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Original Article

Predictor Factors of Tuberculosis Treatment Success in Sleman Regency of Indonesia

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Abstract

Background : Tuberculosis (TB) is the leading cause of mortality worldwide. Several studies have created risk scores to predict treatment success in TB patients. However, cohort study did not consider other clinical forms of TB such as negative AFB smears and extrapulmonary TB. The objectives of this study was to knowing the predictor factors for the success of TB treatment in Sleman Regency by taking into account other clinical forms of TB such as negative smear and extrapulmonary TB.
Methods : The type and design of this study was an analytical study using a cross-sectional design conducted on TB patients in Sleman Regency from 2015 – 2018. Data were collected from TB 01 or TB 03 register of the Sleman District Health Office, including age, sex, BMI at the beginning of treatment, OAT (Antituberculosis Drugs) guideline, anatomic location, initial AFB status, AFB conversion status in intensive phase, type of TB patient, and treatment outcome. Chi-Square analysis and logistic regression were used to determine the predictors of TB treatment success.
Results : The research sample was 2308 people, 2158 successful treatments and 150 patients who failed. AFB conversion in the intensive phase was the only variable to have a role in the TB treatment success (OR = 6.655, 95% CI: 3.354–13.207, $p = 0.000$).
Conclusion : Conversion of AFB status in the intensive phase is a variable that contributes to the success of TB treatment. Age, sex, BMI at the beginning of treatment, OAT guidelines, anatomic location, initial AFB status, and type of TB patient are not predictors of TB success.

Keywords : Predictors, Treatment success, Tuberculosis

BACKGROUND

Tuberculosis (TB) is the primary cause of mortality globally. According to the World Health Organization (WHO), around 16% of the 9 million individuals suffering from TB in 2013 died with 95% of deaths occurring in low and middle–income countries.[1] Indonesia is the country with the second-largest number of new cases in the world after India in 2020. Tuberculosis remains the 10 highest cause of death in the world.[1]Three factors influence the success of treating TB patients: medicine, the disease, and the patients.[2] One of the drug factors is the guidelines and proper drug dosage.[2] Extensive lesions and comorbid diseases cause disease factors.[2] Patient factors such as age, sex, occupation, and medication adherence are essential.[2] Nutritional disorders can affect the treatment outcomes of TB patients due to decreased immunity.[3] Although many studies have evaluated risk factors for mortality in TB patients,[3] evidence regarding the relationship between Body Mass Index (BMI) and mortality is still limited and inconsistent.[4,5] Three studies found that a lower BMI was significantly associated with a higher risk of death among hospitalized patients.[4,5] In developing countries, determinants of mortality during TB therapy are largely non-infectious comorbidities, negative smears of acid-fast bacteria (AFB), alcohol, and drug abuse.[6]

Research conducted in Japan created a risk score to predict mortality in Japanese patients with an average of 65 years old that received hospital services for positive AFB smears. However, their cohort study did not consider other clinical forms of TB (smear-negative smears and extrapulmonary TB).[7] Health care workers need to identify when therapy is started, patients with TB who have a risk of death during therapy, and who have outcomes that can be modified through monitoring and management adjusted.[6] Based on this, the researchers consider it necessary to conduct a study to determine the predictors of TB treatment success in the Sleman Regency.

RESEARCH METHODS

The type and design of this study is an analytical study using a cross-sectional design on the predictors of the TB treatment success in Sleman Regency from 2015 to 2018. Sampling was conducted with non-probability sampling, namely purposive sampling by selecting samples based on consideration of the completeness of the medical record.

The inclusion criteria in this study were TB patients registered in the TB.01 and TB.03 registers of the Sleman District Health Office from 2015 to 2018. The exclusion criteria in this study were patients who had switched treatment to or from other health service units (transfer out) and TB patients with incomplete data at the time of data collection, exclusion criteria are intended to reduce data bias. The independent variables in this study were age, sex, BMI at the beginning of treatment, OAT guideline, location of anatomic disease, initial AFB status, AFB conversion status, and type of TB patients. The dependent variable in this study was the success of the treatment, which consisted of success and unsuccessful criteria.

Treatment success is defined as the outcome/output of treatment carried out by TB patients, considered successful if it was cured or completed treatment on the TB.01 or TB.03 registers, considered unsuccessful if the TB.01 or TB.03 registers are listed as fail, or died or dropped out of treatment (loss to follow-up/default). Age, sex, OAT guideline, anatomic location, initial AFB status, AFB conversion status, and type of TB patient were taken from TB data 03. The BMI variable is calculated from the data comparing patient's weight and height at the start of treatment from the TB data 03.

Chi-Square analysis and logistic regression were used to determine the predictors of TB treatment success. Bivariate analysis using Chi-Square test, if the *p*-value <0.05, then the hypothesis is accepted. In this study, the method of determination is the Prevalence Ratio (PR). The multivariate analysis used was a logistic regression with a 95% confidence level and used the PR determination method. Unknown Initial treatment BMI 1 and 2 category was omitted from the bivariate and multivariate analysis. Patient Type 1 variable was omitted from bivariate and multivariate analysis; the variable categories namely recover, fail, others, and after default, were changed to the repeated treatment category for the patient type variable. All of the statistical analyses were carried out on the statistic computer programs.

The ethics committee approved this research. The approval from the Faculty of Medicine Universitas Gadjah Mada was obtained with the number KE/FK /0291/EC/2019.

RESEARCH RESULTS

The number of TB patients from 2015 to 2018 was 3448 people. Research subjects that met the inclusion and exclusion criteria were 2308 people; 2518 were declared successful therapy while 150 patients were declared unsuccessful (Figure 1).

The number of TB treatment patients in Sleman Regency with successful treatment results was 2158, consisting of 1056 cured patients and 1102 completed treatment patients. Patients with unsuccessful treatment resulted in 150 patients consisting of 59 patients dropping out of treatment, 26 patients failed, and 65 patients died.

Table 1 shows the distribution of TB patients by age group that patients who suffer more TB were the age group > 45 years which was equal to 40.2%; by sex it was revealed that TB patients were more prevalent in the male

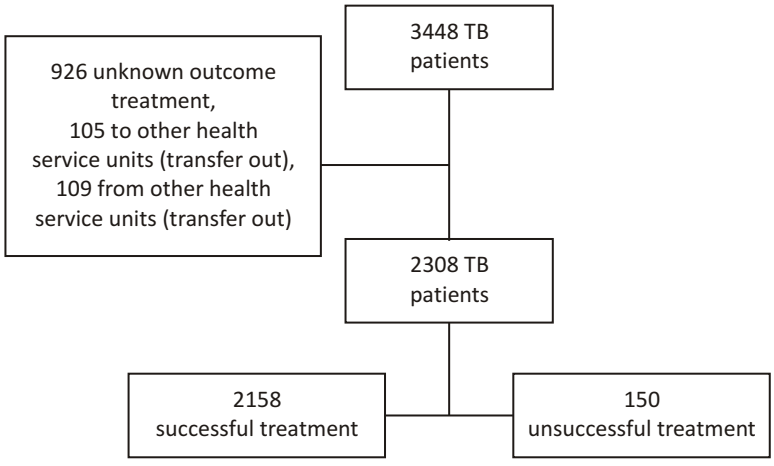

Figure 1. Study Population

TABLE 1
TB patient's characteristics

Characteristics		Treatment Results				*Number*	
		Success		Unsuccess			
		n=2158	%	n=150	%	n=2308	%
Age	<12 years	152	7.0%	3	2.0%	155	6.7%
	12–25 years	441	20.4%	15	10.0%	456	19.8%
	26–45 years	719	33.3%	51	34.0%	770	33.4%
	>45 years	846	39.2%	81	54.0%	927	40.2%
Sex	Male	1203	55.7%	88	58.7%	1291	55.9%
	Female	955	44.3%	62	41.3%	1017	44.1%
Initial treatment BMI 1	<18.5	356	16.5%	33	22.0%	389	16.9%
	18.5–24.9	384	17.8%	31	20.7%	415	18.0%
	25–29.9	36	1.7%	4	2.7%	40	1.7%
	≥30	6	0.3%	0	0.0%	6	0.3%
	Unknown*	1376	63.8%	82	54.7%	1458	63.2%
Initial treatment BMI 2	Normal	384	17.8%	31	20.7%	415	18.0%
	Unknown*	1376	63.8%	82	54.7%	1458	63.2%
	Abnormal	398	18.4%	37	24.7%	435	18.8%
OAT Guideline	Category 1	1887	87.4%	143	95.3%	2030	88.0%
	Child Category	175	8.1%	1	0.7%	176	7.6%
	Category 2	96	4.4%	6	4.0%	102	4.4%
Anatomic location	Extra lungs	379	17.6%	15	10.0%	394	17.1%
	Lungs	1779	82.4%	135	90.0%	1914	82.9%
Initial AFB Status	Positive	1103	51.1%	76	50.7%	1179	51.1%
	Not Conducted	374	17.3%	16	10.7%	390	16.9%
	Negative	681	31.6%	58	38.7%	739	32.0%

Characteristics		Treatment Results				*Number*	
		Success		Unsuccess			
		n=2158	%	n=150	%	n=2308	%
AFB Conversion Status	Yes	924	83.8%	17	22.4%	941	79.8%
	No	179	16.2%	59	77.6%	238	20.2%
Patient Type 1**	New	2062	95.6%	144	96.0%	2206	95.6%
	Cured	66	3.1%	3	2.0%	69	3.0%
	Fail	19	0.9%	1	0.7%	20	0.9%
	Others	4	0.2%	1	0.7%	5	0.2%
	After default	7	0.3%	1	0.7%	8	0.3%
Patients Type	New	2062	95.6%	144	96.0%	2206	95.6%
	Repeated Treatment	96	4.4%	6	4.0%	102	4.4%

*This category was omitted from the bivariate and multivariate analysis, **This variable was omitted from bivariate and multivariate analysis

TABLE 2
Bivariate analysis between independent variables with the TB patients treatment success

Characteristics		Treatment Outcomes				*P*	OR	CI 95%	
		Success		Unsuccess					
		n	%	n	%				
Age	<12 years	152	98.1%	3	1.9%	0.008	4.851	1.513	15.555
	12–25 years	441	96.7%	15	3.3%	0.000	2.815	1.603	4.942
	26–45 years	719	93.4%	51	6.6%	0.106	1.350	.938	1.943
	>45 years	846	91.3%	81	8.7%				
Sex	Male	1203	93.2%	88	6.8%	0.486	0.888	0.634	1.242
	Female	955	93.9%	62	6.1%				
Initial treatment BMI 1	<18.5	356	91,5%	33	8,5%	0.596	0.871	0.522	1.452
	>24.9	42	91,3%	4	8,7%	0.768	0.848	0.285	2.518
	18.5–24.9	384	92,5%	31	7,5%				
Initial treatment BMI 2	Normal	384	92.5%	31	7.5%	0.578	1.152	0.700	1.894
	Abnormal	398	91.5%	37	8.5%				
OAT Guideline	Category 1	1887	93.0%	143	7.0%	0.654	0.825	0.355	1.914
	Child Category	175	99.4%	1	0.6%	0.028	10.937	1.298	92.184
	Category 2	96	94.1%	6	5.9%				
Anatomic Locations	Extra Lungs	379	96.2%	15	3.8%	0.019	1.917	1.112	3.306
	Lungs	1779	92.9%	135	7.1%				
Initial AFB Status	Positive	1103	93.6%	76	6.4%	0.242	1.236	.867	1.763
	Not Conducted	374	95.9%	16	4.1%	0.017	1.991	1.129	3.512
	Negative	681	92.2%	58	7.8%				
AFB Conversion Status	Yes	924	98.2%	17	1.8%	0.000	17.92	10.205	31.450
	No	179	75.2%	59	24.8%				

Characteristics		Treatment Outcomes				*P*	OR	CI 95%	
		Success		Unsuccess					
		n	%	n	%				
Patient type 2	New	2062	93.5%	144	6.5%	0.796	0.895	0.386	2.077
	Repeated Treatments	96	94.1%	6	5.9%				

TABLE 3
Multivariate analysis with logistic regression for the TB treatment success

Characteristics		*P*	OR	CI 95%	
Age	<12 years	1.000	38166026.749*	0.000	∞**
	12–25 years	0.322	1.778	0.569	5.553
	26–45 years	0.595	0.819	0.391	1.713
OAT Guideline		0.897	0.922	0.269	3.163
Anatomic Location		1.000	30223115.578*	0.000	∞**
AFB Conversion Status***		0.000	6.655	3.354	13.207

*High OR number in age and anatomic location occurred due to analysis of empty cell, so ** CI 95% was infinite, this value can be ignored since the *p*>0,05. *** Initial AFB status in table 3 was missing due to remarkably high with AFB conversion status, this happened because the whole AFB conversion status samples came from positive initial AFB status.

group that was equal to 55.9%. Based on the initial BMI of treatment as many as 63.2% of TB patients did not know their BMI, in the group which had a BMI the results showed that the group that suffered TB the most was the group with a BMI range of 18.5–24.[9] by 18%. Moreover, based on OAT guidelines it was known to suffer more in the category 1 group at 88%; based on the anatomical location of the disease, pulmonary TB group was most prevalent that was equal to 82.9%; based on the initial AFB status, it was found that more suffered in the positive AFB category, namely 51.1%; based on the status of AFB conversion it was known that more suffered in the TB group who experienced AFB conversion that was equal to 85.1%; based on the type of patient it was revealed that more suffer in the new patient type that was equal to 95.6%.

Table 2 shows age (OR=2.815, 95% CI:1.603–4.942, *p*=0.000), OAT guideline (OR=10.937, 95% CI: 1.298-92.184, *p*=0.028), anatomic location (OR=1.917, 95% CI: 1.112–3.306, *p*=0.019), initial AFB status (OR=1.991, 95% CI: 1.129–3.512, *p*=0.017), AFB conversion status (OR=17,92 95% CI: 3.354–13.207, *p*=0.000) shows significant relationship with TB treatment success. Sex, initial BMI treatment 1 and 2, and patient Type 2, however, were not.

The initial BTA status variable in the multivariate analysis was lost because it had a very high correlation with BTA conversion status; this happened because all samples of BTA conversion status came from positive initial BTA status. The multivariate statistical tes with logistic regression in Table 3 shows that AFB conversion (OR=6.655, 95% CI: 3.354–13.207, *p*=0.000) has a significant correlation with TB treatment success, while age, OAT guideline, and anatomic location are not.

DISCUSSION

In this study smear conversion in intensive phase was an independent variable as a predictor of successful TB treatment (OR = 6.655, 95% CI: 3.354–13.207, *p*=0.000) (Table 3). The results of this study were the same as the study which stated that smear sputum examination at the end of the initial phase (intensive phase) is related to the success of treatment.[8] Patients who do not experience a change from positive smear to negative smear are a poor indication of response to treatment, have the possibility of being persistent and are at risk of extending the duration of treatment and have a low rate of treatment success.[9] Medical professionals can use AFB conversion status to predict treatment success, if the patient does not have AFB conversion, more attention is needed on the patient to reduce the chance of treatment failure.

Data distribution of patient characteristics in Table 1 shows that the highest percentage of TB patients in Sleman Regency was found in the age group ≥ 45 years. This study shows that the age group ≥ 45 years has the highest proportion of unsuccessful treatment (Table 1). It aligns with several previous types of research that the

elderly group has a risk of not succeeding in treatment because of their non-adherent to treatment and inability to make regular visits to health care facilities. At that age, the body's immunity begins to decrease, resulting in an increase of coinfection with other diseases that will result in unsuccessful treatment of pulmonary TB.[10–13] This research shows the older age has a higher proportion of treatment failures because the researchers only obtained secondary data, and the data did not include those causes as explained above.

This study shows that men had a higher percentage of treatment failures than women (Table 1); this is possible because women pay more attention to health than men. In addition, the same results were obtained in studies conducted in Ethiopia and Morocco.[12,14]

This study found that there was no difference in the status of BMI on the success of TB treatment (Table 2); This may be due to an improvement in nutrition in the low BMI group or the high BMI group which changes to normal, so to find out it is necessary to include data on changes in body weight during treatment, whereas in this study there was none. In the data group where BMI results were known, the highest TB treatment failure was in the BMI group <18.5 by 22%. In the previous research results said lower BMI / thin was associated with risk factors for treatment failure.[15] Low body mass index (BMI) is an important risk factor for TB development and the failure of TB therapy.[16]The study results show that all patients with BMI ≥ 30 experienced treatment success (Table 1). Moreover, there is growing evidence that high BMI is a protective factor for TB, and epidemiological data previously reported that obesity is associated with a reduced risk of active TB in the body's response to treatment dose[15,17] TB patients, based on the initial BMI of treatment or 63.2% of TB patients, did not know their BMI because many data about body weight and height were not filled in by the officer on the patient register sheet. TB sheet 03, starting in 2018, does not include information on body weight and height, so research with complete initial BMI data is needed to AFB in better statistical results.

In this study, OAT guidelines did not affect the success of TB treatment. In contrast to some previous studies, TB patients who have never undergone prior treatment or new patients receiving category 1 treatment will be associated with successful treatment. TB patients who had undergone prior treatment would increase the risk of being lost to treatment and cause treatment failure.[18] This indifference might be because OAT guidelines have been adjusted to new or repeat patients' status.

Table 3 shows that the anatomic location of the disease did not affect the success of TB treatment. In contrast to some research, the treatment success rate in patients with extrapulmonary TB is lower than in patients with pulmonary TB.[10] Extrapulmonary TB disease is more common in individuals with advanced HIV stage, making them more susceptible to failure in OAT treatment than pulmonary TB patients.[10] No difference in the study still needs proof because no other diseases accompany it or the treatment is the same for all TB patients. Unfortunately, this study does not have supporting data. The distribution of TB patients based on the anatomic location of the disease suffered more in the pulmonary TB group at 82.9% because pulmonary TB patients had a greater chance of transmitting the disease to others than patients with extrapulmonary TB.

Table 3 shows that the initial AFB status did not affect the success of TB treatment. In contrast, previous studies stated that there could be two possibilities: the number of bacteria in the body indicates the increased proliferation of TB germs, which will increase the difficulty of treatment because more and more germs need to be killed, and TB cases with negative AFB are more common in individuals with HIV, making them more susceptible to failure in OAT treatment than pulmonary TB patients.[10]

IIn this study, the type of patient did not affect the success of TB treatment (Table 2), which was different from several previous studies, where TB patients who have never undergone prior treatment or new patients are associated with treatment success. Patients who underwent the first treatment program had a higher rate of treatment success than patients with a history of previous treatment. Because patients who have received previous treatment are closely related to the drugs used, the risk of resistance to the drug becomes higher. Therefore, further treatment is likely to influence the success of subsequent treatments.[10]

The conclusion is that the conversion of AFB status in the intensive phase is a variable that contributes to the success of TB treatment. Age, sex, BMI at the beginning of treatment, OAT guidelines, anatomic location, initial AFB status, and type of TB patient are not predictors of TB success.

The research design in this study only used secondary data, so that a good and complete recording of patient data by health workers on the registration form is very important. There were some incomplete patient data written by health workers. In addition, data on side effects, complications, comorbidities and chronic diseases suffered by patients before undergoing treatment and during treatment could not be obtained on the TB register form.

Further research needs to be done on the factors associated with the successful treatment of TB patients with a prospective cohort design so that they can see risk factors that cannot be obtained using secondary data. In addition, it is also necessary to conduct qualitative research to address the factors influencing TB treatment success.

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