Determinan Keterlambatan Pengobatan Pada Pasien Tuberkulosis Resisten Obat di Provinsi Banten Tahun 2020

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Abstract

Indonesia is currently ranked 2nd with the most tuberculosis cases in the world, after India and China. is ranked 2nd with the most tuberculosis sufferers in the world, after India and China. Tuberculosis control in Indonesia faces many challenges, one of which is the increase in patients with drug-resistant tuberculosis (DR TB). In 2019, the number of tuberculosis sufferers in Indonesia reached 543,874 cases, with drug-resistant tuberculosis cases reaching 11,463 (2.1%). Banten is one of the provinces with the highest number of Tuberculosis sufferers in Java, which is 223 people per 100,000 population, with a national TB rate of 203 people per 100,000 population, of which only 58.3% take medication regularly. This study aims to determine the determinants of treatment delay in drug-resistant tuberculosis patients in Banten province in 2020. The study design was a retrospective cohort. The sampling technique was a total sampling of the list of DR TB cases at South Tangerang city General Hospital and dr. Drajat Prawiranegara Serang. Secondary data search was carried out on the TB Information System (SITB) and patient medical records. The study population was 114 respondents, obtained 90 respondents who fit the inclusion and exclusion criteria. Univariate, bivariate analysis with chi-square test and multivariate with logistic regression statistical test were performed to obtain a fit final model. The results of the bivariate analysis showed a significant relationship between age (p=0.030) and employment status (p=0.003). The final multivariate model, showing employment status with delayed treatment (p = 0.008), with OR 18,788 (95% CI: 2,122 – 166.329), meaning that respondents who have jobs have 18.8 times risk for late treatment compared to respondents who do not have jobs after being controlled by variables of age, gender, history of TB, and education level. The researcher concludes that the determinants of delay in treatment of DR TB patients in Banten province in 2020 are employment status and age. It is recommended that the Banten Provincial Health Office can coordinate cross sectors, to ensure the treatment of DR TB patients until they are cured.
Keywords: epidemiology, tuberculosis, drug-resistant

Introduction

Tuberculosis or commonly called TB, is an infectious disease caused by the bacteria Mycobacterium tuberculosis. This disease accounts for more than one million deaths worldwide. In 2019, there were ten million people suffering from tuberculosis, of which 1.4 million died. This disease is transmitted through the air; It is generally transmitted when sufferers talk, cough or sneeze. Tuberculosis generally attacks the lungs, but can also attack other organs besides the lungs (extra-pulmonary). Currently, tuberculosis is still a big problem in the world because it is a deadly infectious disease, even above HIV/AIDS.(1)

Indonesia is currently ranked 2nd as the highest number of Tuberculosis sufferers in the world, this condition is hampering Indonesia in achieving the MDGs target (2). In 2019, according to the Ministry of Health, 543,874 cases of Tuberculosis were found. Of this figure, 45% comes from residents in the three large provinces on the island of Java, namely West Java, Central Java and East Java (2).

Tuberculosis prevention in Indonesia faces many obstacles. One of these is the increase in drug-resistant tuberculosis (TB RO) sufferers. Drug-resistant tuberculosis is resistance to tuberculosis germs caused by spontaneous mutations in chromosomes. RO TB sufferers in Indonesia reached 11,463 people in 2019. This figure increased by more than 100% from 2017 which reached 5070 people (1). However, from these figures it is known that only 5531 patients started treatment. Often patients make excuses such as being afraid of side effects, the distance to the TB RO referral hospital, not being able to leave work, choosing alternative medicine, or because they feel they are already healthy (3) (4).

Tuberculosis drug resistance can occur in new patients, namely patients who have never had Tuberculosis treatment at all before. When compared with patients who already have a history of Tuberculosis treatment, fewer new patient criteria were found (5). Patients with a history of Tuberculosis treatment have a 10 times greater chance of contracting RO TB germs than those who have never had a history of Tuberculosis (6). Patients with a history of Tuberculosis who do not take medication regularly is one of the causes of drug resistance (7). Tuberculosis patients do not regularly or stop taking medication for various reasons, such as forgetting, not having OAT available at the TB RO referral hospital, not being able to tolerate the side effects, the treatment period feels long, not being able to buy Tuberculosis medication, not having regular treatment, and feeling like they have had enough. healthy (8).

Determination of the diagnosis is carried out by a rapid molecular test (TCM) using GeneXpert. With this tool, RO TB suspects can be diagnosed within two hours, compared to the old method using culture which took weeks (9).

Banten is one of the provinces with a high number of tuberculosis sufferers on the island of Java. According to the Indonesian Ministry of Health, in 2019, there were 223 people suffering from Tuberculosis per 100,000 population, above the national average of Tuberculosis sufferers of 203 people per 100,000 population (2). However, of the total number of tuberculosis sufferers in Banten province, only 58.3% take medication regularly (8). It is feared that this will increase the number of RO TB sufferers so that the goal of the Banten province program to be free of Tuberculosis by 2030 will be difficult to achieve.

Limited access to TB RO treatment is one of the problems in controlling TB RO in Banten province. In its efforts, the Provincial Health Service is collaborating with 13 health facilities spread across seven districts/cities to install TCM check tools. Apart from that, the Banten Provincial Health Office is also collaborating with hospitals to open TB RO services. Until 2020, only 2 hospitals had opened TB RO referral services in Banten province, namely RSU Kota South Tangerang and RSUD dr. Drajat Prawiranegara Serang Regency. Until now, the Banten Provincial Health Service is still working to increase the number of TB RO referral

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services to facilitate access to services needed by TB RO patients considering that the coverage of these two hospitals is still small compared to the area of Banten province.

Based on data from eTB Manager and SITB during the 2019 – 2020 period, there were 490 patients diagnosed with RO TB using the GeneXpert machine. However, from this data there are still 120 TB RO patients who have not started treatment or around 25% of the total TB RO patients (10)¬-(11). There are also patients who start treatment, not all of them start treatment immediately or experience treatment delays (delays), while referring to the Ministry of Health's latest technical guidelines regarding RO TB treatment, treatment must be started at least 7 days after the diagnosis is made (5). Based on the results of the clinical audit of MDR-TB patients in 2020 at RSU South Tangerang City, from 30 samples, 11 patients experienced delays in treatment or around 36.7%.

Patients with Tuberculosis have the potential to infect 10 to 15 people in one year (12). Delays in treating MDR-TB patients will increase the risk of transmission (13). Of course, this will become a new problem because it can continue to cause an increase in the number of RO TB patients in the community.

The aim of this research is to determine and explain the determinants of treatment delays in RO TB patients in Banten province in 2020.

METHOD

This type of research is quantitative with a retrospective cohort design. The research was conducted at two TB RO referral hospitals in Banten province, namely RSU Kota South Tangerang and RSUD dr. Drajat Prawiranegara Serang Regency. When the research was conducted in July 2021. The population of this study was all RO TB patients who were registered and treated at South Tangerang City General Hospital and Dr. Drajat Prawiranegara of Serang Regency in 2020 as many as 141 people. The sample taken was the total population, but based on inclusion and exclusion criteria, 90 respondents were

obtained. The bivariate research analysis used chi-square analysis, while the multivariate analysis used multiple logistic regression analysis.

RESEARCH RESULT

Table 1. Frequency Distribution of Variables: respondent characteristics, distance to health facilities, history of TB, HIV status and time of LPA results with treatment delays in 2020

Variable	n	%
Patient Lateness		
≤ 7 days	9	10%
> 7 days	81	90%
Age		
≥ 38 years	46	51,1%
< 38 years	44	48,9%
Gender		
Female	38	42,2%
Male	52	57,8%
Education		
High	54	60%
Low	36	40%
Occupation		
Not Working	37	41,1%
Working	53	58,9%
Health Center Distance		
< 10 km	17	18,9%
≥ 10 km	73	81,1%
TB History		
New	16	17,8%
Old	74	82,2%
HIV Status		
Negative	86	95,6%
Positive	4	4,4%
LPA Duration		
≤ 7 days	33	36,7%
> 7 days	57	63,3%

Based on table 1 above, it can be seen that of the 90 RO TB patients, the majority had a delay of > 7 days, namely 90%, age > 38 years 51.1%, male gender 57.8%, higher education 54%, 58.9% of those working, distance to TB RO health facility > 10 km 81.1%, TB history 82.2%, HIV negative status 95.6% and time to LPA

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results > 7 days 63.3%.

Table 2 Relationship between respondent characteristic variables, distance to health facilities, history of TB, HIV status and time of LPA results with treatment delays

Variabel	Keterlambatan Pengobatan		P-Value
	≤ 7 hari	> 7 hari	
Patient Lateness			
≤ 7 days			
> 7 days			
Age			
≥ 38 years	8 (17,4%)	38 (82,6%)	
< 38 years			0,030
Gender			
Female	1 (2,3%)	43 (97,7%)	
Male			
Education			
High			
Low			
Occupation			
Not Working	6 (15,8%)	32 (84,2%)	
Working			0,160
Health Center Distance			
< 10 km	3 (5,8%)	49 (94,2%)	
≥ 10 km			
TB History			
New			
Old			
HIV Status			
Negative	3 (5,6%)	51 (94,4%)	
Positive			0,148
LPA Duration			
≤ 7 days	6 (16,7%)	30 (83,3%)	
> 7 days			
Patient Lateness			
≤ 7 days			
> 7 days			
Age			
≥ 38 years	8 (21,6%)	29 (78,4%)	
< 38 years			0,003
Gender			
Female	1 (1,9%)	52 (98,1%)	
Male			
Education			
High			
Low			
Occupation			
Not Working	2 (11,8%)	15 (88,2%)	0,676
Working			
Health Center Distance			
< 10 km	7 (9,6%)	66 (90,4%)	
≥ 10 km			
TB History			
New			
Old			
HIV Status			
Negative	3 (18,8%)	13 (81,3%)	
Positive			0,196
LPA Duration			
≤ 7 days	6 (8,1%)	68 (91,9%)	
> 7 days			
Patient Lateness			
≤ 7 days			
> 7 days			
Age			
≥ 38 years	9 (10,5%)	77 (89,5%)	
< 38 years			1,000
Gender			
Female	0	4 (100%)	
Male			
Education			
High			
Low			
Occupation			
Not Working	2 (6,1%)	31 (93,9)	
Working			0,477
Health Center Distance			
< 10 km	7 (12,3%)	50 (87,7%)	
≥ 10 km			

Based on table 2, the results of analysis using chi-square show that the variables associated with delays in RO TB treatment are age and occupation. with a P-value <0.05. Meanwhile, variables that were not related to delays in RO TB treatment were gender, education, distance to health facilities, history of TB, HIV status and time of LPA results.

Table 3 Multivariate Analysis Variable Selection

Variable	p-value	Candidate
Age	0,030	**Candidate**
Gender	0,160	**Candidate**
Education	0,148	**Candidate**
Occupation	0,003	**Candidate**
Health center Distance	0,676	No
TB Histpry	0,196	**Candidate**
HIV Status	1,000	no
LPA Duration	0,477	No

After After the selection was carried out from 8

independent variables, only 5 were multivariate candidate variables, namely; age (p = 0.003), gender (p = 0.160), education level (p = 0.148), employment status (p = 0.003), and history of TB (p = 0.196). After selecting variables for multivariate analysis with the condition that the p value is> 0.25, they will be excluded from further modeling testing, which can be seen in the following table:

Table 4 Initial Multivariate Modeling

Variable	P value	RR	RR²
Age	**0,037**	**11,473**	
Gender	0,904	1,114	
Education	0,294	0,365	0,410
Occupation	**0,023**	**13,690**	
TB History	0,305	2,805	

Pada pemodelan awal analisis multivariat (Full Model), variabel kandidat multivariat diujikan dengan analisis regresi sederhana dengan metode "Enter". Hasil yang didapat ditunjukkan pada tabel 4 di atas. Berdasarkan hasil tersebut permodelan selanjutnya akan memasukkan variabel usia RR = 11,473 dan *p value* = 0,037 dan pekerjaan RR = 13,690 dan *p value* = 0,023.

Table 5   Final Model

Variable	P value	RR	CI 95%	RR²
Age	0,024	12,541	1,397-112,547	0,376
Occupation	0,008	18,788	2,122-166,329	

Based on Table 5 above, the final modeling results show that the two variables tested have a significant relationship with delays in RO TB treatment. Judging from the p value obtained, the employment status variable with RR = 18.788 (CI95% 2.122 − 166.329) and p value = 0.008 is the variable with the most dominant influence. Next is the age variable with RR = 12.541 (CI95% 1.397 − 112.547) and p value = 0.024.

DISCUSSION

a. Age

In this study, it was found that age was a factor that had a significant relationship with treatment delays. This result is also the same as research (14). Treatment delays often occur in patients of productive age. In this age category, patients have to go to work so they do not have time to go to a health facility to start treatment. In another study examining delay factors in TB patients, it was also found that patients aged 15 – 24 years who experienced long delays in treatment tended to have their treatment delayed (15). There is concern that if they continue to follow the treatment process it will take a long time so that their time to find a source of income will be reduced.

b. Gender

The subjects of this research were predominantly male, namely 52 people out of the 90 subjects studied. However, the gender variable did not find a significant relationship with treatment delays ≥ 8 days after the patient was diagnosed with RO TB.

In line with this research, research also examines the same variables. In his research involving 143 female subjects, he did not find a significant relationship with treatment delay (16). Other studies also obtained similar results where no significant relationship was found between gender and delays in treatment of TB patients (14).

However, this is different from the results of research conducted by Cheng (2013). In research conducted in China, female gender had a significant relationship with treatment delays. This may be due to the role of women who have to take care of household work and care for children. Women in the role of housewives are often unable to leave their children to go to health facilities and undergo treatment. (13)

Level of education

In previous studies, the level of education was one of the factors that was considered to have an influence on delays in RO TB patients. With a high level of education, it is hoped that patient awareness will arise about the importance of immediately starting RO TB

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treatment. This is intended to break the chain of transmission of TB germs.

In this study, no significant relationship was found between the educational level variable and treatment delay. The same results were also found in research in Uzbekistan, where there was no significant relationship between education level and treatment delays in TB patients (17). Not unlike Belkina, research conducted in Yogyakarta also found that there was no relationship between education level and treatment delays (18).

a. Job status

It is hoped that RO TB treatment can be initiated as quickly as possible to prevent wider transmission. However, there are often obstacles for patients to visit TB RO health facilities to start treatment. Patients need to take the time to visit the TB RO referral health facility. In this study, a significant relationship was found between the educational level variable and treatment delays. This is clarified by research conducted by Evans, D. Et al (16). His research shows that patients who work often have treatment delayed because workers tend to only want to seek treatment if the health facility where the treatment is located is close to their place of work. Apart from that, worry about being dismissed from work is one of the reasons why patients do not undergo treatment (19).

b. Distance to TB RO Health Facilities

RO TB treatment facilities are still limited in number. Unlike TB SO (Drug Sensitive) which can be treated at Community Health Centers, TB RO treatment can only be done at TB RO referral hospitals. At the time this research was conducted, Banten province only had two TB RO referral hospitals running. The two hospitals are South Tangerang City Hospital and Dr. Dradjat Prawiranegara. With limited referral hospitals in Banten province, patients are forced to travel long distances from their homes to reach TB RO referral hospitals.

Previous research found many results that stated there was a relationship between the distance to health facilities and delays in treatment. Research conducted by Andriani &

Prameswari (2018) found that patients with a distance from residence to a health facility of >3 km had a tendency to start treatment more late (4). Similar results were also shown by research conducted by Mekonnen (2014) which stated that patients who lived >10 km from health services had three times the chance of treatment being delayed three times compared to patients who lived ≤10 km (20).

Although this study did not find a significant relationship between the distance to TB RO health facilities and treatment delays, this may be influenced by other factors such as easy road access, availability of public transportation, and the availability of shelters or halfway houses for TB RO patients who are undergoing treatment in TB RO referral hospital.

a. History of TB

In this study, no significant relationship was found between history of TB treatment and delay in treatment. This research is in line with research conducted by Andriani & Prameswari (2018) which obtained a p value = 0.279 (p > 0.05) on the TB treatment history variable (4).

The researchers' considerations for including the variable history of TB treatment in this study were based on previous research which had the results of a significant relationship between history of TB treatment and delay in treatment. Research conducted by Tefera (2019) found that patients with a history of previous TB treatment, especially with streptomicyn injection therapy, had twice the chance of delaying treatment. Patients complain of side effects after treatment and are afraid to restart TB treatment (21). Another study in China conducted by Xu, Z. et al (2017) obtained similar results. This is because patients who have received TB treatment consider themselves to have recovered from TB and are reluctant to undergo TB treatment again in health services (22).

b. HIV status

The TB elimination program in Indonesia refers to WHO decisions where TB and HIV are very closely related. Patients diagnosed with TB are required to undergo an HIV test in the

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laboratory. This procedure causes people with HIV-AIDS to be reluctant to go to health facilities to be checked and treated for TB if it is confirmed that they have a TB germ infection in their body. They feel embarrassed and worried if their HIV status becomes known to others, thereby hindering the initiation of TB treatment (23). In another study, a significant relationship was also found between the patient's HIV status and treatment delay — 1.85 (95% CI 1.21-2.82) (24). Although in this study no relationship was found between the patient's HIV status and delays in TB treatment, this needs to be of concern because TB patients with HIV status have four times the chance of experiencing a worse end to TB treatment compared to TB patients who do not have HIV status (25).

LPA Result Time

The use of the LPA method is intended to determine the resistance of TB germs to second-line OAT. This can be seen in research conducted by Singla et al (2014) which showed a decrease in lost to follow-up rates in the period when the LPA method was used compared to the period when the LPA method was not used (26).

The long lag time for LPA examination results results in delays in treatment because the Clinical Expert Team (TAK) is waiting for the LPA results as a consideration for determining the therapy to be given to RO TB patients. Delays in treatment caused by non-ideal LPA intervals can have fatal consequences for RO TB patients. Evans, D. Et al (2017) found that patients died before treatment due to the long notification time for drug resistance (16).

The bivariate analysis carried out in this study resulted in a p value = 0.477, which means that there was no relationship found between the time of LPA results and treatment delay ($p>0.05$).

CONCLUSION

The conclusion obtained by the 8 independent variables studied, it turns out that the variables that are related are age and occupation, for 6 other variables that are not related, namely gender, education level, distance to TB RO health facility, history of TB treatment, HIV status and time of LP results with dependent variable. Meanwhile, the most influential factor in delays in RO TB treatment in Banten province in 2020 was employment status with an RR value of 18.788 and p value = 0.008, then the age factor with an RR value of 12.541 and p value = 0.024. The suggestions from this research are that the Provincial/Regency/City Health Service hopes to increase the role of TB RO communities and/or cadres as patient supporters by increasing capacity and commitment in assisting TB RO patients since TB RO is confirmed. Apart from that, the Provincial/Regency/City Health Service is also advised to carry out outreach and coordination with companies through company health clinics regarding the rights of RO TB patients to receive treatment.

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