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INTERLEUKIN LEVEL 10 AS A BIOMARKER IN IMPROVING TREATMENT OF PULMONARY TUBERCULOSIS BEFORE TREATMENT AND AFTER 2 MONTHS OF ANTI TUBERCULOSIS TREATMENT

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Abstract

Background

Tuberculosis (TB) is an important community health problem in the world. Indonesia ranks third in the world after China and India. The cause of TB is Mycobacterium tuberculosis. The disease is the result of chronic interactions between intracellular microorganisms and the immune system response. Interleukin 10 (IL-10) is ananti-inflammatory cytokine. These cytokines are produced by macrophages and T cells during tuberculosis infection. The success of TB control is highly dependent on the diagnosis and appropriate treatment and evaluating its treatment. Many TB sufferers who are undergoing further anti tuberculosis treatment have difficulty sputum removal for acid-resistant bacillus smear examination, so that the therapeutic monitor is not optimal

Methods

Observational research with a cohort - prospective data collection method. Thirty subjects with positive smear pulmonary TB were taken blood samples, before treatment and after 2 months of anti *tuberculosis* treatment to assess changes in IL-10 levels

Results

From 30 patients with positive smear pulmonary TB disease, the IL value of 10 before receiving anti tuberculosis treatment was 17.9 ± 28.5 and after 2 months of treatment decreased to 13.6 ± 10.5,although this difference was not statistically significant ($P < 0.05$). By using the Spearman correlation obtained a significant correlation between IL-10 levels before and after treatment ($p < 0.05$) the correlation strength being moderate ($r = 0.72$)

Conclusions

From the results of the study concluded that there were nosignificant differences in IL-10 levels before and after two months of intensive phase treatment.

Introduction

Tuberculosis (TB) is an infectious disease that is still a problem for world health and will continue to be a challenge for the world's population today. Tuberculosis ranks second as a cause of death from infection in the world, after the human immunodeficiency virus (HIV). Tuberculosis cases worldwide are estimated at 9.6 million with a death rate of 1.5 million cases in 2014. Indonesia ranks third in the world with an incidence of 550000 - 1 300 000 cases based on data from the World Health Organization (WHO) in 2017 after India. Tuberculosis case detection is still considered to be quite difficult and necessary recognized Mycobacterium tuberculosis infection quickly.[1,2,3]

Bacteriological examination is very instrumental in establishing the diagnosis of TB. Sputum examination serves to establish the diagnosis, assess the success of therapy and determine the potential for transmission. Re-examination of sputum smear is an important way of assessing the results of treatment progress. The success of TB disease control depends on the diagnosis and appropriate treatment. It also affected efforts to monitor and

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

evaluate treatment. Ineffective monitor TB treatment can lead to the development of multi-drugs resistant strains (MDR).[4,5,6.]

Many TB patients who are undergoing treatment anti-tuberculosis medicine have difficulty issuing sputum for acid-fast bacilli smear examination in the second month, so that the maximum monitor the therapy. Therefore, this study examined the levels of IL-10 plasma at the beginning of the second month of treatment and to determine its relationship with sputum conversion and treatment success. It is expected to determine changes in the levels of IL-10 may be a clue to predicting the success of TB therapy.[7,8,9.]

Research Purposes

Seeing the therapeutic response smear positive pulmonary tuberculosis patients before treatment and after 2 months of treatment received antituberculosis drugs.

Material and Methods

This study is an observational study with a cohort data collection methods – prospective. The study was conducted at the Department of Clinical Pathology, Faculty of Medicine USU / Adam Malik Hospital in collaboration with the Department of Pulmonology and Respiratory FK USU / Dr H. Adam Malik, starting in October 2018 - May 2019. The affordable population of this study was TB patients who had fulfilled the inclusion and exclusion criteria.

Results

A research has been conducted which aims to determine the comparison of Interleukin-10 levels in the blood of pulmonary tuberculosis patients before treatment and after 2 (two) months of intensive phase treatment. A total of 30 people with tuberculosis were included as subjects in this study. The characteristics of the subjects in this study can be seen in table 1 below:

Table 1 Characteristics of Research Subjects

Characteristics		n	%
Gender	Male	21	70.0
	Female	9	30.0
Age	< 40 years	10	33.3
	40 - 49 years	6	20.0
	50 - 59 years	6	20.0
	≥ 60 years	8	26.7
Acid-resistant bacteria Smear	Scanty	3	10.0
	Positive 1	8	26.7
	Positive 2	8	26.7
	Positive 3	11	36.7
Total		30	100.0

Of the entire study group, 70% of patients with male sex and only 30% are female. Pulmonary tuberculosis patients were subjects in this study more are in the age range under 40 years old (33.3%). The sufferers who are in the age range 40-49 years and 50-59 years each amounted to 6 people (20%).

The main objective of this study was to compare the levels of Interleukin-10 (IL – 10) in the blood of patients with pulmonary tuberculosis before and after treatment intensive phase for 2 months. The changes in IL-10 levels can be seen in the following table 2.

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

Table 2. Comparison of IL-10 levels before and after treatment

	IL - 10 (pg/ml)		p value
	mean ± SD	median (min - max)	
Before treatment	17.9 ± 28.5	9.7 (4.0 - 162.0)	0.66
After treatment	13.6 ± 10.5	11.4 (2.5 - 50.0)	

Wilcoxon test

Table 2. shows the change in the levels of IL-10 in patients with pulmonary tuberculosis before and after treatment for 2-month intensive phase. Normality test results show that IL-10 levels both before and after treatment are not normally distributed, and therefore statistical analysis is carried out with the Wilcoxon test to see mean differences before and after treatment.Based on table 2, it can be seen that the levels of IL-10 pulmonary tuberculosis patients decreased from 17.9 pg / ml to 13.6 pg / ml, although this difference was not statistically significant ($p > 0.05$).

Table 3.Interleukin -10 (IL – 10) correlation before and after treatment

	IL-10
p value	0.01*
coefisient (r)	0.42

*) significant with the Spearman Correlation Test

Based on table 3, there is a significant correlation between Interleukin (IL-10) levels before and after treatment ($p < 0.05$), with the correlation strength being moderate ($r = 0.42$).

Discussion

Tuberculosis is a disease that generally attacks the lungs. Inhalation of droplets in phagocytes by alveolar macrophages. Macrophages are trying to destroy pathogens and transport it to the lymph nodes drain. Granulomatous lesions that contain the bacteria formed later. Granules do not directly cause disease. The risk of developing the disease remains, because the bacteria are not eradicated. In individuals with immune system compromise, the disease will develop after the primary infection. In individuals with immunodeficiency, tuberculosis develops more quickly.[10,11,12]

The production of anti-inflammatory cytokines such as IL-10 (produced by Th2 cells) in response to tuberculosis bacteria can decrease the immune response and limit tissue damage by inhibiting an excessive inflammatory response. These cytokines if produced too much can cause a failure to control the infection that causes the expansion of tuberculosis.[13,14,15]

Various studies have identified that IL-10 correlates with susceptibility to tuberculosis, both in humans and in experimental animals (mice). In patients with tuberculosis IL-10 can be found in serum and bronchoalveolar fluid. IL-10 is considered possible to be an important clinical biomarker of disease progression.Various studies show that the expression of IL-10 can increase significantly in patients with active tuberculosis.[16,17,]

The results obtained in this study are in line with the results obtained by Emizola, et al who measured IL-10 levels in 22 people with smear (+) pulmonary TB in Malang. She found that in the first 2 months of treatment, there was a decrease in IL-10 levels from 123.2 ± 79.9 pg / ml before treatment to 114.0 ± 65.6 pg / ml at the end of the second month ($p > 0.05$). [18]

A study conducted by Abdalla and Lambert in China in 2016 in experimental animals stated that IL-10 can increase the survival of intracellular TB bacilli and TB bacilli growth by inhibiting nitric oxide production, phagosome maturation, and cytotoxic effects mediated by gamma IFN. IL-10 also suppresses T-cell priming activity by presenting cell antigens by inhibiting macrophage apoptosis. In addition, IL-10 can also modulate granuloma formation by inhibiting TNFα, Th17 cells and T-cell expansion.[19]

By Moreira et al in 2017 in London stating that in humans, monocytes isolated from TB patients has been shown to produce IL-10 levels higher than the monocytes from healthy controls. Decreased levels of IL-10 as treatment became evident that TB-infected monocytes has also been reduced and thus may reflect the success of therapy.[20]

In this study found that there was a decrease in IL-10 levels from before treatment (17.9 pg / ml) to 13.6 pg / ml after undergoing intensive phase of treatment for 2 months, although this difference was not statistically significant ($p > 0.05$). This is consistent with the theory which states that IL-10 is a cytokine that inhibits the work of macrophages in phagocytosis of TB bacilli. High levels of IL-10 will cause failure of macrophages and cytotoxic T cells to eliminate bacilli. Thus, the levels of IL-10 should be decreased during the treatment period so that the immune system is able to eliminate TB bacilli, and these studies find that the expected results.

Conclusion

- There was no relationship between the level of BTA sputum density with increased levels of IL-10 in the blood of new cases of pulmonary tuberculosis patients
- There was a decrease in IL-10 levels in patients with new cases of pulmonary TB after undergoing intensive phase of treatment for 2 months, but not statistically significant ($p > 0.05$)
- There was no difference in IL-10 levels between pulmonary TB patients who experienced sputum conversion and those who did not experience sputum conversion after two months of treatment ($p > 0.05$)
- There was a positive correlation between IL-10 levels before and after treatment ($p = 0.01$; $r = 0.42$)
- It is estimated that more advanced research to study other factors that affect the levels of IL-10 and increased with the success of the treatment of tuberculosis.

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