

Relationship Between a Levels of Aspartate Aminotransferase (Ast), Alanine Aminotransferase (Alt), Sedimentation Rate of Blood (Led) and Interleukin (Il)-6 in Patients with Tuberculosis (Tb) and Latent After 2 Months Treatment of Tuberculosis (Tb)

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Article History	Abstract
<p>Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 10 Nov 2023</p>	<p><i>The aims to determine the relationship between aspartate aminotransferase (AST), alanine aminotransferase (ALT) Blood Sedimentation Rate (LED) and Interleukin (IL)-6 levels. The methods used are Laboratory Observation, Enzymatic Thermo Scientific Indiko, Ves Matic Easy, Enzyme Linked Immunosorbent Assay (ELISA). The samples in this study were tuberculosis and latent after 2 months of treatment, the samples used were 30 samples, statistic tests were normality tests with Shapiro Wilk and Independent sample tests. The results of the research that has been done, it can be concluded that aspartate aminotransferase (AST) levels, blood sedimentation rate (LED) levels, interleukin (IL)-6 levels in tuberculosis patients and latent after 2 months of treatment obtained significant results. At alanine aminotransferase (ALT) levels in tuberculosis patients and normal latent is not significant. There is a relationship with the results of aspartate aminotransferase (AST) examination, blood sedimentation rate (LED), interleukin (IL)-6 in tuberculosis (TB) patients and latent after 2 months of tuberculosis (TB) treatment.</i></p>
<p>CC License CC-BY-NC-SA 4.0</p>	<p>Keywords: 2 Months Treatment Tuberculosis, Latent T BC, AST, ALT, LED and Interleukin 6 levels</p>

1. Introduction

Tuberculosis or often called tuberculosis is a disease that attacks the lungs caused by germs (*Mycobacterium Tuberculosis*). In patients infected with positive tuberculosis, these germs can enter the human body through the circulatory system, lymph system, air way or directly to other parts of the body. This infection can be in a latent or active state, during the treatment period [1].

Latent tuberculosis infection (LTBI) is a condition in which the body's immune system responds to M. tuberculosis antigens without showing symptoms of active tuberculosis disease. Approximately 30% of the global population is estimated to have been infected with M. tuberculosis, but only approximately 10% of infected individuals ultimately develop clinically active tuberculosis disease. In contrast, approximately 90% of infected individuals are in the latent phase. People with LTBI usually have no symptoms of active tuberculosis and feel well, but it is possible that tuberculosis may develop in the future. This process is known as tuberculosis reactivation, and the risk of this reactivation is estimated to be around 5-10% in individuals who have LTBI, especially in people who are also infected with HIV. Active tuberculosis disease usually begins to develop within the first five years after initial infection. However, the risk of developing tuberculosis after infection depends on various factors, the most important of which is the immune status of the host [2].

The source of transmission of tuberculosis (TB) lies in individuals who suffer from TB and have positive results on the acid-fast bacteria (BTA) test when coughing or sneezing. TB sufferers release bacteria in the form of droplets (sputum splashes) into the air. Droplets containing this bacterium can

survive in the air for several hours at room temperature. People can become infected if they inhale droplets containing this bacterium into the respiratory tract. After tuberculosis bacteria enter the body, they can spread from the lungs to other parts of the body through the blood circulation, respiratory tract, or through direct spread to various other parts of the body. The occurrence of tuberculosis infection in a person is influenced by the concentration of droplets in the air and the duration of time they breathe air containing these droplets [3].

Treatment of tuberculosis 1 to 6 months is isoniazid, rifampicin, INH and pyrazinamide from drugs containing hepatotoxic metabolites that cause mild to severe liver damage, with increased liver enzymes secreted by the liver cytoplasm the presence of molecules that act as transaminase biocatalysts in plasma occurrence increased levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), sedimentation rate of blood (LED) and levels of interleukin (IL)-6 indicate tissue damage [4].

The liver is the largest organ located in the upper right part of the abdominal cavity, just below the diaphragm. The liver weighs around 1,500 grams or around 2.5% of the normal body weight of an adult. In living conditions, the liver has a dark red color because it has an adequate blood supply. The liver is divided into two main lobes, namely the right lobe and the left lobe, which are separated by a structure called the falciform ligament. The right lobe is larger than the left lobe and consists of three main parts, namely the right upper lobe, caudate lobe and quadratus lobe [5].

Drugs that can cause liver injury include halothane, isoniazid (causing diffuse or diffuse hepatocyte damage, acute or chronic hepatitis), rifampin (causing hepatocyte damage, macro vesicular fatty necrosis, central bus). The main or first-line anti-tuberculosis drugs given at the beginning of the intensive phase of treatment for tuberculosis sufferers have quite high levels of hepatotoxicity, especially rifampin and isoniazid, both types of drugs can cause hepatotoxicity in the liver which can result in increased activity of the AST and ALT enzymes [6].

The two enzymes, the ALT enzyme, are considered more specific in detecting liver damage because they are located in liver systole and in low concentrations elsewhere. Drug reactions can occur in anyone who experiences drug accumulation due to consuming a certain amount of medication. Most tuberculosis sufferers can complete treatment without side effects. However, a small percentage may experience side effects, therefore monitoring the possibility of side effects is very important during treatment [7].

Examination of liver function levels in patients with pulmonary tuberculosis aspartate aminotransferase (AST), alanine aminotransferase (ALT), is very important because it can be used to control ALT levels, AST in the body. Blood sedimentation rate (LED) examination [8].

Examination of blood sedimentation rate (LED) in tuberculosis patients identifies that in tuberculosis infection conditions there are levels of fibrinogen and plasma globulin associated with acute phase reactions of inflammation resulting in an increase in blood sedimentation rate (LED) values [9].

The relationship between ESR and tuberculosis. One of the examinations to support the diagnosis of pulmonary TB inflammation is the ESR examination. The use of LED in the diagnosis of pulmonary TB is still widely used in clinical laboratories in Indonesia, it is a simple, fast and cheap examination. ESR examination in lung diagnosis shows that in pulmonary TB infection an inflammatory process occurs, where in the inflammatory process, there is an increase in fibrinogen and plasma globulin which is related to the acute phase reaction, causing the ESR value to increase. ESR values can also vary in other infectious or inflammatory conditions, so ESR is not specific for TB. However, LED is useful for monitoring the success of therapy before the value is high [10].

IL-6 is a pleiotropic cytokine that has various roles in human pathogenesis. This cytokine is produced by various types of cells, including mononuclear phagocytes, fibroblasts, endothelial cells, and T and B lymphocytes. One of the main roles of IL-6 is to stimulate the synthesis of acute phase proteins, especially C-reactive protein, in response to various stimuli [11].

Examination of interleukin (IL)-6 levels involves measuring these proinflammatory cytokines, which are produced by different types of cells including activated cells, T cells, endothelial cells, and smooth muscle cells. These cytokines trigger an immune system response during infection. Interleukin (IL)-6 has a dual role as a proinflammatory and anti-inflammatory cytokine, so it can be used in the context of medical examinations [12]. Based on the background, the aim of this research is to determine the relationship between aspartate aminotransferase (AST), alanine aminotransferase (ALT) Blood Sedimentation Rate (LED) and Interleukin (IL)-6 levels.

2. Materials And Methods

The type of research used is *Laboratory Observation* with a Descriptive design of this study for examination of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood sedimentation rate (LED) and interleukin (IL)-6 in tuberculosis (TB) patients and latent after 2 months of tuberculosis (TB) treatment. The sampling technique was taken by *accidental sampling*, the researcher took samples he encountered at that time patients with tuberculosis (TB) and latent tuberculosis after 2 months of treatment. The method used is Enzymatic Thermo Scientific Indiko, Ves Matic Easy, *Enzyme Linked Immunosorbent Assay* (ELISA). The results of descriptive research display the mean value, beside the standard (standard deviation), median, minimum value, maximum value of each variable. The data normality test is performed using the *Shapiro-wilk S* test because this data shows a normal distribution, and then continued with the *Independent* test. The normally distributed test data sample is said to have a relationship obtained *p value* < 0.05. The samples in this study were tuberculosis (TB) patients and had entered the latent phase after undergoing 2 months of tuberculosis (TB) treatment as much as 30 tol.

3. Results and Discussion

Results of measurements of aspartate aminotransferase (AST), alanine aminotransferase (ALT), sedimentation rate of blood (LED) and interleukin (IL)-6 in patients with tuberculosis (TB) and latent after 2 months of tuberculosis (TB) treatment.

Table 1. Frequency Distribution of Interleukin (IL)-6 in tuberculosis patients and Latent after 2 months of tuberculosis treatment by Sex

Gender	Number (of people)	Percentage (%)
Man	13	43 %
Woman	17	57 %
Total	30	100 %

The results of the study can be in Table 1, it is known that patients can be identified based on the sex of tuberculosis patients and latent tuberculosis after 2 months of treatment of 17 women with a percentage (57%) with a total sample of 30 people.

Table 2. Descriptive Analysis of AST, ALT, LED and Interleukin (IL)-6 levels in tuberculosis and latent patients after 2 months of tuberculosis treatment

Parameters	Categories Tuberculosis and latent	Standard			
		N	Mean	Deviation	P Value
AST	tuberculosis	15	33,15	10,99	0,044
	Latent tuberculosis	15	25,60	8,43	
ALT	tuberculosis	15	14,27	6,85	0,429
	Latent tuberculosis	15	16,40	6,69	
LED	tuberculosis	15	11,93	9,03	0,027
	Latent tuberculosis	15	30,20	28,96	
INTERLEUKIN (IL) 6	tuberculosis	15	26,18	6,15	0,001
	Latent tuberculosis	15	17,22	3,40	

From table 2, it can be seen that the mean levels of aspartate aminotransferase (AST), tuberculosis 33.15 U / L and latent tuberculosis 25.60 U / L = *p* 0.044. The mean at alanine aminotransferase (ALT) levels, tuberculosis 14.27 U/L and latent tuberculosis 16.40 U/L = *p* 0.429. The mean at the level of sedimentation rate (LED), tuberculosis 11.93 mm / hour and latent tuberculosis 30.20 mm / hour = *p* 0.027 and the mean at the level of interleukin (IL)-6 tuberculosis 26.18 pg / mL and latent tuberculosis 17.22 pg / mL = *p* 0.001.

Based on Table 2 it can be seen that tuberculosis and latent the highest percentage is 17 people (54%) with female sex. This is because hormonal changes in women during menstruation can affect the body's immunity so that the risk of infection and other diseases increases. While in the male sex 13 people with a percentage (43%).

The results of this study support previous findings that tuberculosis sufferers are more in women with a percentage of 53.75% and men with a percentage of 46.25% of the total sample of 80 patients [13].

In this study, the activity of aspartate aminotransferase (AST), tuberculosis sufferers after 2 months of treatment and undergoing AST examination with normal values were 7 people and tuberculosis sufferers with high values were 8 people, the mean value for tuberculosis was 33.15 U/L. For latent tuberculosis AST, the normal value was 11 people and for latent tuberculosis, the high value was 4 people, the mean value was 25.60 U/L.

Based on the results of the analysis, AST levels are higher in tuberculosis patients than in latent tuberculosis. This is because tuberculosis patients often consume anti-tuberculosis drugs so that liver function is disrupted and liver cell damage reaches mitochondria, excessive activity and irregular eating patterns, and smoking habits result in higher AST levels. While in tuberculosis patients who do not experience an increase or normal AST despite taking anti-tuberculosis drugs, liver function does not show significant damage or increase.

The results of this study support previous research on AST which showed that of 30 participants, 5 people (around 17%) had AST activity above the normal threshold before treatment, and after 1 month of treatment, as many as 25 people (around 83%) experienced increased activity. AST that exceeds normal values. These results indicate liver damage caused by the use of anti-tuberculosis drugs [14].

In the erythrocyte sedimentation rate (ESR), there were 5 people with normal values for tuberculosis and a mean value of 11.93 mm/hour. There were 10 people with high values for tuberculosis with a mean of 30.20 mm/hour. There was an increase in the ESR in latent tuberculosis with inflammatory reactions. Low levels that occur in the body which causes the immune system to still try to resist incoming tuberculosis, so that the inflammatory reaction causes changes in the blood so that red blood cells become faster. There are factors that influence the time of sampling so that hemoconcentration occurs, the results of which can go up and down. Based on the increase in the mean value of ESR levels in latent tuberculosis, it indicates inflammation, namely tissue damage so that fibrinogen and globulin indicate a chronic and acute disease.

The increase in ESR values in this study is also in line with previous research which noted that almost all patients (97%) infected with the Beijing strain and non-Beijing strain of *M. tuberculosis* experienced an increase in ESR. This increase in ESR reflects the presence of an inflammatory process. A high level of ESR indicates the severity of the disease [15].

The results of the study showed that IL-6 levels were 13 people with a mean value of 26.18 pg/mL with tuberculosis and latent tuberculosis after 2 months of treatment and IL-6 levels were 17 people with a mean value of 17.22 pg/mL. This causes an increase in IL-6 levels in tuberculosis sufferers, a type of cytokine or chemical substance and is produced by a type of cell that enters the body as an immune response to fight tuberculosis and the spread of infection shows severe results that cause death. IL-6 induces acute phase proteins and fibrinogen in tuberculosis with intracellular growth of bacterial microbes in monocytes. IL-6 appears to be important in resistance to tuberculosis.

This study is also in line with previous studies on active pulmonary tuberculosis, the current study showed that IL-6 blood levels were significantly higher at 8.6 pg/mL compared with the healthy group. This IL-6 is directly correlated with the level of bacterial infection, increasing levels of IL-6 in serum is associated with the development of the infectious process [16].

Results of research on the relationship between aspartate aminotransferase (AST), alanine aminotransferase (ALT), erythrocyte sedimentation rate (ESR) and IL-6 levels in latent and tuberculosis sufferers after 2 months of tuberculosis treatment and mean values. The three parameters showed a significant relationship with AST (p 0.044), latent tuberculosis LED (p 0.027), IL-6 tuberculosis (p 0.001). This causes an increase in IL-6 which damages the liver and can affect AST and ESR levels due to its impact on blood viscosity.

For 1 parameter, there was no significant relationship with latent tuberculosis, alanine aminotransferase (ALT) activity, mean 16.40 U/L and tuberculosis mean 14.27 U/L (p 0.429). The results of data analysis and discussion show that clinical results have no improvement or normal values despite taking anti-tuberculosis drugs.

At the sedimentation rate of blood (LED) tuberculosis patients with normal values amounting to 5 people and mean values of 11.93 mm / hour tuberculosis patients high values amounting to 10 people with a mean of 30.20 mm / hour, an increase in LEDs in latent tuberculosis low inflammatory reactions that take place in the body that causes the immune system to still try to contain incoming tuberculosis, So that the inflammatory reaction causes changes in the blood so that red blood cells are faster. There

are things that affect factors at the time of sampling so that hemoconcentration occurs whose results can go up and down. Based on an increase in the mean value, LED levels in latent tuberculosis indicate inflammation, namely tissue damage, so fibrinogen and globulin indicate a chronic and acute disease.

The results of the study of interleukin (IL)-6 levels there were 13 people with a mean value of 26.18 pg / mL patients with tuberculosis and latent tuberculosis after 2 months of treatment and IL-6 levels 17 people with a mean value of 17.22 pg / mL. This causes an increase in IL-6 levels in tuberculosis patients, one type of cytokine or chemical and produced types of cells that enter the body as an immune response to fight tuberculosis and the spread of infection shows severe results that cause death. IL-6 induces acute-phase proteins and fibrinogen in tuberculosis with intracellular growth of bacterial microbes in IL-6 monocytes appears to be important in resistance to tuberculosis.

The study is also in line with previous research on active pulmonary tuberculosis, the current study showed that IL-6 levels in the blood were significantly higher by 8.6 pg/mL compared to the healthy group. It is IL-6 directly correlated with the rate of bacterial infection, increased levels of IL-6 in serum associated with the development of the infectious process [16].

The results of the study related aspartate aminotransferase (AST), alanine aminotransferase (ALT), sedimentation rate of blood (LED) and interleukin (IL)-6 in tuberculosis patients and latent after 2 months of tuberculosis treatment and mean value. Three parameters showed a significant association with AST (p 0.044), latent LED tuberculosis (p 0.027), IL-6 tuberculosis (p 0.001). This is an increase in IL-6 which damages the liver so that it can affect AST levels, LEDs because of its impact on blood viscosity.

For 1 parameter showed no significant association in latent tuberculosis alanine aminotransferase (ALT) levels, mean 16.40 U/L and tuberculosis mean 14.27 U/L (p 0.429). The results of data analysis and discussion showed that clinical results did not increase or normal values despite taking anti-tuberculosis drugs.

This research is also in line with previous research on 186 pulmonary tuberculosis sufferers who underwent anti-tuberculosis drug therapy (OAT), it was found that 138 tuberculosis sufferers had normal ALT levels, while 48 tuberculosis sufferers showed high AST levels with OAT treatment [17].

4. Conclusion

From the results of the research that has been done, it can be concluded that there are significant differences in aspartate aminotransferase (AST) levels, blood sedimentation rate (LED) levels and interleukin (IL)-6 levels between tuberculosis patients and latent tuberculosis after 2 months of treatment. However, in this case alanine aminotransferase (ALT) levels there is no significant difference between tuberculosis and latent patients. These results show a relationship between aspartate aminotransferase (AST) levels, blood sedimentation rate (LED) and interleukin (IL)-6 with the condition of tuberculosis patients and latent after 2 months of tuberculosis (TB) treatment.

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