



# The relationship between the length of treatment for pulmonary tuberculosis patients in the intensive phase and hemoglobin levels

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## Abstract

**Background:** Tuberculosis (TB) medication can alter hematological parameters, including hemoglobin levels. Hemoglobin levels due to anti-TB drugs have the potential to cause anemia. Therefore, it is important to know the risk of anemia during intensive phase TB treatment therapy. **Objectives:** This study aims to determine the relationship between the length of treatment for TB patients in the intensive phase and hemoglobin levels. **Materials and Methods:** The sample was selected using the accidental sampling method. The number of samples obtained was 31 consisting of 17 respondents from the *Kedungmundu* Community Health Center, 14 respondents from the *Bangetayu* Community Health Center. EDTA blood was analyzed using a KX21-N hematology analyzer. The relationship between the duration of treatment and hemoglobin levels in TB patients was statistically tested using Pearson correlation test. **Results:** Most of the intensive phase TB patients are in the 15-24 years age group. The percentage of female patients is 54.8%, and 45.2% male. TB patients with a treatment duration of 5-8 weeks are 34.1% and a treatment duration of 1-4 weeks is 65.9%. Normal hemoglobin levels are 51.6%, and low hemoglobin levels are 48.4%. The results of the Pearson correlation test have a significance level of 0.862. **Conclusion:** There is no correlation between the duration of treatment of intensive phase TB patients and hemoglobin levels. The importance of monitoring hemoglobin levels during intensive phase treatment, in order to monitor the effectiveness of treatment or the presence of complications such as anemia.

## Keywords

Drug, Hematological parameters, Red blood cells, TB, Therapy period.



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## 1. Introduction

Tuberculosis (TB) is an infectious disease that causes of death worldwide. An estimated 10.1 million people contracted TB in 2020, increasing by 4.5% to 10.6 million people in 2021. Indonesia is one of the countries with the second largest TB burden after India. TB incidence in India is 28% while in Indonesia it is 9.2%. TB is caused by the *Mycobacterium tuberculosis* bacillus, which spreads when people with TB expel the bacteria into the air (e.g. through coughing) (World Health

Organization, 2020). The notification rate of all tuberculosis cases in Central Java Province in 2022 was 179 per 100,000 population, an increase from 110 per 100,000 population in 2021. Semarang City still ranks as the highest regency/city with a Case Notification Rate (CNR) of all TB cases of 348 per 100,000 population (Dinas Kesehatan Provinsi Jateng, 2022). TB sufferers in Semarang City in 2022 amounted to 4,653 cases, this figure has increased compared to 2021. Kedungmundu District is the District with the highest number of pulmonary TB cases with a total of 186 cases and Bangetayu District is in second place with a total of 158 pulmonary TB cases (Dinas Kesehatan Kota Semarang, 2022a)(Dinas Kesehatan Kota Semarang, 2022b). To prevent and control TB infection, it must be done early diagnosis and treatment, and monitoring of TB patients during treatment. TB treatment monitoring aims to ensure the success of treatment.

The success rate of Semarang City's treatment has not reached the national target (90%) (Dinas Kesehatan Kota Semarang, 2022b). According to the results of Berliana (2020), non-compliance with regular treatment is one of the obstacles to achieving recovery. High non-compliance with treatment has an impact on high resistance (OAT) to pulmonary anti-tuberculosis drugs which causes the duration of treatment to increase (Berliana et al., 2020). One of the efforts needed to achieve the cure rate is pulmonary tuberculosis treatment. TB treatment is carried out in the intensive phase for the first 2 months or can go to the advanced phase (Achmad et al., 2022). Based on the previous findings, long-term TB treatment causes problems of non-compliance. Non-compliance in tuberculosis treatment can have a negative impact on clinical outcomes and public health (Sazali et al., 2023) .

TB treatment causes reversible changes in hematological parameters. Studies have shown that hematological abnormalities are common in TB patients such as leukocytosis, monocytosis, lymphocytosis, thrombocytosis, lymphopenia, and anemia (Bonsome, 2017) (Fayed et al., 2018). Anti-TB drugs such as isoniazid and rifampicin can cause hemolytic anemia or metabolic disorders that affect Hb levels (Mursalim et al., 2022). Decreased hemoglobin concentration is also interpreted as anemia. The criteria for anemia are based on hemoglobin levels, in men HgB <13 g/dL and women <12 g/dL (Saxena et al., 2018) (Kementerian Kesehatan RI, 2018).

Shadrina's (2019) study on pediatric patients before treatment showed that out of 110 children, 56 children were found with Hb levels of less than 11 g/dL (Shadrina & Atikah, 2019). The previous study also showed a significant decrease in hemoglobin levels in Tuberculosis patients before undergoing Anti-Tuberculosis Drug treatment (Shah et al., 2022). Although hematological abnormalities in hemoglobin associated with tuberculosis have been documented, there has been

no study detailing the length of the intensive phase in relation to hemoglobin levels. Therefore, this study is important to determine the risk of anemia during intensive phase TB therapy.

## 2. Materials and Methods

### 2.1 Type of research

This type of research is a quantitative descriptive study conducted in April 2023 at Puskesmas Kedungmundu and Puskesmas Bangetayu Semarang City. The population of this study were TB patients at Kedungmundu and Bangetayu Health Center. The samples in this study were pulmonary tuberculosis patients in the intensive phase of treatment, which were selected using accidental sampling method. The number of samples obtained was 31 respondents consisting of 17 respondents from Puskesmas Kedungmundu and 14 respondents from Puskesmas Bangetayu.

The data collected came from two types of data, namely primary data and secondary data. Primary data was in the form of hemoglobin examination result data and secondary data obtained from Kedungmundu and Bangetayu Health Center Medical Record data regarding sample code, age, gender, and length of treatment of pulmonary tuberculosis patients who came and underwent intensive phase treatment.

### 2.2 Research methods

This study utilized instruments like informed consent, result sheets, hematology analyzer tools, and blood sampling materials. Blood was collected through venous puncture and analyzed using the KX21-N hematology analyzer, which displayed results on an LCD screen (Booth & Mundt, 2019) (Corporation, 2014).

The collected data were processed and presented in a descriptive table, then continued with the Spearman rank test. Hypothesis determination shows that if the  $p$  value  $> 0.05$ , then there is no significant relationship between the duration of treatment of intensive phase pulmonary tuberculosis patients and hemoglobin levels. Conversely, if the  $p$  value  $< 0.05$ , then there is a significant relationship between the duration of treatment of intensive phase pulmonary tuberculosis patients and hemoglobin levels. Inclusion criteria were pulmonary tuberculosis patients undergoing intensive phase treatment. This study has been approved by the research ethics committee of the Health Polytechnic of the Ministry of Health Semarang on January 05, 2023 with the number 003/EA/KEPK/2023.

### 3. Results and Discussion

#### 3.1 Results

Characteristics of intensive phase pulmonary tuberculosis patients based on age, and gender can be seen in table 1 as follows

Table 1. Sample Characteristics Based on Age and Gender

Variable	n	%
Age (years)		
0-14	1	3.2
15-24	12	38.7
25-34	4	12.9
35-44	6	19.4
45-54	3	9.7
55-64	3	9.7
≥ 65	2	6.5
Gender		
Men	14	45.2
Women	17	54.8

The characteristics of intensive phase pulmonary tuberculosis patients based on age and gender were found to be mostly in the age group of 15-24 years. The percentage of female patients was 54.8%, and male patients were 45.2%. The length of treatment of pulmonary tuberculosis patients in the intensive phase was 34.1% with a length of treatment of 5-8 weeks and a length of treatment of 1-4 weeks as much as 65.9% (Table 2).

Table 2. Distribution of samples based on length of treatment

Length of Treatment (week)	Respondent	
	n	%
1-4	15	48,4
5-8	16	51,6
Total	31	100

The distribution of samples in the study based on hemoglobin levels of pulmonary tuberculosis patients in the intensive phase can be seen in Table 3.

Table 3. Distribution of samples based on hemoglobin levels

Variable	Respondent		Hemoglobin level			Std deviation
	n	%	Min (g/dL)	Max (g/dL)	Mean (g/dL)	

Normal Hb levels	16	51,6				
Low Hb levels	15	48,4	9,9	17,3	12,735	1,9506
Total	31	100				

The hemoglobin level of the study respondents obtained normal levels as much as 51,6%, and low hemoglobin levels as much as 48,4%, with a minimum hemoglobin level of 9.9 g/dL, a maximum of 17.3 g/dL, and an average of 12.735 g/dL.

**Table 4.** Shapiro-Wilk Normality Test

Variable	Statistik	df	Sig.
Length of treatment	0.638	31	0.000
Hemoglobin level	0.947	31	0.130

The results of the normality test for length of treatment, and hemoglobin levels in intensive phase pulmonary tuberculosis patients using Shapiro Wilk obtained a p-value <0.05 which states that the data is not normally distributed as seen in Table 4.

**Table 5.** Pearson Correlation Test

Variable	df	Sig.
Length of treatment	31	0.862
Hemoglobin level		

The results of the relationship test after using the Pearson correlation test had a significance level of 0.862. This shows that there is no relationship between the length of treatment of pulmonary tuberculosis patients in the intensive phase with hemoglobin levels.

### 3.2 Discussion

The age characteristics of patients with intensive phase pulmonary tuberculosis are most commonly found in the 15-24 age group. This study differs from the previous study in Deli Serdang, where the highest number of respondents was found in the age group of 60-72 years (Situmorang, 2020). The results of the study were also different, TB cases at Adam Malik General Hospital, Medan were mostly found in the 45-54 year age group (Purba, 2021). The characteristics of female respondents (53%) are more numerous than male (47%). The characteristics of female respondents (53%) are greater than male respondents (47%). This result is different when compared to national TB case data where the number of cases in men (58.0%) is greater than in women (42.0%) (Kementerian Kesehatan RI, 2023). According to the WHO in 2023, the number of TB cases will be higher in men compared to women (World Health Organization, 2023). This is not in line with the

study from Situmorang (2020), in this study the majority of TB patients were male, 14 respondents (66.7%), and women were 7 respondents (33.3%). This study explains that men are more often active outside the home and are more at risk of being exposed to or contaminated by microorganisms than women. This is also supported by the opinion that smoking habits and poor adherence to taking medication make men more at risk of being exposed to TB (Situmorang, 2020).

The duration of treatment is the length of time a patient undergoes pulmonary tuberculosis treatment which is divided into two phases, namely the intensive phase for the first two months, and the continuation phase for four months after that. In the intensive phase for the first two months, pulmonary tuberculosis patients consume more drugs than in the continuation phase, where patients must consume four different types of drugs, namely isoniazid, rifampicin, pyrazinamide, and ethambutol (Ulfah, 2022). This aims to kill the *Mycobacterium tuberculosis* bacteria so that patients can recover, and prevent relapse. (OAT) Antituberculosis drugs have an important function as a factor in the length of treatment by taking the drug according to the dosage according to the established rules (Rojali & Noviatuzzahrah, 2018).

Pulmonary tuberculosis can cause reversible abnormalities in the peripheral blood. Abnormalities can occur in hemoglobin. Hemoglobin is a protein molecule containing iron found in red blood cells that functions to transport oxygen from the lungs to the body's tissues. Hemoglobin is a protein pigment that gives red blood cells their red color. Hemoglobin is measured to detect anemia and its severity, as well as to monitor the response of anemia patients to treatment (Dabbagh, 2009) (Kahar et al., 2022). The normal hemoglobin level in women is 12-14 g/dL, while in men it is 14-18 g/dL (Greer et al., 2019).

The results of hemoglobin level measurements in intensive phase pulmonary tuberculosis patients in this study found that 51.6% had normal hemoglobin levels and 48.4% had low hemoglobin levels. Pulmonary tuberculosis patients have low hemoglobin levels due to malnutrition, which worsens *Mycobacterium tuberculosis* infection so that patients have difficulty breathing and coughing up blood. This can also result in non-compliance with treatment by patients (Maulidiyanti, 2020). According to the research conducted by Permana (2020), hemoglobin levels become low in pulmonary tuberculosis patients due to the initial infection process, and the use of anti-tuberculosis drugs disrupts B6 metabolism, causing patients to experience sideroblastic anemia and hemolytic anemia (Permana, 2020).

Our findings indicate that there is no relationship between the duration of treatment and hemoglobin levels. (p value 0,862). This is because the number of TB patients with normal hemoglobin levels is greater than the number of patients with low hemoglobin levels. This research is in line with the study conducted by Purba, which states that there is an increase in hemoglobin levels after consuming OAT (*obat anti tuberculosis*). The duration of patient care can result in an increase in hemoglobin levels after the patient undergoes the initial phase of treatment if the patient's nutritional intake meets the requirements for hemoglobin formation. Consuming high-calorie and protein-rich foods plays a role in increasing hemoglobin (Purba, 2021). However, this is different from Situmorang's (2020) study, which found many TB patients with low hemoglobin levels. The decrease in hemoglobin levels occurs as a side effect of anti-tuberculosis medication (OAT) that is not accompanied by a good diet (Situmorang, 2020).

Anemia is functionally defined as a decrease in the blood's ability to carry oxygen to the tissues, resulting in tissue hypoxia. The term anemia refers to a decrease in the concentration of hemoglobin and/or erythrocytes. Low hemoglobin levels or anemia is a condition in which the hemoglobin level in men is <13 g/dL and in women <12 g/dL. Measurement of hemoglobin (Hb) levels is an important part of managing anemia patients. The diagnosis of anemia is usually made after a decrease in hemoglobin concentration is found from the CBC results (Saxena et al., 2018) (Kenzie & Williams, 2015).

The mechanism of anemia in pulmonary TB patients is explained as follows: bacterial invasion activates T lymphocytes and macrophages, which induce the production of cytokines (IFN- $\gamma$ ), (TNF- $\alpha$ ), Interleukin-1 (IL-1) and interleukin-6 (IL-6) which will cause the transfer of iron in the reticuloendothelial system causing a decrease in iron concentration in plasma thereby reducing the number of red blood cells available for hemoglobin synthesis, inhibition of erythroid progenitor cell proliferation and erythropoietin production and activity (Kassa et al., 2016) (Sheetal et al., 2020).

#### 4. Conclusions

The results of the study showed that there was no relationship between the length of treatment for pulmonary tuberculosis patients in the intensive phase and hemoglobin levels. There was a limited number of samples obtained in this study and some patients were reluctant to have their blood samples taken so the number of samples was minimal. The authors suggest further study using a larger sample size, adding variables such as age, nutritional status, or comorbidities and



conducted on patients with intensive and advanced phases of tuberculosis.

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**Author Contributions:** ANF: concept, methodology, writing original manuscript. RJW: supervision, concept, editing, review, validation.

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