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**Description of Liver Function on the Effect of Treatment on Pulmonary  
Tuberculosis Patients at the Manado City Health Center**

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## **Abstract**

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*. This bacterium usually attacks the lungs, but TB bacteria can also attack other parts of the body such as the kidneys, spine, and brain. Anti Tuberculosis Drugs (OAT) is the most important component in TB treatment. TB treatment is one of the most efficient efforts to prevent the further spread of TB. Research conducted by Ashford et al (2015), the risk of hepatotoxicity in the use of first-line OAT increases at the age of 60 years. Also a study conducted by Prihatni et al (2005) as many as 62.5% of subjects who used hepatotoxic Rifampicin in the second week after treatment, this study also showed an increase in serum ALT (alanine aminotransferase) due to the combination of OAT with rifampicin. The purpose of this study was to determine the description of liver function on the effects of treatment for pulmonary TB patients at three health centers in Manado city.

Thirty pulmonary TB patients at the Ranotana Weru, Tuminting and Tikala Health Centers were interviewed and their blood samples taken for examination of AST, ALT and bilirubin levels in the laboratory. The results showed that the ALT/SGPT enzyme activity value in patients with pulmonary tuberculosis in the normal range was 10-29 U/L in 24 (80%) patients and the abnormal value was 34-82 U/L in 6 (20%) patients. The value of AST/SGOT enzyme activity in patients with pulmonary tuberculosis in the normal range was 12-30 U/L in 25 (83.4%) patients and an abnormal value of 33-100 U/L, in 5 (16.6%) patients. Bilirubin levels in all pulmonary TB patients within normal limits are 0.22 – 1.30 mg/dl. Undesirable effects that arise during the treatment of pulmonary tuberculosis are itching and redness of the skin, joint pain, tingling and burning in the legs, red urine and sweat, nausea and vomiting. Suggestion, for health workers can provide health education to patients and their families monitoring OAT about the conditions and effects related to the dose of the drug given, the patient's family as OAT monitors must be able to ensure that patients with pulmonary tuberculosis who are in the treatment stage are obedient to taking medication and seek to recognize their condition. or signs and symptoms complained of due to the effects of the drug by the patient

Keywords: Patients with TB, ALT, AST, Bilirubin

## **BACKGROUND**

Tuberculosis (TB) is caused by the bacterium *Mycobacterium tuberculosis*. These bacteria usually attack the lungs, but TB bacteria can also attack other parts of the body such as the kidneys, spine, and brain. Not all people infected with TB bacteria become sick, so there are two conditions related to TB, namely latent TB infection (LTBI) and TB disease. (Harsh Mohan, 2010)

The number of new TB cases in Indonesia was 420.994 cases in 2017 (data per 17 May 2018). Based on gender, the number of new TB cases in 2017 in males was 1.4 times greater than in females. Even based on the Tuberculosis Prevalence Survey, the prevalence in men is 3 times higher than in women. The same is happening in other countries. This may be because men are more exposed to TB risk factors, such as smoking and lack of medication adherence. This survey found that 68.5% of all male participants smoked and only 3.7% of female participants smoked. (Indah, 2018)

Treatment for TB control is carried out by all First Level Health Facilities (FKTP) and Health Facilities. Advanced Reference (FKRTL). Anti Tuberculosis Drugs (OAT) for TB control are provided by the government and are given free of charge. Handling of cases in TB control is carried out through case management activities to break the chain of transmission and/or treatment of patients, which consists of treatment and handling of side effects in Health Service Facilities; monitoring adherence to swallowing medication; and monitoring of treatment progress and treatment outcomes; and tracking of lost to follow-up cases. (Permenkes RI No. 67 of 2016, 2016)

Adequate treatment must meet the following principles, given in the form of an appropriate combination of OAT containing at least 4 kinds of drugs to prevent resistance, given in the right dose, swallowed regularly and directly supervised by the PMO (Drug Swallowing Supervisor) until completion of treatment and treatment is given within a sufficient period of time divided into two (2) stages, namely the initial stage and the advanced stage, as adequate treatment to prevent recurrence. (Permenkes RI No. 67 of 2016, 2016)

Anti Tuberculosis (OAT) drugs consist of Rifampicin, Pyrazinamide, Isoniazid and Ethambutol. Treatment of pulmonary TB disease takes up to 6 months. The duration of the treatment has a risk of unwanted effects during treatment. *Drug-induced liver injury* (DILI) is one of the most common side effects of taking OATs, especially with the three main first-line drugs: isoniazid (INH), rifampin (RMP) and pyrazinamide (PZA). (Chang *et al.*, 2018)

Research conducted by Hosford *et al* (2015), the risk of hepatotoxicity in the use of first-line OATs increases at the age of 60 years (Hosford *et al.*, 2015). Also a study conducted by Prihatni *et al* (2005) as many as 62.5% of subjects who took hepatotoxic at 2

weeks after treatment, this study also showed an increase in serum ALT (alanine aminotransferase) due to the combination of OAT (Prihatni *et al.*, 2007) . The purpose of this study was to determine the description of liver function on the effect of treatment in patients with pulmonary tuberculosis in three locations of the Manado City Health Center

## **RESEARCH METHODS**

Design was a descriptive study by looking at the effect of anti-tuberculosis drug treatment (OAT) on pulmonary tuberculosis patients. on liver function, namely the activity of *alanine transaminase* (ALT) or serum *glutamate pyruvate transaminase*(SGPT), *aspartate aminotransferase* (AST) or serum *Glutamic Oxaloacetic Transaminase* (SGOT) enzymes and total bilirubin levels. This study also explored information about side effects and patient complaints. Pulmonary TB while taking OAT. The independent variables in this study were: characteristics of pulmonary TB patients undergoing OAT treatment including: age, gender, length of treatment, education level, type of work, duration of treatment, complaints and side effects of treatment. The dependent variables in this study were the serum activity values of ALT/SGPT, AST/SGOT and total bilirubin levels.

Data Collection Techniques The, recruitment of respondents in this study was carried out in 3 health centers, namely Ranotana Weru Health Center, Tikala Baru Health Center and Tuminting Health Center located in the Manado City Region. Taking into account the inclusion criteria, namely patients with pulmonary tuberculosis who are undergoing treatment at the Puskesmas and are willing to sign the IC and PSP and the exclusion criteria are patients with a history of liver disease or disorders. Respondents who were patients with pulmonary tuberculosis were then interviewed and taken 3 ml of blood samples by Puskesmas staff. Then the blood sample was examined at the Laboratory of the Health Laboratory Support Center of the North Sulawesi Provincial Health Office. The clinical chemistry parameters examined were AST/SGOT, ALT/SGPT and Total Bilirubin. The data obtained are presented in tabular form and discussed in descriptive form.

## **RESULTS AND DISCUSSION**

A total of 30 respondents who were patients with pulmonary TB at 3 Puskesmas in the City of Manado were interviewed and then blood was taken by the Puskesmas staff and then examined at the BPLK of the Health Office of North Sulawesi Province and obtained data according to the table of research results below.

Characteristics of respondents with pulmonary TB based on age, education, occupation and complaints of side effects of treatment can be seen in Table 1 below:

**Table 1.** Characteristics of Respondents with Pulmonary Tuberculosis Based on age, education, occupation and Complaints of Side Effects of Treatment at Ranotana Weru, Tikala Baru and Tuminting Health Centers in 2019.

Characteristics of Pulmonary TB Patients	(%)
<b>Age</b>	
17-25	2 (6%)
25-35	6 (20%)
36-45	5 (17%)
46-55	10 (32%)
56-65	5 (17%)
> 65	2 (6%)
<b>Total</b>	<b>30 (100%)</b>
<b>Education</b>	
Elementary	6 (20%)
Junior high	7 (23%)
High school	17 (57%)
Diploma	0 (0%)
Bachelor	0 (0%)
<b>Total</b>	<b>30 (100%)</b>
<b>Occupation</b>	
Civil Servant	3 (10%)
Private	3 (10%)
Self	10 (23%)
IRT	6 (17%)
Worker	14 (47%)
<b>Total</b>	<b>30 (100%)</b>
<b>Complaints/Side effects Treatment</b>	

Itching and redness of the skin	3 (10%)
Joint pain	30 (100%)
Tingling to burning sensation in the legs	23 (76, 6%)
Urine and sweat are red	30 (100%)
Nausea and vomiting	25 (83.3%)

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**Primary Data Sources in 2019**

Based on Table 1 above, the age of respondents with pulmonary TB is mostly at the age of 46-55 years with a total of 10 (32 %) people and the lowest at the age of 17-25 years is 2 (6%) people and over 65 years old is only 2 (6%) people. According to Chang et al., the increase in pulmonary TB patients with smoking is in line with the increasing age of smokers, so that at the age of 40-50 years the number of pulmonary TB patients with smokers increases due to smoking habits at ages ranging from 15 years so that it can be predicted at the age of 40-50 years in the future. These smokers have a high risk of developing pulmonary TB. The percentage of pulmonary TB patients then decreases at the age above 55 years. (Haoran Zhang, Henan Xin, Xiangwei Li, Hengjing Li, Mufei Li, Wei Lu, Liqiong Bai, Xinhua Wang, Jianmin Liu, Qi Jin, 2017) 25-55 years is a productive age at this age sufferers easily interact with other people with high activities so as to facilitate the transmission of pulmonary TB disease from the environment. (Nurkumalasari and Ningsih, 2017)

Based on the education level of respondents with pulmonary TB patients with an equivalent high school education level the highest number is 17 (57%) people, then followed by respondents with junior high and elementary education levels, while respondents with Diploma and Bachelor education levels are not found. The level of education greatly determines public health behavior. The higher the level of education, the better the individual's understanding of health status. Based on the survey results, generally the level of education infected with pulmonary tuberculosis in the working area of the Puskesmas is high school where this age is a very productive period of activity with a fairly high and wide level of association so that this has a high risk of contracting pulmonary TB disease

Based on the type of work the number of respondents The highest number of patients with pulmonary TB worked as a handyman with a total of 14 (47%) people, while the lowest worked as a civil servant with a total of 1 (3%) people. According to Fitriani (2013) there is a relationship between the level of family income with pulmonary TB sufferers. (Eka Fitriani,

2013) The type of work will greatly affect family income in terms of fulfilling the nutritional intake of all family members. The better the family's nutritional intake will increase the body's resistance to infection with pulmonary TB disease pathogens. Carpenter work is one of the menial jobs with a minimal level of income so that the head of the household is not able to meet the needs of good nutrition for family members and themselves.

Based on the types of complaints and side effects of drugs that arose during the respondent's treatment of pulmonary tuberculosis with the most complaints/side effects being joint pain and red urine and sweat where all respondents (100%) complained of the same thing and the lowest side effect complaints were itching and 3 (10%) people complained of redness of the skin. Drug side effects on the use of anti-pulmonary TB drugs often appear in the first week of treatment until the eighth week of treatment. According to Abbas (2017), side effects that often arise during the treatment of pulmonary TB are joint pain, nausea, vomiting, stomach pain, visual disturbances, lack of appetite, dizziness, tingling (Akmadi Abbas, 2017). The staining of urine and sweat occurs due to the red nature of rifampin and is excreted through urine and sweat so that urine and sweat will appear red.

The results of laboratory tests on blood serum of patients with pulmonary tuberculosis on liver function parameters are as shown in the table below

**Table 2.** ALT/SGPT enzyme activity values. AST/SGOT and Total Bilirubin in Blood Serum of Pulmonary Tuberculosis Patients undergoing treatment at Ranotana Weru, Tikala Baru and Tuminting Health Centers in 2019

Examination Parameters	n (%)
ALT/SGPT (10-29 U/L)	24 (80%)
Abnormal (34-82 U/L)	6 (20%)
Total	30 (100%)
AST/SGOT Normal (12-30 U/L)	25 (83.4%)
Abnormal (33-100 U/L)	5 ( 16.6%)
Total	30 (100%)
Bilirubin Normal	30 (100%)
Abnormal (>1.5 mg/dl)	0 (0%)

Total	30 (100%)
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**Primary Data Sources in 2019**

Based on Table 2 above, the normal value of ALT/SGPT enzyme activity ranges from a value of 10-29 U/L obtained from measuring blood samples of pulmonary TB patients who are undergoing treatment with a total of 24 (80%) people while abnormal values range from at a value of 34-83 U/L as many as 6 (20%) people. The normal value of AST/SGOT enzyme activity ranges from a value of 12-30 U/L obtained from measuring blood samples of pulmonary TB patients who are undergoing treatment with a total of 25 (83,4%) people, while the value of ab Normal values range from 33-100 U/L as many as 5 (16.6%) people. Rifampicin 85-90% is metabolized in the liver and its active metabolite is excreted through the urine and gastrointestinal tract, acting synergistically with INH. Patients with liver disorders will find higher serum rifampin levels. Rifampin will induce the cytochrome P450 enzyme system which will continue for up to 7–14 days after the drug is discontinued. The hepatotoxic effect is influenced by the dose used, and the drug metabolism process is influenced by factors of age, sex, the environment in the stomach and liver disease. (Katzung, Masters and Trevor, 2009) (Prihatni *et al.*, 2007)

One of the main liver functions is Excretion of bilirubin, this liver function can be disrupted if there is damage to liver function. This impaired excretion of bilirubin causes an increase or decrease in serum bilirubin levels. Bilirubin will increase if there has been moderate liver damage. In this study, the increase in the AST/ALT enzyme occurred in the first and second months, this increase was not seen again at the 3rd to 6th month of treatment, so it could not increase the total bilirubin value. At the beginning of treatment, the increased liver function values were AST and ALT values, while bilirubin had not increased significantly. (Made Agastya Darma Putra Wesnawa, 2016)

Variations in the activity values of AST/SGOT, ALT/SGPT and total bilirubin in the blood serum of Pulmonary Tuberculosis Patients undergoing treatment based on gender can be seen in table 3 below.

**Table 3.** Value of ALT/SGPT Enzyme Activity. AST/SGOT and Total Bilirubin by Gender of Pulmonary Tuberculosis Patients who are undergoing treatment at Ranotana Weru, Tikala Baru and Tuminting Health Centers in 2019

Examination Parameters	Normal	Abnormal
	n (%)	n (%)

AST/SGOT

Male	16 (53.4 %)	3 (10.0%)
Female	9 (30.0%)	2 (6.6%)
Total	25 (83.4%)	5 (16.6%)
Male	16 (53.4 %)	3 (10%)
Female	8 (26.6%)	3 (10%)
Total	24 (80%)	6 (20%)
Total Bilirubin		
Male	19 (63%)	0 (0%)
Female	11 (36,7%)	0 (0%)
Total	30 (100%)	0 (0%)

#### Primary Data Sources in 2019

Based on Table 3 above, it shows that 3 (10%) men have the highest AST/SGOT enzyme activity values. This abnormal number is higher than women, while the normal value of AST/SGOT enzyme activity with the highest number of patients is also male, namely 16 (53.4%) and then 9 (30%) female. The abnormal value of the AST/SGOT enzyme is empirically not influenced by gender, so in this study the frequency of occurrence is low and cannot be used as a risk factor for liver damage. (Prihatini *et al.*, 2007)

Table 3 above also shows that 3 (10%) male and female sexes have abnormal ALT/SGPT enzyme activity values, while normal ALT/SGPT enzyme activity values with the highest number of patients are male. namely 16 (53.4%) people and 8 (26.6%) women. The same thing also happened to the abnormal value of ALT/SGPT where this value was not influenced by gender. (Prihatni *et al.*, 2007) The bilirubin value did not show abnormal changes based on the sex of the patient with pulmonary TB

Enzyme activity AST/SGOT and ALT/SGPT based on The duration of treatment in patients with pulmonary TB who are undergoing treatment can be seen in Table 4 below.

**Table 4.** Values of ALT/SGPT and AST/SGOT enzyme activities based on duration of treatment for pulmonary tuberculosis patients who are undergoing treatment at Ranotana Weru, Tikala Baru and Tuminting Health Centers in 2019

Parameters of	Normal	Abnormal
	n (%)	n (%)

AST/SGOT		
1 month	5 (16.7)	4 (13.4)
2 months	6 (20.0)	2 (6.60)
3 months	2 (6.60)	0 (0)
4 months	7 (23.3)	0 (0)
5 months	3 (10.0)	0 (0)
6 months	1 (3.30)	0 (0)
<b>Total</b>	<b>24 (80.0)</b>	<b>6 (20)</b>
ALT/SGPT		
1 month	6 (20)	4 (13.3)
2 months	6 (20)	1 (3.30)
3 months	2 (6.60)	0 (0)
4 months	7 (23.3)	0 (0)
5 months	3 (10.0)	0 (0)
6 month	1 (3,30)	0 (0)
<b>Total</b>	<b>25(83,4)</b>	<b>5 (16,6)</b>

**Source of Primary Data in 2019**

Based on Table 4 above shows AST/SGOT enzyme activity based on duration of treatment in patients with pulmonary tuberculosis who are undergoing treatment . The highest number of patients with pulmonary tuberculosis with abnormal AST/SGOT values with a duration of treatment of 1 month was 4 (13.4%) people and then followed by 2 months of treatment, namely 2 (6.60%) people while the length of treatment was 3 to 6 months. did not show abnormal AST/SGOT activity values. On the other hand, 7 (23.3%) people had normal AST/SGOT values during treatment for 4 months and the lowest was 6 months of treatment, which was 1 (3.30%) people. An increase in AST/SGOT values at the start of treatment is very likely a consequence. In patients with pulmonary TB, abnormal ALT/SGPT values with 1 month of treatment were 4 (13.3%) people and then followed by 2 months of treatment, namely 1 (3.3%) people, while 3 to 6 months of treatment did not show any indications. abnormal ALT/SGPT activity values. On the other hand, the normal ALT/SGPT values at 4 months of treatment were 7 (23.3%) people and the lowest was 6 months of treatment, which was 1 (3.30%) people.

Hepatotoxic at 2 weeks after treatment. Based on the WHO classification, hepatotoxicity is mild to moderate, therefore treatment is continued. With the consideration that like other cells in the body, when hepatocytes experience trauma, both physical and chemical, they will immediately try to regenerate. Trauma at the cellular level will result in irreversible changes within the first 20–60 minutes. Irreversible changes that will end in cell death include cell membrane damage, lysosomal swelling and mitochondrial vacuolization with decreased ATP-forming capacity. ATP depletion and decreased ATP synthesis are usually caused by hypoxia and chemical (toxic) trauma. If there has been a disruption of mitochondrial function and cell membranes, the hepatocyte cells will secrete transaminase enzymes. Elevated transaminase enzymes are early markers of hepatotoxicity. (Prihatni *et al.*, 2007)

### **CONCLUSION AND RECOMMENDATION**

The value of ALT/SGPT enzyme activity in patients with pulmonary tuberculosis was 10–29 U/L in 24 (80%) respondents and 34–82 U/L in as many as 6 (20%) respondents. The value of AST/SGOT enzyme activity in patients with pulmonary tuberculosis was 12–30 U/L in 25 (83.4%) respondents and a value of 33–100 U/L in 5 (16.6%) respondents. Bilirubin levels in patients with pulmonary TB 0.22 – 1.30 mg/dl. Undesirable effects that occur while the patient is undergoing treatment for pulmonary TB disease are itching and redness of the skin, joint pain, tingling and burning sensation in the feet, red urine and sweat, nausea and vomiting. Suggestion, for health workers can provide health education to patients and their families monitoring OAT about the conditions and effects related to the dose of the drug given, the patient's family as OAT monitors must be able to ensure that patients with pulmonary tuberculosis who are in the treatment stage are obedient to taking medication and seek to recognize their condition. or signs and symptoms complained of due to the effects of the drug by the patient.

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