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Relationship between duration of treatment and urine protein in pulmonary tuberculosis patients

Randy Sadid¹✉, Maulidiyah Salim¹, Ari Nuswantoro¹, Mohd Yunus²

¹Department of Medical Laboratory Technology, Politeknik Kesehatan Kementerian Kesehatan Pontianak, Pontianak, West Kalimantan, Indonesia

²Faculty of Medicine, Jalalabad State University, Jalal-Abad, Kyrgyzstan

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Abstract

Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. TB treatment is an efficient way to prevent the spread of the bacteria. The goals of TB treatment include curing, maintaining the patient's quality of life and productivity, preventing death from active TB or its sequelae, preventing relapse, reducing transmission to others, and preventing drug resistance. Most TB patients complete treatment without significant side effects, but a minority experience significant side effects. The duration of drug consumption can affect other organs such as the kidneys. Proteinuria is a condition in which there is protein in the urine beyond normal limits. The purpose of this study was to determine the relationship of length of treatment to urine protein in TB patients in Meliau District. This research method is analytical observational with a cross-sectional approach and consecutive sampling technique, with a total sample of 47 respondents. The results showed 10 respondents (21.27%) experienced proteinuria, while 37 respondents (78.73%) did not. Chi-Square analysis showed a relationship between length of treatment and urine protein in TB patients in Meliau District, as evidenced by a p-value of 0.015 (<0.05). In conclusion, there is a relationship between length of treatment and urine protein in TB patients in Meliau District.

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Corresponding Author:

✉ Randy Sadid

Department of Medical Laboratory Technology, Politeknik Kesehatan Kementerian Kesehatan Pontianak, Pontianak, West Kalimantan, Indonesia

Email: randycik8@gmail.com

INTRODUCTION

Despite its deadly nature, tuberculosis (TB) remains undetected in many countries (Sankineni, et al., 2023). Due to the possibility of TB patients who do not receive proper treatment becoming a source of transmission in the community, this adds to the global TB problem (Kaona et al., 2004; World Health Organization, 2010; Kompala, Shenoi, & Friedland, 2013; Dheda et al., 2017; Chakaya, et al., 2021). In , untreated TB infection increases mortality rates, especially in HIV (*Human Immunodeficiency Virus*) patients (Ministry of Health, 2020). *Mycobacterium tuberculosis* is the bacterium that causes tuberculosis, a chronic infectious disease. Because of its rod-like structure and resistance to acid, it is often referred to as acid-resistant bacillus (BTA). Although most tuberculosis (TB) germs are often found infecting the lung parenchyma and causing pulmonary tuberculosis (TB), these bacteria can also cause extra-pulmonary tuberculosis (TB) in other human organs such as the pleura, lymph nodes, bones and other extra-pulmonary organs. A single sneeze can release up to one million tiny droplets and a cough can release up to 3,000 tiny droplets. In contrast, TB infection requires 1 to 10 bacilli to materialize. Patients whose sputum test results are +3 or more are indicative of the most infectious cases. People who get negative findings from sputum tests are less contagious. There are almost never cases of extrapulmonary TB that are contagious, unless the patient also has pulmonary TB. Patients with latent TB are not contagious because the germs that cause the infection do not multiply or spread to other living things (Ministry of Health, 2020).

Worldwide an estimated 10.6 million people (95% UI: 9.9 - 11.4 million) have tuberculosis in 2022, up from best estimates of 10.3 million in 2021 and 10.0 million in 2020. A decline back to pre-pandemic conditions is likely in 2023 or 2024. The global gap between the estimated number of people with TB (incident cases) and the number of people newly diagnosed with TB (notified cases) reported narrows to a best estimate of 3.1 million in 2022, down from about 4 million in 2020 and 2021, and returns to pre-pandemic levels in 2019. The estimated global tuberculosis incidence rate (new cases per 100,000 people per year is 133 (95% UI: 124-143) in 2022. The net reduction from know 2015 to 2022 is 8.7%, well short of the WHO TB end strategy milestone of 50%. In 2022, eight countries accounted for two-thirds of total global tuberculosis cases: India (27%), Indonesia (10%), China 7.1%), Philippines (7.0%), Pakistan (5.7%), Nigeria (4.5%), Bangladesh (3.6%), and Democratic Republic of Congo (3.0%). These thirty countries have the highest burden of tuberculosis (WHO, 2023). Based on data from the Sanggau District Health Office, in 2023 the number of TB suspected patients who were examined for sputum samples was 5119 with positive results of 929, and for Meliau District the number of TB suspected patients who were examined for sputum samples was 199 with positive results of 59 (Health Office of Sanggau, 2023).

One of the most effective ways to stop the spread of the bacteria that cause tuberculosis is to treat the disease. Curing tuberculosis (TB) and maintaining patient productivity and quality of life is one of the goals of therapy. Other goals include avoiding the development and spread of drug resistance, preventing death from active TB or its side effects, preventing recurrence of TB, and minimizing the spread of TB to others. There are two phases of TB treatment: the basic phase and the advanced phase. Each day is dedicated to the first phase of therapy. This stage of treatment aims to reduce the impact of a small number of bacteria that may have become resistant before the patient received treatment, while effectively reducing the overall number of germs present in the patient's body. All new patients must undergo two months of initial therapy. To help the patient recover and stop relapse, the next phase of therapy focuses on eliminating any persistent germs that may still be present in the body. The advanced phase lasts for four months. Most TB patients are able to complete their therapy without any side effects. However, a small percentage may have serious side effects that make it difficult for them to do their daily

chores. Throughout therapy, it is important to monitor the patient's clinical symptoms so that any side effects can be identified quickly and treated efficiently (Ministry of Health, 2020).

Long-term use of the drug can also have negative effects on other organs, such as the kidneys, which are used for excretion and elimination. Kidney failure is one of the possible consequences. The excretion process removes drugs from the body either in their original form or converts them into metabolites. When it comes to eliminating drugs and their metabolites, the kidneys are the most important organ (Djasang, & Saturiski, 2019). Streptomycin and rifampicin are nephrotoxic or can impair kidney function. Nephrotoxic means harmful or damaging to kidney cells. Finding elevated levels of protein in the urine, or proteinuria, is one indicator of kidney damage (Tangkin, Mongan, & Wowor, 2016). Based on research conducted by Tangkin, et al., (2016) with the title Overview of urinary protein in adult patients with pulmonary TB at the Hospital. Prof.Dr.R.D. Based on these findings, most patients with pulmonary tuberculosis have negative urine protein results, and some patients with positive proteinuria results have risk factors that can interfere with urinalysis results.

The anti-tuberculosis drugs rifampicin, pyrazinamide, and isoniazid all cause hepatotoxic side effects. The liver breaks down isoniazid to make a molecule called diacetylhydrazide. Nicotinamide acetyl dehydrogenase is an enzyme whose levels can be altered by pyrazinamide. Both of these drugs have the potential to produce free radicals that can harm hepatocyte cells. Conjunctive hyperbilirubinemia, caused by rifampicin's interference with bilirubin transport, can harm hepatocyte cells. Damage to hepatocyte cells leads to impaired liver function (Nursidika et al., 2017). Patients diagnosed with tuberculosis will be provided with six months of standardized treatment, as well as medication monitoring, which is also part of the national tuberculosis prevention and treatment program. The goals of TB treatment include curing, maintaining the patient's quality of life and productivity, preventing death from active TB or its sequelae, preventing relapse, reducing transmission to others, and preventing drug resistance.

METHOD

This research was conducted in an observational analytical manner with a cross-sectional approach, namely a research design that studies the dynamics of the correlation between the independent variable and the dependent variable, by means of observation, data collection at one time. While the sample technique used in this study is non-probability sampling consecutive sampling approach, namely samples that meet the criteria at a certain time (Sugiyono, 2013). The population in this study were all tuberculosis patients in Meliau District, with a sample of all patients taking OAT in Meliau District.

The data used in the study are primary data, namely OAT collection time and urine protein readings. The data will then be analyzed by univariate analysis and bivariate analysis. The measurement data were summarized in tabular, graphical, and statistical measurement formats. The chi square test was used in this investigation to apply non-parametric statistics (Notoadmojo, 2018). Bivariate analysis is used to determine the relationship between two or more variables studied, called bivariate analysis, namely the length of OAT taking with urine protein values.

RESULTS AND DISCUSSION

Meliau sub-district is one of the sub-districts located in Sanggau Regency. The boundaries of Meliau sub-district are north with Tayan hilir sub-district, south with Kapuas sub-district, east with Ketapang district and west with Toba sub-district. In Meliau sub-district there are 19 villages with a total population of 51,108 people. A total of 47 respondents who were willing to be used as research samples were observed and interviewed for research. Before the research was carried out, the respondents first received an explanation related to the research being conducted, then the respondents' willingness to volunteer was proven

by filling out the willingness to be a respondent form. The following are the results of the analysis of the data that has been collected:

Table 1. Characteristics of Respondents Based on Gender

Variables	Total	Percentage (%)
Male	25	53.19
Female	22	46.81
Total	47	100

Based on the data in the table 1, 47 respondents with male gender 25 people (53.19%), and female gender 22 people (46.81%).

Table 2. Characteristics of Respondents Based on Age

Variables	Minimum	Maximum	Mean
Age	17	76	44

Based on the table 2, the minimum age of respondents is 17 years and the maximum is 76 years with an average age of 44 years.

Table 3. Characteristics of Respondents Based on Duration of Treatment

Variables	Total	Percentage (%)
Duration of Medication		
Initial Phase (0-2 months)	21	44.68
Advanced Phase (3-6 months)	26	55.32
Total	47	100

Based on Table 3, it can be seen that there were 47 respondents with a length of medication in the initial phase (0-2 months) as many as 21 respondents (44.68%) and in the advanced phase (3-6 months) as many as 26 respondents (55.32%).

Table 4. Characteristics of respondents based on gender

Variables	Total	Percentage (%)
Urine protein		
Positive	10	21.27
Negative	37	78.73
Total	47	100

Table 4 shows that there were 47 respondents with positive protein results as many as 10 respondents (21.27%) and negative protein as many as 37 respondents (78.73%).

Table 5. Relationship between Length of Treatment and Urine Protein

Variables	Positive	(%)	Negative	(%)	Percentage
Take medicine					
Initial	1	4.76	20	95.23	100
Continued	9	34.61	17	65.38	100
Total	10	21.27	37	78.72	100

Table 5 shows that there were 47 respondents with positive protein results as many as 1 respondent (4.76%) and negative protein as many as 20 respondents (95.23%) in the initial phase, and with positive protein results as many as 9 respondents (34.61%) and negative protein as many as 17 respondents (65.38%) in the advanced stage.

Table 6. Crosstabulation of Length of Treatment with Urine Protein

Duration of Treatment			Positive	Negative
		Expected Count		
	Initial		4.5	16.5
	Continued		5.5	20.5

Based on Table 6 above, there is a result of 1 cell expected count value that is less than 5, namely 4.5, because the chi square test requirement cannot have 1 cell that has an expected count of less than 5 so it must be continued with the Fisher's Exact test.

Table 7. Chi-Square Analysis of the Relationship between Length of Treatment and Urine Protein

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.181 ^a	1	.013		
Continuity Correction ^b	4.527	1	.033		
Likelihood Ratio	7.072	1	.008		
Fisher's Exact Test				.015	.014
Linear-by-Linear Association	6.050	1	.014		
N of Valid Cases	47				

a. 1 cell (25.0%) has an expected count less than 5. The minimum expected count is 4.47.

b. Computed only for a 2x2 table

The results of statistical analysis with the *fisher's exact test* obtained a *p* value of 0.015 (<0.05) indicating a relationship between the length of treatment with urine protein in patients with pulmonary tuberculosis in Meliau District.

DISCUSSION

Mycobacterium tuberculosis infection is the main cause of tuberculosis (TB), a direct infectious disease. Patients who test positive for tuberculosis are the source of infection, and the disease is easily transmitted through the air. Patients release germs into the air through sneezing or coughing which releases sputum droplets. Extra-pulmonary tuberculosis is the term used to describe tuberculosis infections that affect not only the lungs but also other organs of the body. About 80% of tuberculosis cases are of the pulmonary type. The only type of tuberculosis that is easily transmitted is tuberculosis (TB) that attacks lung tissue. Based on the results of the study, there were 47 respondents with 22 women (46.81%) and 25 men (53.19%). Men are often more likely to get TB than women because this disease is associated with smoking and lack of hygiene so that it can potentially reduce the immune system which makes it easier to exposed to germs that cause tuberculosis.

It can be seen that the minimum age of respondents is 17 years old and the maximum is 76 years old, which is 44 years old on average. In line with the research findings (Sunarmi et al 2022) which stated that the age range of 15 to 55 years (productive age) accounted for the majority of pulmonary tuberculosis cases. People in this age range work until their energy runs out, reducing their rest time, thus reducing their immune system and increasing the risk of developing tuberculosis. In addition to attacking people of productive age due to mobility, tuberculosis can also attack people over 55 years of age because a person's immune system decreases with age, making them vulnerable to various diseases, including pulmonary tuberculosis. At the stage of consuming drugs, 47 respondents were seen with a length of taking medication in the initial phase (0-2 months) as many as 21 respondents (44.68%) and in the advanced phase (3-6 months) as many as 26 respondents 55.32%.

From the results of urine protein examination as many as 47 respondents with positive protein results as many as 10 respondents (21.27%) and negative proteins as many as 37 respondents (78.73%), and at the stage of taking drugs many as 47 respondents with positive protein results as many as 1 respondent (4.76%) and negative proteins as many as

20 respondents 95.23%) in the initial phase, and with positive protein results as many as 9 respondents (34.61%) and negative proteins as many as 17 respondents (65.38%) in the advanced stage. Based on the analysis of urine protein levels in individuals who used anti-tuberculosis drugs for less than two months, 10 (90.9%) received negative results and 1 (9.1%) received positive results. Furthermore, eight respondents (57.1%) who had used anti-tuberculosis drugs for more than two months but less than six months had negative urine protein findings, while six respondents (42.9%) had positive results.

In this study, in the advanced phase, there were more positive urine protein examination results than the initial phase. This is in line with the results of research conducted by (Tangkin, et al 2016) based on the analysis of urine protein levels in individuals who used anti-tuberculosis drugs for less than two months, 10 (90.9%) got negative results and 1 (9.1%) got positive results. Furthermore, eight respondents (57.1%) who had used anti-tuberculosis drugs for more than two months but less than six months had negative urine protein findings, while six respondents (42.9%) had positive results. A positive urine protein result is an indication or marker of impaired renal function. This means that if the drug is frequently used in large doses, it can have adverse effects on the kidneys. It is intended that drug chemicals that are not metabolized can be excreted through the kidneys which function as the body's excretory organs. Rifampicin is nephrotoxic and can interfere with kidney function. Nephrotoxic substances are harmful or damaging to kidney cells. Kidney function may be indicated by positive protein findings. On the other hand, a number of diseases can cause proteinuria without causing kidney injury, a condition known as transient proteinuria. Many factors, including intense physical exercise, dehydration, mental stress, fever, and exposure to cold, can cause transient proteinuria. After rest, transient proteinuria is temporary, reversible, and returns to normal.

The results of statistical analysis with *Fisher's Exact Test* obtained a *p value* of 0.015 (<0.05) indicating a relationship between the length of treatment with urinary protein in pulmonary tuberculosis patients in Meliau District. This is in accordance with research by Choirunnisa, Ujjani, and Kusuma (2022) which found a weak correlation between the occurrence of proteinuria in TB patients and the length of OAT therapy. The study by (Choirunnisa et al. 2022) did not address the possibility that TB patients have other risk factors, such as comorbidities, that may influence positive proteinuria results. The researchers in this study were also unaware of any other risk factors that respondents may have, such as a history of diabetes mellitus or hypertension, which can also affect the presence of indicators of kidney damage, one of which is the presence of protein in the urine.

CONCLUSION

In conclusion, there is a relationship between length of treatment and urine protein in TB patients in Meliau District.

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