

THE EFFECT OF ANTI-TUBERCULOSIS DRUGS AGAINST THE INFLAMMATION  
PROCESS OF THE DISEASE THROUGH ERYTHROCYTE SEDIMENTATION  
RATE TEST IN PUKESMAS TUMINTING, MANADO

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ABSTRACT

The general purpose of this study was to assess the progress of treatment on Tuberculosis (TB) patients through ESR examination while the specific purposes were to know the average of ESR examination results in both stages of treatment of TB Category 1 patients and to prove that there is a relationship between administered of anti-TB drugs against ESR on TB patient. The study design was cross-sectional with laboratory tests. Venous blood samples from 30 adult TB Patients that fulfilled inclusion criteria were examined for ESR. 13 patients were in the initial phase while 17 patients were in the continuation phase. Some samples were withdrawn when patients came to Health Center to seek treatment and some patients were taken by visiting their houses. The result of the study found that mean of ESR from each stage of treatment is different, from 21,5 mm/hour in the initial phase decreased to 11,35 mm/hour in the continuation phase. To assess the effect of anti-tuberculosis drugs on the inflammation process in each phase of treatment, statistical analysis was used using a correlation test. The correlation r-value was -0,457 with a p-value of 0,006 shows that there was a significant effect of administration of the anti-tuberculosis drugs in decreasing ESR in patients from initial phase to continuation phase. The study concludes that anti-tuberculosis drugs are effective in decreasing the inflammation process of tuberculosis.

**Keywords:** tuberculosis; phases of treatment; TB Category 1; ESR.

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INTRODUCTION

Pulmonary tuberculosis (TB) is an infected or communicable disease that is caused by *Mycobacterium tuberculosis* and spread from a sick person to another through droplets when that sick person coughed. WHO stated that TB is one of the top 10 causes of death worldwide and also the leading cause of death from single infectious drugs (WHO, 2020). TB still stands as the disease of poverty and destitute community and infects people in productive age groups. Indonesia's MOH stated that about 75% of TB cases in Indonesia occurred in the 15-54 age group, and one sick person can introduce the basil to another 10-15 people in one year (Kemenkes RI, 2018). Of 34 provinces in Indonesia, North Sulawesi Province is in the third position in terms of TB Case Detection Rate (CDR) and Case Notification Rate (CNR). Manado city, the capital of North Sulawesi, is one of 15 districts/municipalities in the province that has the most cases of TB from year to year (Dinkes Kota Manado, 2018). Two health centers in the city have the most TB cases compare with other fifteen which are Puskesmas Tuminting and Puskesmas Ranotana Weru. Both are alternately in the top position of Puskesmas with most TB cases year by year.

Treatment of TB cases depends on the classification of the patient because that will determine the selection of appropriate standard treatment policy (WHO, 2000). Appropriate in treating the patient may prevent death, relapse, acquires drug resistance, spread TB in the community. In Puskesmas Tuminting, the average number of TB cases every year is 250 cases, most of them are the new case. Diagnosing TB in Puskesmas is made by doctors and trained staff according to the anatomical site of disease, history of previous treatment, bacteriological result, HIV status, and treatment. The purpose of TB treatment is to cure patients and improving productivity and life quality, to prevent death caused by TB, to prevent TB relapse, to reduce TB transmission, and to prevent drug resistance and transmission of drug resistant TB (WHO, 2000). TB treatment is given within two phases which are the initial and continuous phases. Each phase of treatment should be given in a different regimen.

Erythrocyte Sedimentation Rate (ESR) is an old hematology examination that is usually carried out by health facilities such as hospitals as a laboratory marker that reflects the systemic inflammation in any condition,

even though it is a nonspecific test. ESR is the most frequently utilized laboratory method and has been found useful in monitoring response to clinical therapy, especially in tuberculosis (Mahalakshamma. V, Raju. A and Jhansi. K, 2016). Westergren's method is considered the standard method for measuring ESR. The general purpose of this study was to assess the progress of treatment on Tuberculosis (TB) patients through ESR examination while the specific purposes were to know the average of ESR examination results in both stages of treatment on TB patients and to know the effect of anti-TB drugs against the inflammation process through ESR test.

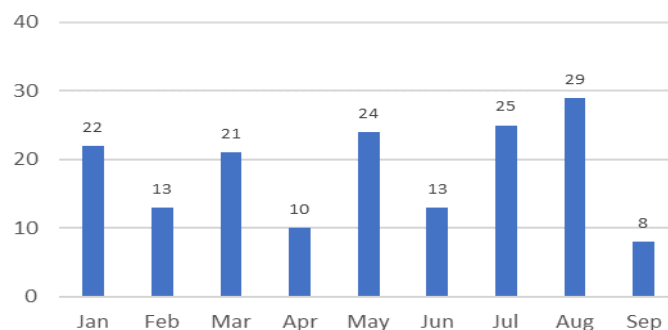
### METHODS

The study design was cross-sectional with a laboratory test. The study was performed by collecting 30 EDTA venous blood samples from TB patients from both the initial and continuation phase. The population was all patients who were diagnosed with pulmonary TB and have received anti-TB drugs in the initial phase (within the first two months since the first day of drug drank) and in the continuation phase (within four months after finishing the initial phase or not more than 6 months since the first-day drug taken) in Puskesmas (Health Center) Tuminting. The sample is withdrawn by accidental sampling. Some samples were taken from patients when they came to get the anti-TB drugs and other samples were gained after directly visiting their houses according to data from HC staff. Sample collection was made within two weeks in August 2019. All of the patients were diagnosed with a new case. There were thirteen patients in the initial phase and seventeen in the continuation phase. For the patient who was visited, blood specimens were kept in a cold box before bringing to HC for examination. Westergren's method in which the standard method for measuring ESR was conducted in the laboratory of HC. The questionnaire is used to obtained information related to patients' background, including sex, age, while other information such as the number of household contacts, and bacteriology laboratory results is obtained from patients' records in HC. Informed consent is Data collected then analyzed using statistical software. The research hypothesis is: There is a relationship between administered anti-TB drugs against ESR on TB patients. The study was declared by Health Research Ethics Committee, Manado Health Polytechnic as ethically appropriate under 7 (seven) WHO 2011 Standard.

### RESULTS

Puskesmas Tuminting is located in Tuminting subdistrict in Manado municipality. There are ten villages in this subdistrict of which eight of ten were the villages where the patients in this study came from. Sindulang 1 was the village that has the most TB patients. In Puskesmas Tuminting, the discovery of pulmonary TB cases is done passively where the patient comes to the health center with symptoms of tuberculosis, such as coughing, bleeding, or not bleeding. Throughout 2019, from January to September there were 165 new TB cases found, as seen as in figure 1.

Figure 1. Number of the new TB cases in 2019 by month



The study involved 16 males and 14 females in which the greatest number of patients is in the 41-50 age group that is eight patients, followed by seven patients in the age group of 31-40 and 51-60, as seen in table 1.

Table 1. Age and sex characteristic of patients.

Characteristics	frequencies	percentage
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Sex	Male	16	53.3
	Female	14	46.7
Age group			
	20-30	6	20.0
	31-40	7	23.3
	41-50	8	26.7
	51-60	7	23.3
	61-70	1	3.3
	71+	1	3.3

From the patients' records, the study found that 20 patients have positive AFB smear, followed by 10 patients with negative AFB Smear and positive with thorax photo, 14 TB patients with diabetes mellitus. In terms of the phase of treatment, there were 13 patients in the initial phase and 17 in the continuation phase, as seen in table 2.

Table 2. Characteristics of patients related to the status of TB

Characteristics	Frequencies	Percentage	
Number of household contact			
	0-1	7	23.30
	3-5	18	60.00
	6-8	3	10.00
	NA	2	6.70
Laboratorium status			
	AFB 1+	13	43.30
	AFB 2+	5	16.70
	AFB 3+	3	6.70
	AFB (-), Rontgen +	10	33.30
With DM			
	Yes	4	13.30
	No	14	46.70
	NA	12	40.00
Phase of treatment			
	Initial	13	43.30
	Continuation	17	56.70

Of the 30 samples examined, there were six samples (the largest number) who had received treatment for 12 weeks or 3 months and 4 samples who just received treatment (the first days). The longest duration of taking medication was 24 weeks (2 samples) as shown in table 3. The mean was 12.5 weeks.

Table 3. Distribution of patients by duration of drugs administered

Duration of drugs taken (weeks)	frequencies	percentage
0	4	13.3
3	2	6.7
5	2	6.7
6	1	3.3
7	3	10
8	1	3.3
12	6	20
14	1	3.3
15	1	3.3
17	1	3.3
20	1	3.3
21	2	6.7
23	3	10
24	2	6.7

The results of the ESR test from samples that were in the initial phase and samples in the continuation phase can be looked at figure 2.



Correlation test	Variabel	n	Nilai r	Nilai p / Sig.(1-tailed)
Pearson	ESR -- phase of treatment	30	- 0,457*	0,006
Spearman's rho	ESR -- phase of treatment	30	- 0,457*	0,007

Since the p-value <0.01 then hypothesis 0 is rejected and the alternative hypothesis is accepted, namely there is a significant/moderate correlation between the treatment phase and the ESR value or in other words, there is an effect of giving OAT in the early/intensive phase to the ESR value compared to giving OAT in the advanced phase of the LED value.

### DISCUSSION

Studies on the relationship between ESR and inflammatory status in tuberculosis have often been carried out and generally get results where the ESR in tuberculosis patients tends to be higher than in normal patients (Alende-Castro et al., 2019; Mahalakshamma. V, Raju. A, & Jhansi. K, 2016; Martins, De Castro Gama, Valcarenghi, & De Borba Batschauer, 2014). The erythrocyte sedimentation rate is not an examination of the analyte, but is related to a physical phenomenon. The normal values for the LED according to the Westergren method are <15 mm/hour (for women) and <10 mm/hour (for men). The difference in normal values for men and women is because the number of erythrocytes in women is relatively less than in men and androgen hormones in men can inhibit ESR (Stuart & Whicher, 1988). The erythrocyte sedimentation rate is a measure of overall inflammation because it depends on the concentration of circulating acute-phase proteins, particularly fibrinogen; these proteins increase the dielectric constant in the blood and neutralize the negative charge on the surface of red blood cells, which repel each other and physiologically oppose aggregation

This study looked at the effect of the stage of treatment of TB patients with anti-TB drugs on the speed of the ESR. Although it cannot be used to diagnose diseases, especially pulmonary TB, the use of LEDs in monitoring the effect of treatment can be done (Alende-Castro et al., 2019; Watson et al., 2019)., Furuhashi (2014) reported ESR examination was used for diagnosis and monitoring of progress TB disease where they concluded that ESR proved to be good marker in diagnosing and monitoring pulmonary TB (Furuhashi, Shirai, Hospital, & Suda, 2012). The study found that mean of ESR values in the initial phase of TB treatment was higher than in the continuation phase.

It is indicating that the patient is still in the inflammatory stage or the inflammation that occurs in the patient is still quite high. ESR in patients who were in the lower advanced stage of treatment showed that the level of inflammation had significantly decreased when compared to the initial stage. These results are in agreement with several previous studies (Abdelkareem, Hashim, & Abdelazeem, 2015; Furuhashi et al., 2012; Lee et al., 2012; Okafor, Eyo, Okon, & Akpan, 2013). The effect of the drug is expected to reduce the (Brajedenta & Sumaerah, 2019; Zumla et al., 2015)inflammatory process in the patient's lungs, so that systemic markers of inflammation can be measured and decreased (Brajedenta & Sumaerah, 2019; Zumla et al., 2015).

In this study, other factors that might interfere with ESR results due to the effect of antituberculosis drugs were not investigated and may become the weakness of this study. Diabetes Mellitus, which is often co-morbid with tuberculosis, was not studied. There are data about DM suffered by respondents but it is too small to be analysed. Further studies need to be conducted using more samples to determine the effect of other factors that can increase ESR in TB patients according to the stages of treatment (Goovaerts & Kestens, 2015).

### CONCLUSION

The study revealed that average of ESR values from TB patients in the continuation phase were lower than in the initial phase. There is a relationship between administration of anti-TB drugs against ESR on TB patient. the inflammatory process in the advanced phase becomes better indicated by a lower ESR value compared to the initial phase. It is recommended for the Puskesmas to carry out ESR checks to monitor the progress of treatment so that they can provide appropriate counseling to patients.

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