadel Lubis study (2021), showed that 75% of pulmonary TB patients who received treatment for two months had normal leukocyte counts, while 25% had increased leukocytes[5]. Hairani's study (2019) found that the

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leukocyte count decreased significantly after two months of treatment, indicating a positive immune response to anti-tuberculosis drugs[6].

Despite an increase in drug-sensitive and Drug-Resistant TB cases based on Hulu Sungai Utara P2P data (2022-2023), no local study has specifically examined changes in the number and type of leukocytes in TB patients as an indicator of treatment effectiveness.

This study not only measured general leukocyte counts but also analyzed changes in the complete leukocyte profile (basophils, eosinophils, neutrophils, lymphocytes, and monocytes) at 0 months and 2 months of treatment. This focus on hematologic profiles makes an important contribution to the understanding of immunologic mechanisms in TB patients and may serve as a reference for similar studies in the future. So, this study aims to determine the difference in length of treatment with leukocyte profiles in pulmonary TB patients in Central Amuntai, Hulu Sungai Utara. The length of treatment studied was 0 months and 2 months, while the leukocyte profile analyzed included the number and type of leukocytes.

MATERIALS AND METHODS

This study was an analytic survey study with a cross-sectional design. Researchers took a sample of 60 tuberculosis (TB) patients who underwent treatment at 0 months and 2 months. Samples were selected using a purposive sampling technique. Inclusion criteria were TB patients with bacteriological confirmation of TB and willing to become respondents. Exclusion criteria were patients with drug-resistant TB, glandular and other TB, and patients with a history of HIV or diabetes mellitus. The independent variable was the length of treatment (0 months and 2 months), while the dependent variable was the number and type of leukocytes in pulmonary TB patients.

We used a Hematology Analyzer Swelab to check leukocyte counts, microscopes and slides to count leukocyte types, and equipment such as syringes, tourniquets, 70% alcohol swabs, dry swabs, and gloves. Materials used included alcohol, EDTA, Giemsa solution, methanol, aqua dest, and venous blood of TB patients. Primary data were obtained from laboratory examination results. In contrast, secondary data were medical record data for 0 months of anti-tuberculosis drugs treatment duration (0 to < 1 month) and with 2 months of anti-tuberculosis drugs treatment duration (2 to < 3 months) at UPT Puskesmas Sungai Malang and UPT Puskesmas Sungai Karias in June, July, and August 2024.

The study procedure began with the operation of the Hematology Analyzer Swelab to measure the leukocyte count. Blood samples that have been mixed with anticoagulants are examined by entering patient data on the device and waiting for the output results. Leukocyte type examination was performed by Giemsa staining method. Blood was smeared on a glass slide, dried, fixed with methanol, and stained using Giemsa solution. After rinsing and drying, the sample was observed under a microscope (Olympus) at 1000x magnification. Leukocytes were systematically counted until they reached 100 cells using a differential cell counter or Schilling hemogram.

Statistical analysis was performed using SPSS software with the Shapiro-Wilk test for normality. Non-normally distributed data were analyzed using the Mann-Whitney test, while normally distributed data were analyzed using the independent t-test. This research

obtained an ethical test certificate from the Research Ethics Commission of the Poltekkes Kemenkes Banjarmasin, number 743/KEPK-PKB/2024.

RESULTS AND DISCUSSION

Respondent Characteristics

Research conducted in June-August 2024 showed pulmonary TB patients with 0 months and 2 months of treatment obtained a total of 60 people. General characteristics of respondents with a total of 60 people based on gender and age as in figures 1 and 2.

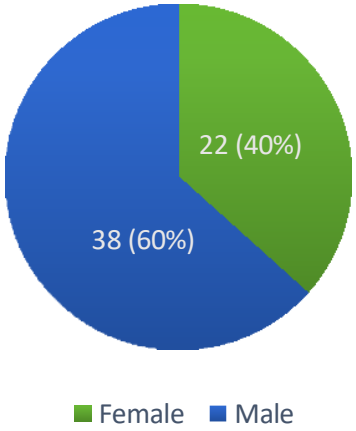

Figure 1. Characteristics of Respondents at 0 Months and 2 Months of Treatment by Gender

Based on Figure 1, it can be seen that pulmonary TB patients with 0 months and 2 months of treatment have 22 people (40%) female respondents and 38 people (60%) male.

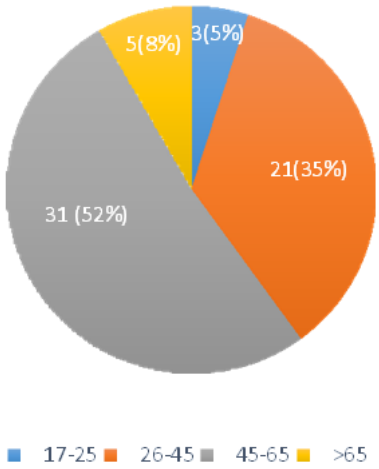

Figure 2. Characteristics of Respondents at 0 and 2 Months of Treatment by Age

Based on Figure 2, it can be seen that pulmonary TB patients with 0 months and 2 months of treatment have 3 respondents (5%) in the age range of 17-25 years, 21 people (35%) respondents in the age range of 26-45 years, 31 people (52%) respondents in the age range of 45-65 years, and 5 people (8%) respondents in the age range > 65 years.

Leukocyte Count and Type Results

Table 2 shows the mean counts of leukocytes, basophils, eosinophils, stab neutrophils, segment neutrophils, lymphocytes, and monocytes at 0 months and 2 months of treatment. These data show the average changes in each parameter after 2 months of treatment.

Table 2. Mean Leukocyte Count and Type at 0 Month and 2 Months of Treatment

Parameters	Normal value	Average (0 Months)	Average (2 Months)
Leukocyte Count (/mm3)	4.500-11.000	9.877	6.678
Basophils (%)	0-2	0.2	0.13
Eosinophils (%)	2-4	1.53	2.23
Neutrophil Stab (%)	0-10	3.67	3.27
Segment Neutrophils (%)	51-67	68.73	51.33
Lymphocytes (%)	21-35	21.07	37.33
Monocytes (%)	4-8	4.8	5.7

Table 2 shows the changes in mean leukocyte counts and types in TB patients after treatment for 0 months and 2 months compared to normal values. The mean leukocyte count decreased significantly from 9,877/mm³ at 0 months to 6,678/mm³ at 2 months (normal value 4,500- 11,000/mm³). Basophils decreased from 0.2% to 0.13% (normal value 0-2%). In contrast, eosinophils increased from 1.53% to 2.23%, although they remained within the normal range of 2-4%. Stab neutrophils decreased slightly from 3.67% to 3.27% (normal value 0-10%), while segment neutrophils decreased significantly from 68.73% to 51.33%, close to the lower limit of normal value 51-67%. Lymphocytes increased significantly from 21.07% to 37.33%, exceeding the normal value of 21-35%. Monocytes also increased from 4.8% to 5.7%, remaining within the normal range of 4-8%.

Distribution of Differences in the Number and Type of Leukocytes in Pulmonary TB Patients with 0 Months and 2 Months of Treatment

Differences in the number and type of leukocytes in pulmonary TB patients with 0 months and 2 months of treatment can be seen using the t-independent test. This study first carried out a normality test using the Shapiro-Wilk test. The table below shows the differences in the number and type of leukocytes in pulmonary TB patients with 0 months and 2 months of treatment.

Table 1. Normality Test Results of Leukocyte Count and Type at 0 Month and 2 Months of Treatment

Shapiro Wilk	Sig.
Leukocyte Count	0.034
Basophils	0.000
Eosinophils	0.001
Lymphocytes	0.791
Neutrophil Segment	0.041
Neutrifil Stab	0.001
Monocytes	0.001

Based on the above results, statistically obtained data on the number of leukocytes, basophils, eosinophils, segment neutrophils, stab neutrophils, and monocytes data are not normally distributed because Sig. <0.05. So proceed with the Mann-Whitney test, while in lymphocytes, the data is normally distributed because Sig. >0.05, so proceed with the t-Independent test.

The results of differences in the number and type of leukocytes in pulmonary TB patients with 0 months and 2 months of treatment can be seen using the t-independent test, and Mann Whitney to Table 3 shows the results of a study comparing the length of treatment with leukocyte profiles in pulmonary TB patients.

Table 3. Results of Mann Whitney Test and Independent t-test on Leukocyte Counts and Types at 0 Month and 2 Months of Treatment

Variables	Statistical Test	P Value	Conclusion
Leukocyte Count	Mann Whitney	0.000	There is a difference
Basophils	Mann Whitney	0.741	No difference
Eosinophils	Mann Whitney	0.253	No difference
Neutrophil Seg	Mann Whitney	0.000	There is a difference
Neutrophil Stab	Mann Whitney	0.360	No difference
Lymphocytes	Independent t-test	0.000	There is a difference
Monocytes	Mann Whitney	0.056	No difference

Based on Table 3. shows the results of statistical analysis of the Mann-Whitney Test for leukocyte count and Neutrophil Segment, that is, Sig value. (2-tailed) <0.05, so it is stated that there is a significant difference in the number of leukocytes and the count of segment neutrophils of pulmonary TB patients with 0 months and 2 months of treatment, while for the count of basophils, eosinophils, stab neutrophils, and monocytes obtained Sig. (2-tailed) >0.05, then it is stated that there is no significant difference in the types of basophils, eosinophils, stab neutrophils, and monocytes of pulmonary TB patients with 0 months and 2 months of treatment. Based on the results of the statistical analysis of the Independent t-test for the lymphocyte count, the value of Sig. (2-tailed) <0.05, then it is stated that there is a significant difference in the lymphocyte count of pulmonary TB patients with 0 months and 2 months of treatment.

Based on the results of a study of 60 respondents who underwent anti-tuberculosis drug treatment for 0 months and 2 months, it was found that pulmonary TB patients were more common in men (60%) than women (40%). Research by Sunarmi et al. (2022) supports this finding, stating that the prevalence of TB is higher in men due to factors such as smoking and alcohol consumption, which reduce the immune system. Reduced respiratory immunity due to cigarette smoke toxins can damage mucocilia and inhibit antigen response, thus increasing the risk of pulmonary TB. In addition, men's routine of being outside more is also a risk factor for transmission[7].

Patient age also affects the incidence of pulmonary TB. This study showed that the majority of patients were in the age range of 45-65 years (52%), followed by age 26-45 years (35%), age >65 years (8%), and age 17-25 years (5%). These results are consistent with the research of Sutrisna et al. (2022), which states that TB is more prevalent in productive age (15-58 years) due to busy lifestyles, lack of rest, and decreased immunity,

which increases the risk of infection[8].

This study also recorded various anti-tuberculosis drug side effects that patients complained about, including dizziness (7 people), itchy skin (21 people), joint pain (7 people), chest pain (2 people), and indigestion (10 people). These results were reinforced by Caroll's (2012) study on 655 respondents, which reported that the main side effects were digestive disorders (53 people), muscle-joint pain (22 people), psychological disorders (10 people), visual disturbances (9 people), and nervous disorders (8 people). These side effects were more common in patients on second-line therapy, but In the first-line, pyrazinamide most commonly triggered joint pain and gastrointestinal disturbances[9].

Leukocyte count analysis showed a significant difference between 0-month and 2-month treatment, with means of 9,877/mm³ and 6,678/mm³ (Sig. (2-tailed) <0.05). This finding is in line with the research of Ainu'rohmah et al. (2020), which also found significant differences in leukocyte counts before and after treatment (Sig. (2-tailed) < 0.05)[10]. According to Bestari and Adang (2014), TB treatment can reduce the number of leukocytes, which previously increased in number due to infection. A normal leukocyte count is obtained after several months of treatment[3].

This study showed the distribution of leukocyte types analyzed before and after treatment for 2 months. The mean basophils decreased from 0.2% to 0.13%, with Sig. (2-tailed) >0.05, indicating no significant difference. This value remains within the normal range (0-2%). According to Sutedjo (2011), an increase in basophils occurs in leukemia, while a decrease indicates a hypersensitivity reaction. These results indicate that the respondents did not experience leukemia or hypersensitivity[11].

Eosinophils increased from 1.53% to 2.23% but showed no significant difference (Sig. >0.05) compared to normal values (2-4%). Ulya (2018) explained that the increase in eosinophils could be caused by the side effects of Isoniazid, which is bactericidal. However, the questionnaire data did not show signs of allergy in patients, so the increase in eosinophils is more likely to be caused by drug effects[12].

Segmental neutrophils decreased significantly from 68.73% to 51.33% (Sig. <0.05), which is within the normal range (51-67%). This decrease is in accordance with Tiemessen's (2010) study, which showed that anti-tuberculosis drugs can reduce neutrophils through immune complexes that damage granulocytes. Rod neutrophils decreased from 3.67% to 3.27%, but not significantly (Sig. >0.05), and remained within normal values (0-10%)[13].

Lymphocytes increased significantly from 21.07% to 37.33% (Sig. <0.05), exceeding normal values (21-35%). According to Kaihena (2013), the increase in lymphocytes occurs due to stimulation of T lymphocytes, which enhances the immune response to *Mycobacterium tuberculosis*. This increase signifies the body's response to infection and the ongoing healing process[14].

Monocytes increased from 4.8% to 5.7% but showed no significant difference (Sig. >0.05) and remained within normal values (4-8%). According to Wirawan (2011), the increase in monocytes is the body's response to bacterial infection, mainly due to the role of monocytes in the formation of tubercles with macrophages[15]. Diana (2018) adds that monocytes that increase and then return to normal after treatment indicate the success of therapy[16].

The results of this study showed a pattern of changes consistent with the body's immune mechanisms to anti-tuberculosis drug therapy, with significant differences in

segmental neutrophils and lymphocytes, which are important indicators in monitoring treatment effectiveness.

This study highlights specific changes in various leukocyte types, including segmental neutrophils and lymphocytes, which provide important insights into the body's immune response to anti-tuberculosis drug therapy. This study is also clinically relevant, as it can provide a basis for health workers to monitor hematological parameters during TB treatment.

However, this study has several limitations, namely the short scope of treatment time, which only compares leukocyte profiles at 0 months and 2 months, so it cannot provide an overview of long-term changes to the advanced phase of treatment. In addition, the limited sample size of 60 patients from two health centers using a purposive sampling technique may limit the generalization of the results to a wider population. This study also did not examine other factors that may affect leukocyte profiles, such as nutritional status, comorbidities, and medication adherence.

CONCLUSION

This study shows that in pulmonary TB patients with 0 months of treatment, the average leukocyte count is 9.877%, with details of basophils 0.2%, eosinophils 1.53%, stab neutrophils 3.67%, segment neutrophils 68.73%, lymphocytes 21.07%, and monocytes 4.8%. In patients with 2 months of treatment, the mean leukocyte count was 6.678%, with details of basophils 0.13%, eosinophils 2.23%, stab neutrophils 3.27%, segment neutrophils 51.33%, lymphocytes 37.33%, and monocytes 5.7%. There were significant differences in leukocyte, lymphocyte, and segment neutrophil counts between 0 months and 2 months of treatment ($p<0.05$), while basophils, eosinophils, stab neutrophils, and monocytes showed no significant differences ($p>0.05$). Health workers are advised to monitor the development of leukocyte counts in pulmonary TB patients during treatment to detect the body's response and possible side effects. Future studies should expand the analysis with longer treatment duration and larger samples and examine drug interactions in more depth.

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CONFLICT OF INTEREST

The authors declare no conflict of interest and have not received any funds for this study.

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