Jurnal Aisyah: Jurnal Ilmu Kesehatan

Volume 8, Issue S1, 2023, p. 39 – 46
ISSN 2502-4825 (print), ISSN 2502-9495 (online)

Evaluation of the ESR In Monitoring Treatment of Tuberculosis Patients at The Puskesmas Tuminting, Manado

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ARTICLE INFO

Article history:

Received 19 October 2022
Accepted 10 January 2023
Published 20 January 2023

Keyword:

Tuberculosis
Phases of treatment
ESR

A B S T R A C T

Because it may detect inflammation in any condition, the Erythrocyte Sedimentation Rate test is still the most popular laboratory technique for assessing how clinical therapy for infectious infections is working. The goal of the study was to demonstrate that there is a correlation between the administration of anti-TB medications against ESR in TB patients and the progression of treatment for patients with tuberculosis (TB) through ESR. Laboratory testing was part of the descriptive study design. Thirty adult TB patients who met the inclusion criteria had venous blood samples tested for ESR. There were 17 patients in the continuous phase and 13 patients in the starting phase. According to the study, the mean ESR fell from 21,5 mm/hour in the beginning phase to 11,5 mm/hour in the continuation phase. A correlation test was utilized in the statistical analysis. The correlation r-value was -0,457 and the p-value was 0,006, indicating that the decrease in ESR in patients from the first phase to the continuation phase was not statistically significant. Compared to the beginning phase, TB patients' average ESR readings were lower in the continuous phase. In TB patients, there was a moderate correlation between taking anti-TB drugs and ESR

Kata kunci:

Tuberkulosis
Fase pengobatan
LED

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DOI: 10.30604/jika.v8iS1.1683

A B S T R A K

Uji Laju Sedimentasi Eritrosit masih merupakan metode laboratorium yang paling sering digunakan dalam memantau respon terapi klinis pada penyakit infeksi karena dapat mencerminkan inflamasi pada kondisi apapun. Tujuan penelitian adalah untuk menilai kemajuan pengobatan pada pasien Tuberkulosis) melalui LED dan membuktikan bahwa ada hubungan antara pemberian obat anti TB terhadap LED pada pasien TB. Desain penelitian adalah deskriptif dengan uji laboratorium. Sampel darah vena dari tiga puluh pasien TB dewasa yang memenuhi kriteria inklusi diperiksa ESR. Ada 13 pasien fase awal dan 17 pasien fase lanjutan yang terlibat. Hasil penelitian didapatkan rata-rata ESR pada fase awal dari 21,5 mm/jam menurun menjadi 11,5 mm/jam pada fase lanjutan. Analisis statistik yang digunakan menggunakan uji korelasi. Nilai r korelasi sebesar -0,457 dengan nilai p-value 0,006 menunjukkan bahwa terdapat pengaruh yang kecil dari pemberian obat antituberkulosis terhadap penurunan LED pada pasien dari fase awal hingga fase lanjutan. Rata-rata nilai ESR pasien TB fase lanjutan lebih rendah dibandingkan fase awal. Hubungan antara pemberian obat anti TB terhadap LED pada pasien TB tidak cukup kuat

INTRODUCTION

The infectious or contagious condition known as pulmonary tuberculosis (TB) is brought on by the Mycobacterium tuberculosis bacterium and is transmitted from one sick individual to another through cough droplets (Amin & Bahar, 2014). Prior to the coronavirus (COVID-19) pandemic, tuberculosis (TB) killed more people than HIV/AIDS and other infectious diseases combined, according to the World Health Organization. TB is a significant contributor to poor health and one of the world's top causes of mortality. (World Health Organization, 2021). 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 (Pusdatin 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 (Dinas Kesehatan Kota Manado, 2018). Two health centers in the city have the most TB cases compared with the 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.

The classification of the patient will determine the choice of an appropriate standard treatment policy for treating TB cases. (World Health Organization, 2010). Appropriate in treating the patient may prevent death, relapse, acquiring drug resistance, and spread of TB in the community. In Puskesmas Tuminting, the average number of TB cases every year is about 250 cases, most of them new cases. Untreated TB cases or improper TB treatment appear to be factors in the global rise in chronic obstructive pulmonary disease (COPD) and a burden on disease control program efforts. (Ravimohan et al., 2018). In addition to therapy, TB health promotion is thought to be crucial for tuberculosis control. Policymakers and healthcare professionals (HCWs) are the target audience for TB health promotion initiatives that still primarily concentrate on changing individual knowledge and behavior. Multi-sector collaboration is required for TB control, involving public health officials, doctors, policymakers, technical aid organizations, laboratory professionals, and others. (Li et al., 2015). Programs to manage TB must also take into account the population environment, the protection of medical personnel, their clinic, and themselves. Research in the context of PHC in South Africa showed that efforts to develop clinic-specific infection control methods, such as employing natural air, opening windows, and segregating patients with and without coughs, will cost less and be effective (Engelbrecht & van Rensburg, 2013).

Doctors and skilled personnel at Puskesmas make TB diagnoses based on the anatomical site of the disease, history of prior therapy, bacteriological result, HIV status, and treatment. In Indonesia, a bacteriological examination that includes microscopic examination, a fast molecular TB test, and culture is required to first establish the diagnosis of pulmonary TB in adults (Kementerian Kesehatan RI, 2020). Delay in the diagnosis of tuberculosis will have an effect on the patient because it will cause delays in treatment. There are various reasons, particularly in the healthcare system, that cause delays, such as the time required for radiological examinations, the time required for AFB microscope examinations, and suspected TB patients who have coexisting conditions. (Inayati & Majdawati, 2021). The goals of TB treatment include curing patients, enhancing productivity and quality of life, preventing TB-related deaths, TB relapses, reducing the spread of TB, and preventing drug resistance and the spread of drug-resistant TB (World Health Organization, 2010). The early and ongoing phases of TB treatment are divided into two parts. Each step of treatment should follow a different regimen. To combat drug resistance, a variety of medications are used in tuberculosis treatments. Although a medicine combination is quite successful in treating tuberculosis, it may potentially increase toxicity and adverse effects. Rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA), and ethambutol (EMB) or streptomycin (SM) are used in the initial rigorous 2-month regimen for TB treatment to prevent the emergence of mutants resistant to a single antibiotic. Rifampicin and isoniazid are the medications administered after two months (World Health Organization, 2022)

The Erythrocyte Sedimentation Rate (ESR), while being a non-specific test, is the most often used laboratory approach for tracking the effectiveness of therapeutic therapy for infectious infections since it represents systemic inflammation in any condition. The Westergren method, which is dependable, reproducible, and sensitive, is the gold standard for calculating the ESR (Kratz et al., 2017). This test is not just nonspecific in pathophysiological circumstances; numerous physiological conditions, such as pregnancy, menstruation in women, aging, arthritis, and inflammatory bowel disease, can induce an increase in ESR readings. (Čičak et al., 2022). The ESR test is based on the idea that red blood cells settle in plasma when inflammation influences the release of plasma proteins like globulin and fibrinogen (Tishkovsky & Gupta, 2022). Sedimentation, which a solid object in a liquid will experience, is the central idea of this investigation (in this case, erythrocytes in the blood). The erythrocytes will eventually separate from the plasma in the uncoagulated blood sample (given with sodium citrate anticoagulant) and fall to the bottom of the container. The determined rate of erythrocyte sedimentation is then known as the erythrocyte sedimentation rate. This test is less sensitive in terms of aiding in the diagnosis of the condition because the ESR can occasionally also be affected by additional variables, such as iron deficiency anemia, which will reduce the pace of deposition. (Bray et al., 2016). Time-consuming operations using the Westergren Method have led to the development of alternative and modified approaches as a solution. It was reported that the unique alternative strategy could decrease turnaround time by 30 minutes while also possibly lowering human error (Bray et al., 2016). For study purposes, the Westergren method was used.

METHOD

The study design was a cross-sectional study with a laboratory test. All patients with pulmonary tuberculosis who were treated with anti-TB medications in the initial phase (within the first two months after the first day of drug consumption) and the continuation phase (within the next four months after the completion of the initial phase or not more than six months after the first day of drug consumption) at Puskesmas (Health Center) Tuminting made up the population. Samples that meet the inclusion criteria,

such as new case. not suffering from other infectious diseases and are willing to be the respondent, will be selected as respondents.

The sample was withdrawn by purposive 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 PHC staff. Sample collection was made within two weeks in August 2019. The study was performed by collecting 30 EDTA venous blood samples from TB patients from both the initial and continuation phase. There were 13 respondents in the initial phase and 17 in the continuation phase. For the patient who was visited, blood specimens were kept in a cold box before bringing to PHC for examination. Westergren's method which is the standard method for measuring ESR was conducted in the laboratory of PHC.

A respondent's well-mixed blood was drawn into EDTA and diluted with 0.85% sodium chloride at a ratio of four parts blood to one part. Then, a 200-mm column with a minimum internal diameter of 2.55 mm was filled with the diluted sample. The column was put into the rack and left there for 60 minutes at room temperature (18 to 25° C) without being touched. Keep track of how many millimetres the red blood cells have sunk in an hour. Read the tube from the red blood cell sediment at the top to the bottom of the plasma layer. The ESR was used to report the outcome. Therefore, the ESR is the number of red blood cells that drop in an hour, measured in millimetre (Keohane et al., 2016). The reference interval of ESR in male is 0-15 mm 1 hr (for 0-50y) 0-20 mm 1hr (for >50 y) and female is 0-20 mm 1 hr (for 0-50y) 0-30 mm 1 hr (for >50y).

The questionnaire was used to obtain information related to patients' background, including sex, and age, while other information such as the number of household contacts, and bacteriology laboratory results were obtained from patients' records in HC. Informed consent is Data collected and then analyzed using statistical software. The research hypothesis was "There is a relationship between administered anti-TB drugs against ESR on TB patients".

Data were analyzed using computerized programs such as SPSS 20, including univariate analysis to explain the description of the characteristics of each variable studied. The results of the univariate analysis of the respondent's characteristics are presented in the form of a frequency distribution table with absolute numbers and proportions for each category of each variable, namely age, sex, education, occupation, nutritional status, contact history, and incidence of pulmonary TB. Each research variable was subjected to statistical testing as part of the bivariate analysis utilizing a correlation test.

RESULTS

Puskesmas Tuminting is located in Tuminting subdistrict in Manado municipality. There were 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.

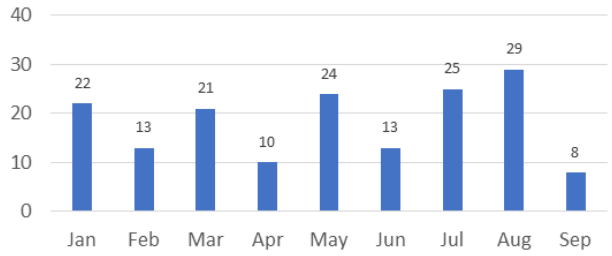

Figure 1. Number of the new TB cases in 2019 by month kin Puskesmas Tuminting

Figure 1 shows that mean of found new TB case within 9 months was 19,6 which is higher compare with other PHCs in Manado. 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
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	23.3
3-5	18	60.0
6-8	3	10
NA	2	6.7
Microscopic status for AFB		
AFB +1	13	43.3
AFB +2	4	16.7
AFB +3	3	6.7
AFB (-), X-ray (+)	10	33.3
With Diabetes Mellitus		
Yes	4	13.3
No	14	46.7
NA	12	40
Phase of treatment		
Initial	13	43.3
Continuation	17	56.7

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 medications taken (weeks)	Frequencies	percentage
0	4	13.3
3	2	6.7
5	2	6.7
6	1	3
7	3	3
8	1	10
12	6	3.3
14	1	20
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.

A

ESR value (mm/hr)	frequencies	percentage
3	1	7.7
8	1	7.7
10	1	7.7
15	1	7.7
18	3	23.1
25	1	7.7
28	1	7.7
30	1	7.7
33	1	7.7
34	1	7.7
35	1	7.7
Total	13	100.0

Mean :21.5 mm/hr

B

ESR value (mm/hour)	frequencies	percentage%
3	1	5.9
4	4	23.5
6	3	17.6
7	3	17.6
9	1	5.9
16	2	11.8
20	1	5.9
35	1	5.9
39	1	5.9
Total	17	100.0

Mean : 13.35 mm/hr

Figure 2. Result of ESR test from samples in the initial phase (A) and in the continuation phase (B)

Figure 2- A shows that the mean of ESR results was 21.5 mm/hour, which was higher than the normal value, although without considering the sex of patients' sample, while the mean of ESR in Table 4 B was 13.35 mm/hour. The result shows that in the initial phase where the patient has just been administered the anti-TB drugs, ESR higher than the normal value. Otherwise, in the continuation phase where the mean ESR value was 13.35 mm/hour that lower than in the initial phase. The scattered diagram in figure 3 shows all ESR values located from samples.

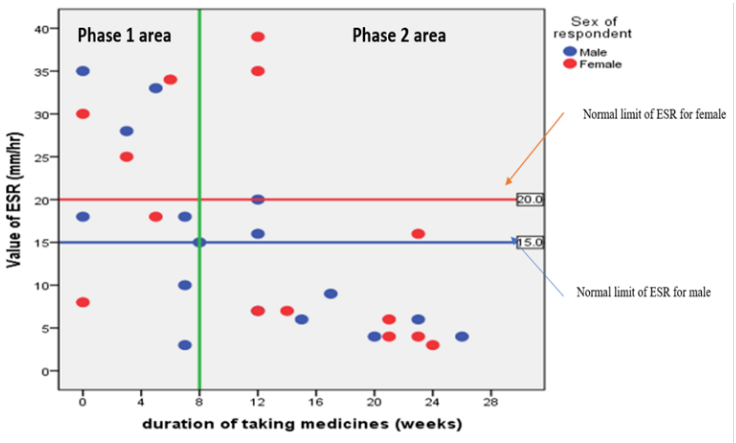

Figure 3. Scatter diagram of ESR value by duration of taking medicine

Figure 3 shows that most of the samples in the phase 1 area were located above the normal limit, while in the phase 2 area, most of the samples were located below the normal ESR limit. That can be concluded that after taking anti-TB

 ISSN 2502-4825 (print), ISSN 2502-9495 (online)

drugs regularly, the inflammation process was gradually decreasing. The length of time the treatment has been carried out affects the value of the erythrocyte sedimentation rate. In Figure 3 it can be seen that in respondents who have been taking drugs for a longer time, the value of the erythrocyte sedimentation rate decreases.

To assess the relationship between administered anti-TB drugs against ESR on TB patients, then the correlation statistic test is used. The Pearson and Spearman's rho correlation test showed the same results, namely that there was a significant effect of taking drugs at different treatment phases on the ESR value with p-value < 0.01, as in figure 4. Although the effect was not strong enough, according to the r-value that it was in the sufficient/moderate category, it can be said that the change of ESR value from high to normal will happen when the initial phase change to the continuation phase, in other word there is the effect of drugs against inflammation process.

Correlation test	Variable	n	r value	p value / 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

Figure 4. The correlation test between the variable ESR and Phase of treatment

The alternative hypothesis, according to which there is a significant/moderate association between the treatment phase and the ESR values, is accepted because the p-value is less than 0.05, which means that hypothesis 0 is rejected. Or, to put it another way, there is less of an impact on the ESR value when OAT is administered during the early/intensive period than when OAT is administered during the continuation phase.

DISCUSSION

Studies examining the connection between ESR and inflammatory status in tuberculosis are frequently conducted, and the results typically show that the ESR in patients with the disease tends to be higher than in healthy patients. (Alende-Castro et al., 2019; Mahalakshmamma. V et al., 2016; Martins et al., 2014). The erythrocyte sedimentation rate is related to a physical phenomenon rather than an analysis of the analyte. The normal values for the LED according to the Westergren method are <15 mm/hour (for women) and <10 mm/hour (for men). The concentration of circulating acute-phase proteins, particularly fibrinogen, determines the erythrocyte sedimentation rate, which is a measure of overall inflammation. These proteins raise the blood's dielectric constant and neutralize the negative charge on red blood cells' surfaces, which repel one another and physiologically prevent aggregation. (Martins et al., 2014). In clinical laboratories, the use of the ESRs in the diagnosis of pulmonary TB is still very common. The measurement of ESR in pulmonary diagnosis reveals that pulmonary tuberculosis infection is accompanied by an inflammatory process, an increase in plasma globulin and fibrinogen levels, and acute phase reactions that raise ESR values.ESR readings also rise in a number of other inflammatory or infectious illnesses, proving that they are not just for TB (Sulochana et al., 2022).

This study looked at the effect of the TB Treatment according to its stage of treatment from TB patients with anti-TB drugs against the ESR. ESR cannot be used to diagnose diseases, especially pulmonary TB, but they can be used to monitor the efficacy of treatment (Alende-Castro et al., 2019; Watson et al., 2019). The results of this study are comparable to those of another study that used an ESR test to identify and monitor the development of TB disease, coming to the conclusion that it was a trustworthy marker for pulmonary TB (Furuhashi et al., 2012). This study found that the average of ESR values in the initial phase of TB treatment was higher than in the continuation phase. It means that the ESR found patients who had inflammation throughout the first stage of treatment, or that the patient's inflammation is still actively. According to the ESR data for individuals who were more advanced in their treatment, there was much less inflammation than at the beginning. These findings are consistent with a number of earlier research (Abdelkareem et al., 2015; Furuhashi et al., 2012; Lee et al., 2012; Okafor et al., 2013). It is anticipated that the treatment will have the effect of lowering the inflammatory process in the patient's lungs, allowing for the measurement of systemic inflammation markers and the discovery of a drop. (Brajedenta & Sumaerah, 2019) (Zumla et al., 2015). Actually, there was information about DM experienced by respondents, but it was insufficient for analysis. To ascertain the impact of additional factors that can raise ESR in TB patients, additional research must be done utilizing more samples.

This study found a moderate association between ESR value at different stages of the TB treatment phase, according to statistical analysis used to evaluate the relationship between anti-TB medications provided against ESR on TB patients. According to the stage of therapy, ESR is not particularly important in assessing inflammation in TB patients while they are taking medication. Side effects of this type of anti-tuberculosis drugs also affect the increase in the value of the erythrocyte sedimentation rate (Ukpe & Southern, 2006). A study found that Rifampicin is known to be hepatotoxic which finally may increase ESR (Alende-Castro et al., 2019).

It is accurate to say that ESR has a low sensitivity and specificity, and a study found that routine ESR testing had little to no effect on patient care other than to raise patient costs and the time required by healthcare workers. (Sorsa, 2020). Some inflammatory and non-inflammatory factors affected ESR readings. Conditions that don't cause inflammation such anemia, kidney disease, obesity, aging, and female sex can increase ESR. (Go et al., 2016).

LIMITATION OF THE STUDY

This study does have some drawbacks. The respondents at the first stage were different from respondents in the continuation phase due to the issue of the length of the treatment time from the initial stage to the continuation phase, which lasts at least 2 months. Lack of a glucose test to confirm that the respondents did not have diabetes mellitus was another drawback.

CONCLUSION AND SUGGESTION

The study found that the average ESR readings for TB patients were lower in the continuous period than in the initial phase. However, an ESR test was unable to differentiate between the stages of TB treatment and the inflammation process. Drugs for tuberculosis had an impact on the inflammation process. The inflammatory process is getting better in the continuous phase, as evidenced by a lower ESR score compared to the initial phase. Despite ESR's limitations in terms of diagnosis, the Puskesmas (PHC) can use it to monitor treatment effectiveness and give TB patients the required counseling.

ACKNOWLEDGEMENT

We are grateful for the study subjects' participation as well as that of the research assistants, manager, and full Puskesmas (PHC) Tumining staff. Likewise, thanks to Manado Health Polytechnics for funding this research.

ETHICAL CONSIDERATIONS

This study had been approved by Health Research Ethics Committee, Manado Health Polytechnics, Ministry of Health No. 500/KEPK/X/2019.

CONFLICT OF INTEREST

No conflict interest exist with this study.

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 ISSN 2502-4825 (print), ISSN 2502-9495 (online)