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The Effect of Initial Anti-tuberculosis Drug Therapy on Transminase Enzymes

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Abstract
Tuberculosis is still a health problem in the world. TB treatment is carried out in 2 phases, namely early and advanced. This study aims to determine changes in serum transaminase enzyme levels (SGOT and SGPT) in pulmonary TB patients before and after initial drug administration. This study was observational with a cohort study design study. Observations were conducted in tuberculosis patients who received initial ATD therapy for 2 months for SGOT and SGPT enzyme levels before and after treatment. The subject of the study was a new case of a pulmonary TB patient aged ≥16 years. Subjects received initial therapy in the form of isoniazid, rifampicin, pyrazinamide, and ethambutol. Recruitment of subjects through successive sampling methods with informed consent. Using a spectrophotometer, SGOT and SGPT enzyme tests were performed on the median blood serum cubital vein. Data analysis using the Wilcoxon Test. The study involved 19 subjects (10 men and 9 women) aged 16-65 years. Before ATD, the mean SGOT was 22.84 IU/L, and SGPT was 21.37 IU/L. After ATD, SGOT increased to 58.63 IU/L (p = 0.023), and SGPT to 80.84 IU/L (p = 0.007). Of the 19 subjects, 8 experienced a significant increase in SGOT and 5 SGPT. Five cases showed an increase in SGPT in line with SGOT, and 3 cases showed an increase in SGOT without SGPT. One case saw an increase in SGOT and SGPT of more than 5 times the reference value. This study confirms an increase in transaminase enzymes during initial therapy with first-line ATD.

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INTRODUCTION

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis (Agapova et al., 2019). Tuberculosis germs attack the lung organs, but can also affect other organs. This disease can infect men and women up to children. This disease is still a public health problem in the world (Cardona & Cardona, 2019). The prevalence of tuberculosis in Indonesia is very high. The 2019 WHO Global Tuberculosis Report states that Indonesia ranks ninth with an incidence of 316 cases per 100,000 population with a total case incidence of 845,000 new cases in 2018 (Organization, 2021).

Treatment of tuberculosis uses antituberculosis drugs (ATDs) which are classified into two groups, namely first-line drug groups and second-line drugs. The first-line group of drugs, namely

isoniazid, rifampicin, ethambutol, streptomycin, and pyrazinamide, show high effectiveness with acceptable toxicity. Second-line antituberculosis is fluoroquinolone antibiotics (ciprofloxacin, ofloxacin, levofloxacin), cycloserine, etionamide, amiksacin, kanamycin, capreomycin, and paraaminosalicylate (Dina et al., 2019). Antituberculosis that has been known based on recent research has the possibility of a Drug-Induced Liver Injury (DILI) in Rifampicin and Isoniazid (Sivapalan et al., 2020).

Hepatotoxic symptoms usually resemble other symptoms of hepatitis. An early marker of hepatotoxic is an increase in serum transaminase enzymes consisting of glutamate oxaloacetate transaminase/aspartate amino transaminase (GOT/AST) which is secreted in parallel with glutamate pyruvate transaminase/alanine aminotransferase (GPT/ALT) which is a more specific marker that is secreted in parallel with glutamate pyruvate transaminase/alanine aminotransferase (GPT/ALT), which is a more specific marker of glutamate to detect liver damage (Salih et al., 2022); (Wang et al., 2016).

Research on the side effects of anti-tuberculosis drugs has been carried out, both regarding risk factors, and their handling. First-line anti-tuberculosis in intoxication with hepatotoxicity. The effect of hepatotoxic on the treatment of tuberculosis in the initial phase can be recognized by examining laboratory functions such as the Serum Glutamate Oxaloacetate Transaminase (SGOT) and Serum Glutamate Piruvic Transaminase (SGPT). Changes in SGOT and SGPT levels before administration of first-line anti-tuberculosis drugs in the initial phase are indications of hepatotoxicity.

According to Clarasanti et al., (2016) A commonly used liver function test is the examination of transaminase enzymes, namely SGOT and SGPT levels which will show an increase if there is damage or inflammation of the liver tissue. The results showed that there were 26% of TB patients with high levels of transaminase enzyme after OAT administration and 74% of TB patients who had normal transaminase enzyme levels after OAT administration. According to Dwi (2020) Of the 200 TB patients who took anti-tuberculosis drugs regularly, 20% had impaired liver function. This study is a descriptive analytical research using secondary data on tuberculosis patients at RSUD Kabupaten Karanganyar in 2018. A total of 66 patient samples were taken by purposive sampling. The most TB patients were men (57.6%). The age group of 46-65 years experienced the most TB (43.9%). Increased transaminase levels occur with the use of 4 combinations of OAT and the duration of therapy <1 month and treatment 1-2 months. Hepatoprotectors were the most consumed drug besides OAT (45.5%). The results of the analysis test using the Wilcoxon SGOT test before and after OAT treatment obtained a significance p = 0.151 (> 0.05). SGPT levels before and after OAT treatment showed significance p = 0.108 (> 0.05). This shows no effect of Anti-Tuberculosis Drugs on SGOT and SGPT levels.

With the very high prevalence of tuberculosis in Indonesia, this research is very important to identify and understand the side effects of anti-tuberculosis drugs, especially hepatotoxic effects that can threaten patients' health. Anti-tuberculosis drugs, such as rifampicin and isoniazid, have been shown to have the potential to cause liver damage. Therefore, this study is urgent to identify the risks and causative factors of side effects of these drugs. With a better understanding of the management and management of side effects of anti-tuberculosis drugs, this research can help in prevention, early detection, and more effective treatment of hepatotoxic effects that may arise. The study also urges to develop methods for early detection of side effects of anti-tuberculosis drugs, in particular hepatotoxic effects, so as to enable more timely and effective interventions. By better understanding the management of side effects of anti-tuberculosis drugs,

this research can make a significant contribution to improving the quality of care for TB patients, including early detection and more effective treatment of side effects that may arise.

The main objective of this study was to evaluate the side effects of anti-tuberculosis drugs, especially hepatotoxic effects that can occur in patients undergoing TB treatment, to identify the risks and causative factors of side effects of anti-tuberculosis drugs, such as rifampicin and isoniazid, which are known to have the potential to cause liver damage, the purpose of this study is also to understand more about the management and management of side effects of drugs anti-tuberculosis, including how to detect, prevent, and treat hepatotoxic effects that may arise and to develop methods for early detection of side effects of anti-tuberculosis drugs, especially hepatotoxic effects, to enable more effective and timely treatment. The benefits of this study can provide a better understanding of the risks and side effects of anti-tuberculosis drugs, thus raising awareness for both patients and medical personnel caring for TB patients, Information obtained from this study can help in the development of safer TB treatment strategies by minimizing the risk of side effects, particularly hepatotoxic effects, which can threaten patient health, By better understanding the management and management of side effects of anti-tuberculosis drugs, this research can contribute to improving the quality of care of TB patients, including early detection and more effective treatment of side effects that may arise, The findings from this study can be used to develop more effective clinical guidelines in the management of side effects of anti-tuberculosis drugs, thus assisting medical personnel in providing appropriate care. The results of this study can be the basis for further research in the field of TB treatment and drug side effects, thus opening up opportunities for the development of better and innovative therapies in the future.

RESEARCH METHODS

The research method used in this study is observational analytic, with a prospective cohort approach that is taking venous blood of tuberculosis patients who have met the diagnostic criteria. Blood sampling is done twice when the patient was diagnosed with tuberculosis (before being given ATD) and 2 months after undergoing ATD therapy (initial phase) including Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol. Determination of research subjects through consecutive sampling with informed consent.

Nineteen subjects were obtained as patients who had the inclusion and exclusion criteria, then the SGOT and SGPT levels were examined on a spectrophotometer. The data obtained were processed using the SPSS 17.0 for Windows computer program. Data obtained from measurements of SGOT and SGPT levels before and after administration of anti-tuberculosis drugs were tested using a data normality distribution test that used the Saphiro-Wilk test. The data was not normally distributed, so the Wilcoxon non-parametric statistical test was performed at the significance level of $p>0.05$.

RESULTS AND DISCUSSION

Table 1. Age Characteristics of The Subjects

Age	n	%
15-25	7	37
26-35	2	10
36-45	3	16
46-55	3	16
56-65	4	21
Total	19	100

Table 2. Gender Characteristics of The Subjects

Gender	n	%
Male	10	53
Female	9	47
Total	19	100

The results showed that the highest percentage of subjects was 16-25 years of age (37%). Subjects with male sex (53%) more than women (47%).

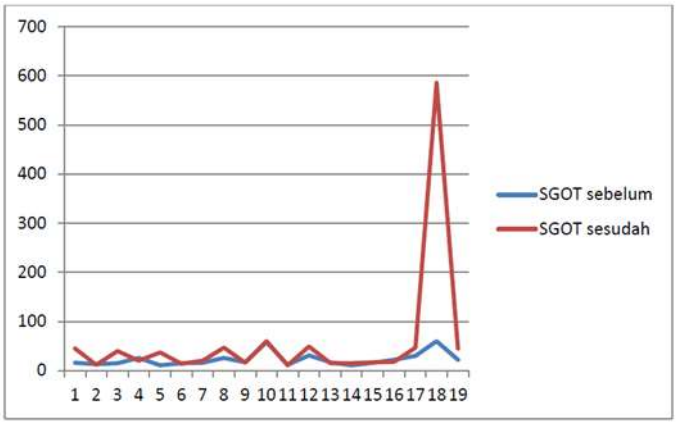

Figure1. Graph of SGOT Levels Before and After Administration of ATD

Figure 1 shows that SGOT levels after the initial phase of ATD administration tend to increase.

Table 3. SGOT Wilcoxon Test Analysis Results

	n	SGOT levels (IU/L) Mean±SD	*p*
Pre initial	19	22,84±14,11	0,023
Post initial	19	58,63±128,69	

The mean SGOT level before giving ATD was 22.84 IU/L, whereas after giving ATD it was 58.63 IU/L. The results of the different test analyses before and after the initial administration of ATD were p = 0.023 (p <0.05). This result means that there was a difference in SGOT levels before and after the initial ATD was given. This showed that there was an effect of initial ATD administration on SGOT levels. Of the 19 subjects, there were 8 people (42%) who had changes in the form of a significant increase in SGOT (compared to the upper limit of the reference value). There was one case that had an increase in SGOT> 5 times the upper limit of the reference value.

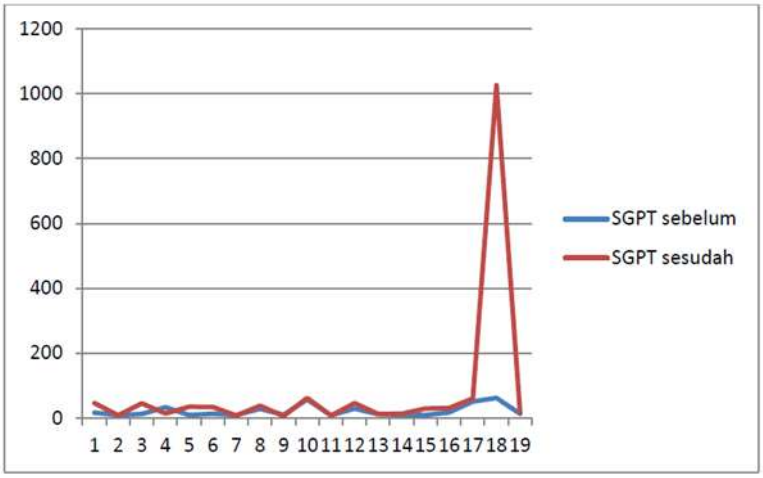

Figure2. Graph of SGPT Levels Before and After Administration of ATD

Figure 2 shows that SGPT levels after the initial phase of ATD administration tend to increase.

Table 4. SGPT Wilcoxon Test Analysis Results

	n	SGPT levels (IU/L) Mean±SD	p
Pre initial	19	21,37±17,42	0,007
Post initial	19	80,84±229,59	

The mean SGPT level before giving ATD was 21.37 IU/L, whereas after initial ATD administration was 80.84 IU/L. The results of the analysis of different tests before and after initial ATD administration were p = 0.007 (p <0.05). This result means that there are differences in SGPT levels before and after the initial ATD is given. This shows the influence of initial ATD administration on SGPT levels.

There were 5 people (26%) who had a change in the form of a significant increase in SGPT (compared to the upper limit of reference value). There was one case that had an increase of> 5 times the upper limit of the reference value. In 5 cases the increase in SGPT was in line with the increase in SGOT.

In this study, most respondents were 16-25 years old (37%). These results were almost the same as the research conducted at Dr. Pirngadi Medan, the highest percentage is the age of 18-25 years (36.5%) (Dasopang et al., 2019). This period is a productive age which has two causes. First, there are no precautions when infected with primary tuberculosis in the environment as a child, so it appears as an adult. Second, there is activity and work environment in the group of adults who interact with people with tuberculosis or environments that make it easier to contract tuberculosis (Permana & Yanti, 2019). The Factors that influence the incidence of tuberculosis over the age of 15 years include age, sex, area of residence, education, and region. It is also influenced by other factors, such as a history of smoking, having been diagnosed with diabetes mellitus, and having lived with a patient with tuberculosis (Pangaribuan et al., 2020).

This study showed the results that based on gender characteristics, the number of male respondents is more than female (n = 10, 53%). The results of the study were in line with research conducted at Omdurman-Sudanyang Hospital, which shows that male respondents are more dominant (n = 84, 84%) (Zhuang et al., 2022). Other studies also mention more men affected by tuberculosis compared with women (Widyastuti et al., 2019). Men have risky behaviors to be

infected with tuberculosis such as smoking, drinking alcohol, as well as more traveling and social contact (Syamsu et al., 2020).

In this study subjects who experienced an increase in SGOT levels were 8 cases (42%) while those who experienced elevated SGPT levels were 5 cases (26%). Subjects who experienced an increase in SGPT in tune experienced an increase in SGOT. Increasing SGPT that harmony with SGOT indicates hepatitis. Meanwhile, an increase in SGOT that is not in harmony with an increase in SGPT (3 cases) was possibly caused by hepatitis. Increasing SGOT without increasing SGPT can occur due to damage outside the liver organ such as skeletal muscle, heart muscle, erythrocytes, kidney, or pancreas (Oh et al., 2017). There was one case that had an increase in SGOT and SGPT more than 5 times of reference value indicating severe hepatitis.

The results of research conducted by SRI EKO (2018) only observed SGOT and SGPT after initial treatment, it was found that the range of SGOT was 10.20-123.90 IU/L and SGPT was 8.70-108.80 IU/L, although the average of both was still within the reference value range.

Our study was in line with the research that was conducted at the Balai Besar Kesehatan Paru Masyarakat Makasar (BBKPMM). The study found that the two groups who were given ATD but with different doses significantly increased levels of SGOT and SGPT (Munawarah et al., 2019)...Hepatotoxicity occurred in 38.2% of tuberculosis patients who received ATD (LASANTU, 2023).

Increasing SGOT and SGPT indicate hepatotoxicity events (Molla et al., 2021). Slow acetylation status is a significant risk factor for drug-induced hepatotoxicity (Luthariana et al., 2017). In this case, including anti-tuberculosis drugs that have hepatotoxicity effects (Bruchfeld et al., 2015).

CONCLUSION

This study highlights the importance of a better understanding of the side effects of anti-tuberculosis drug use, especially hepatotoxic effects that can threaten patients' health. Tuberculosis remains a significant public health problem in Indonesia, with a very high incidence rate. Treatment of tuberculosis uses anti-tuberculosis drugs (ATD), some of which have the potential to cause liver damage. The results showed that there was a significant effect of early treatment of first-line anti-tuberculosis drugs on the increase in SGOT and SGPT. Regular monitoring of SGOT and SGPT levels is necessary before, during, and after initial ATD therapy is administered to determine the effects of hepatotoxicity.

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