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Determinants of Successful Treatment among New Tuberculosis Patients in Brebes Regency

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Abstract

Background: Brebes Regency was ranked first with the highest TB incidence in Central Java in 2020. In 2021 the trend of TB incidence increased and the trend of Success Rate decreased from the previous two years. The study aims to determine the determinants of successful treatment among new TB patients in Brebes Regency.
Method: The study design used was cross-sectional with the subject of new drug-sensitive TB patients in SITB from January 2020 to June 2022. A sample of 565 respondents was taken by simple random sampling. Data were analyzed univariately and bivariately with chi-square and Fisher's tests as well as multivariably using logistic regression test.
Results: Among 565 new TB patients included in this study, 65,1% had successful TB treatment outcomes. In multivariable logistic regression analysis, the categorical variable of pulmonary TB patients (AdjOR: 0,27; 95% CI: 0,08-0,85; p=0,03), ratio of doctors (Q2) (AdjOR: 0,39; 95% CI: 1,18-0,87; p=0,02), microscopic test status at diagnosis (AdjOR: 2,09; 95% CI: 1,08-4,06; p=0,28), duration of treatment Q1 (AdjOR: 9,40; 95% CI: 4,27-20,69; p<0,001), Q2 (AdjOR: 0,08; 95% CI: 0,01-0,43; p<0,001), Q3 (AdjOR: 0,05; 95% CI: 0,01-0,30; p<0,001), and negative smear microscopic test results at month 2 after initiation of treatment (AdjOR: 9,80; 95% CI: 2,10-45,57; p<0,001) has a significant relationship to the successful TB treatment.
Conclusion: Category of pulmonary TB, ratio of doctors 4,4-8,8 per 100,000 population, microscopy test status at diagnosis, length of treatment less than 7 months 11 days-12 months, and negative smear microscopic test results at the end of the 2nd month after the start treatment were determinants of successful treatment among new TB patients in Brebes Regency.

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INTRODUCTION

Tuberculosis (TB) is a disease caused by Mycobacterium tuberculosis that is transmitted from person to person through the air. The bacteria that cause TB not only attack the lungs, but can also affect other parts of the body, such as the brain, kidneys, or spine. If TB is not treated properly, it will be fatal (CDC, 2021). Globally, new cases of TB amounted to 6.4 million, equivalent to 64% of TB incidence (10.0 million). TB remains the 10th leading cause of death in the world with an estimated 1.3 million patients dying (World Health Organization, 2018). Untreated TB patients after 5 years of diagnosis, 50% of them die, patients with good immunity, 25% will recover, and 25% will become chronic infectious cases (World Health Organization, 2021b).

Indonesia is the country with the third highest TB burden and is one of eight countries that account for 2/3 of TB cases in the world (WHO, 2021). In 2021 Central Java is among the zones with the highest estimated number of TB patients at 11,153-18,371 cases. The prevalence of all TB cases in 2018 increased by 2.9% from the previous year (38.8% to 41.7%). Case Notification Rate (CNR) of TB in 2021 was 116.8 per 100,000 population (40,582 cases), a decrease from 2019 and 2018 (211 per 100,000 population and 134 per 100,000 population respectively) (Dinas Kesehatan Provinsi Jawa Tengah, 2021). The Succes Rate in 2021 was 83.5%, this figure has not yet reached the national Succes Rate target (90%) (Indonesia Ministry of Health, 2020).

Central Java consists of 35 regencies/ cities with Brebes Regency being one of them. Brebes alone ranked as the district with the highest TB Incidence (ITB) in Central Java in 2020, at 0.96 (1,840 cases) (Badan Pusat Statistik Provinsi Jawa Tengah, 2020). Based on SITB data of Brebes Regency, the trend of TB case finding in 2021 (55.09%) increased from 2020 (42.84%) and decreased from 2019 (81%). The Success Rate trend has decreased successively by 85% (2019), 84.8% (2020) and 70.6% (2021). In 2021, 7,696 TB cases were reported (36.32% of 21,190 target suspects) with a missing case rate of 44.91%. The target for TB case notification in Brebes is 4,360 (90% of the target suspects) and has only been achieved by 55.09%. Data shows the mortality rate during TB treatment increased from 2019-2021 (1.2 per 100,000 population to 3.0 per 100,000 population) (Brebes Regency Health Office, 2019, 2020, 2021).

The high TB incidence and the increasing trend of TB case finding indicate that the number of new TB patients found and recorded among 100,000 population is still high. New TB patients are patients who have never been treated or have been treated with a combination of drug-resistant OAT for less than one month. Treatment outcomes of new TB patients need to be monitored to determine the success factors of treatment and avoid relapse or the risk of unsuccessful treatment effectively. Most TB patients in Indonesia are in the age range of ≥15 years (adult and productive age groups). Adults and the elderly have a high risk of unsuccessful TB treatment (Gebrezgabiher et al., 2016; Oshi et al., 2014). Male has a higher percentage of unsuccessful TB treatment, this may occur because women pay more attention to health compared to men (Marçôa, 2018; Rajarao & Anjanamma, 2013). Employment is a factor associated with successful TB treatment, with employed patients having better successful treatment rates than unemployed (Apay, 2022).

TB patients can be cured by undergoing routine and regular treatment. The length of treatment for TB patients should be as standardized as 6 months; extending the treatment period can lead to the risk of drug resistance and may cause treatment failure (Lee et al., 2020; World Health Organization, 2017). Positive sputum test results at the end of second month after treatment initiation are significantly associated with unsuccessful treatment outcomes (Wen et al., 2018). Treatment failure and death of TB patients tend to increase especially in patients with comorbid HIV, DM, and pregnant status (Bekker et al., 2016; Lestari et al., 2020; Mohammed et al., 2017; Vrieling et al., 2018). The results showed that the risk of death in patients with extra-pulmonary TB was 5.58 times higher than in patients with pulmonary TB (Rahmanian et al., 2018).

Successful TB treatment is also associated with geographic factors, with urban residents having a higher probability

of successful treatment (Hanson et al., 2015; Mayer et al., 2019). Based on previous studies, the distance from the TB patient's house to the health service center affects the success of TB treatment, the further the distance from the house to the health service center increases the likelihood of failure (Robsky et al., 2020). Accessing quality health services can improve health outcomes, but this is still a challenge due to under-resourced health services (Agustina et al., 2019). Health insurance plays an important role in the integration of TB services, thus having a positive effect on access to services and the quality of health of TB patients (Lestari et al., 2020). Standardized treatment will increase the success rate of TB treatment (Kementerian Kesehatan RI, 2017).

This study aims to determine the determinants of successful treatment among new TB patients in Brebes Regency according to SITB data for 2020, 2021, and 2022. SITB (Tuberculosis Information System) has information that has never been further studied regarding the successful treatment of new TB patients in Brebes Regency.

METHOD

The type and design of this study was an analytic observational study using a cross-sectional design regarding the determinants that influence the successful treatment of new TB patients in Brebes Regency from 2020 to 2022. Data were obtained from secondary data of SITB (Tuberculosis Information System) of Brebes Regency Health Office in January-December 2020, January-December 2021, and January-June 2022. SITB is an integrated platform for recording and reporting TB cases by all stakeholders.

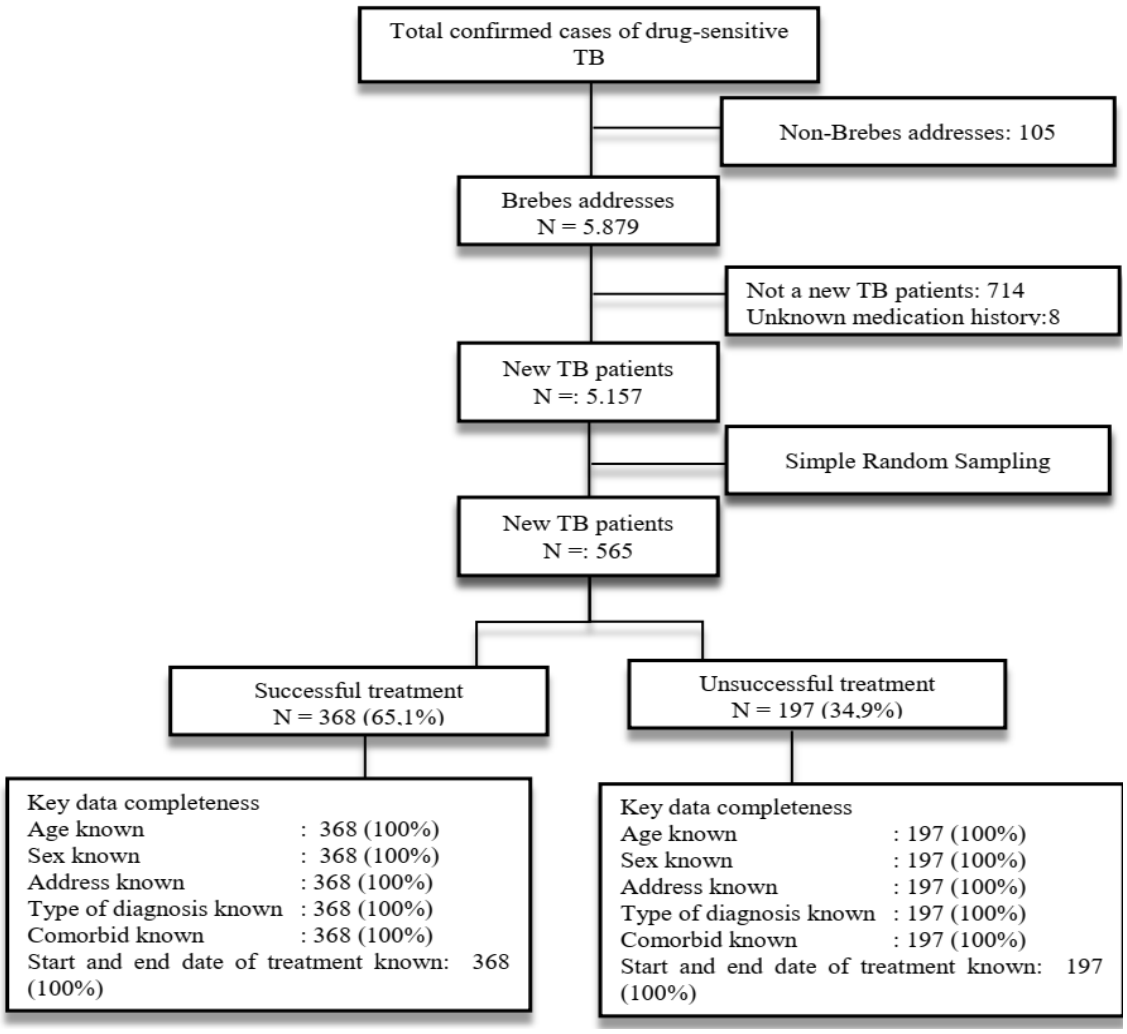

Figure 1. Flowchart of research respondents and key variable completeness

Figure 1 shows the flow of research respondents. From January 1, 2020, to June 30, 2022, a total of 5,984 Drug-sensitive TB patients were recorded in the SITB of the Brebes Regency Health Office for the treatment program. The samples used in this study were samples that met the inclusion and exclusion criteria. The inclusion criteria in this study were new TB patients with treatment results recorded in SITB totaling 5,157 patients, which had been excluded by missing data. The minimum sample size calculation was obtained from the formula in Sample Size Determination In Health Studies by SK. Lwanga and S. Lameshow (Lwanga, Stephen Kaggwa, Lemeshow, 1991). The sample size was determined as 565 samples from eligible SITB and taken by simple random sampling.

TB treatment outcome is the dependent variable in this study. TB treatment outcome decisions are made by doctors or TB clinicians based on laboratory and/or clinical findings. Treatment outcome decisions are made at the end of the 6-month treatment duration for pulmonary TB and up to 1 year for some forms of extrapulmonary TB. In this study, successful treatment was the sum of all cured and fully treated TB cases among all treated and reported TB cases, while unsuccessful treatment consisted of treatment failure, treatment dropout, death, and not evaluated (Indonesia Ministry of Health, 2017; World Health Organization, 2013).

The independent variables in this study included sociodemographic variables and clinical variables. The sex variable is the sex of the TB patient, which consists of male and female. The age variable is the age of TB patients when registered to carry out the treatment process in SITB, categorized into ages <15 years, 15-24, 25-34, and ≥35 years. Working status variable is an activity that TB patients do every day to earn income, categorized into working and not working. Place of residence place is the geographical location of the TB patient's home known from the full address listed in the SITB, categorized into urban and rural areas. Health insurance coverage variable is the status of TB patients as participants in the National Health Insurance or not, known from the National Health Insurance participant number in SITB, categorized into yes and no. Pregnant status is the status of TB patients carrying an embryo or fetus in their body when diagnosed and or undergoing the TB treatment process. DM status is the health condition of TB patients as DM sufferers or not known from the results of a doctor's diagnosis and recorded in SITB, categorized into no and yes. HIV status is the health condition of TB patients as HIV patients or not, which is known from the results of a doctor's diagnosis and recorded in the SITB, categorized into no and yes. Type of health care facility is the health care facility where TB patients are diagnosed, undergo routine treatment, and get help when there is an emergency, categorized into primary health care, hospital, and clinic. The variable distance to a health care facility is the distance from the patient's home address to the nearest health care facility as the location of diagnosis, undergoing routine treatment processes, and obtaining help when there is an emergency, categorized into quartiles: Q1 (<1 km-14.50 km), Q2 (14.51 km-29.50 km), Q3 (29.51 km-44.50 km), and Q4 (44.51 km-60 km). The ratio of doctors per 100,000 population is the ratio of the availability of doctors from primary health care, hospitals, and clinics in the area where TB patients live, the ratio of health workers including the ratio of doctors can describe the quality of health services and the burden of health workers in an area, this variable is categorized into quartiles: Q1 (2.8-4.3), Q2 (4.4-8.8), Q3 (8.9-21.5), and Q4 (21.6-54.5). Category of TB is a grouping of TB patients based on the anatomical location of the disease, categorized into Pulmonary TB and Extrapulmonary TB. Type of TB is a grouping of TB patients based on proven positive results in the examination of biological samples, categorized into BTA positive pulmonary TB, BTA negative pulmonary TB, and extrapulmonary TB. Type of TB diagnosis variable is a grouping of TB patients based on the method of diagnosis, categorized into bacteriologically and clinically confirmed TB patients. Bacteriologically confirmed TB patients were TB patients who tested positive for biological samples (sputum and tissue) through direct microscopic examination,

Rapid Molecular Test (RMT), or culture, while clinically diagnosed TB patients were patients who did not meet the criteria for bacteriological diagnosis but were diagnosed as active TB patients by doctor, and decided to receive TB treatment. The variable of microscopic test status at diagnosis was a variable that showed whether two sputum samples were collected at the time of diagnosis to determine potential transmission and assess treatment success. The treatment status variable is the treatment status of TB patients as determined by health workers, standardized treatment if TB patients take drugs in accordance with the programmed drugs, not standardized treatment if taking drugs outside the programmed drugs. The OAT combination variable is the treatment of TB patients given in the form of an appropriate OAT combination containing at least 4 kinds of drugs to prevent resistance, in this study the selected samples were patients with OAT combination category 1 and child category. Treatment duration is the length of time the patient undergoes the treatment process from diagnosis until the final treatment result is decided by health workers, categorized in the form of quartiles Q1 (0-2 months 14 days), Q2 (2 months 15 days-4 months 26 days), Q3 (4 months 27 days-7 months 10 days), and Q4 (7 months 11 days-12 months). The last variable was microscopic test results at the end of second month, categorized into BTA negative, BTA positive, and not tested, these test results were conducted to monitor and evaluate the treatment process because positive sputum test results at the end of second month after treatment initiation were significantly associated with unsuccessful treatment outcomes (Berhe et al., 2012).

Data analysis included univariate, bivariate, and multivariable analysis. The bivariate analysis was performed with the chi-square test and variables that did not meet the chi-square test were tested using Fisher's test. Furthermore, multivariable analysis was performed with logistic regression test. Bivariate and multivariable analysis with 95% confidence intervals (CI) were used to infer the relationship between independent and dependent variables. Logistic regression analysis was performed to assess the effect of several different variables on one outcome variable. This study was approved by the Health Research Ethics Committee, Universitas Negeri Semarang, Indonesia (402/KEPK/EC/2022).

RESULTS AND DISCUSSION

From January to June 2022, a total of 5,157 new patients were recorded by the Brebes District Health Office, 10.95% of whom were new patients included in this study. 44.4% (251) of patients were female with 57.9% aged ≥35 years. More than half (51.2%) of patients were employed and most patients (82.3%) resided in urban areas. Of the total 565 patients, 140 (24.8%) were enrolled in National Health Insurance. There were 0.5% (3) pregnant patients, 3.77% (21) patients with DM, and 0.7% (4) patients with HIV. 61.4% (347) of patients underwent the treatment process at primary health care, 199 (35.2%) patients at hospitals, and the rest (3.4%) at clinics. 24.1% (136) of patients were from areas with the lowest doctor ratio (2.8-4.3 per 100,000 population) and 75.9% (429) were from areas with a doctor ratio of 4.4-54.5 per 100,000 population. The majority of patients (88.1%) had a residential address that was <1 km-14.50 km from a health care facility. 91.9% (519) were categorized as pulmonary TB patients, 55.9% of patients were bacteriologically diagnosed, and 55.2% were BTA positive.

At diagnosis, 40% (266) had microscopic tests. More than half of the patients (53.8%) did not have microscopic tests at the end of second month, 46.2% of patients had tests done with 241 of them being negative. Patients whose treatment was not standardized accounted for 2.3% (13). New TB patients who were treated with OAT combination category 1 accounted for 92.6% (527), and pediatric category accounted for 6.7% (38) with most patients (67.1%) undergoing treatment for 4 months 27 days to 7 months 10 days (Table 1).

This study showed a successful TB treatment rate of 65.1% (368) of all new TB patients in Brebes Regency during 2020-2022. Among patients with successful TB treatment outcomes, 68% ended up as fully treated patients and 32% were cured. In addition, among patients with unsuccessful treatment outcomes, 0.5% failed, 26.9% dropped out of treatment, 9.6% died, and 62.9% were not evaluated. The

successful treatment rate in new patients in this study was almost 3/4 of the target success rate (90%) for TB treatment among new TB patients and patients with previous treatment history. This is in line with previous studies that stated a lower percentage of successful treatment was in patients with previous treatment than in new TB cases. Previously treated patients are more likely to develop multi-drug resistance to Mycobacterium tuberculosis (Gadoev et al., 2015; Kempker et al., 2015; Stosic et al., 2018; Xi et al., 2022).

Table 1. Respondent Characteristic Distribution (n=565)

Characteristic	Frequency (n = 565)	Percentage (%)
TB Treatment Outcome		
Successful treatment	368	65,1
Unsuccessful treatment	197	34,9
Sex		
Female	251	44,4
Male	314	54,6
Age		
<15	45	8,0
15-24	93	16,5
25-34	100	17,7
≥35	327	57,9
Working Status		
Working	289	51,2
Not working	276	48,8
Type of Residence Place		
Urban	465	82,3
Rural	100	17,7
Health Insurance Coverage		
Yes	140	24,8
No	425	75,2
Pregnancy Status		
Not pregnant	562	99,5
Pregnant	3	0,5
DM Status		
No	544	96,3
Yes	21	3,7
HIV Status		
No	561	99,3
Yes	4	0,7
Type of Health Care Facility		
Primary health care	347	61,4
Hospital	199	35,2
Clinic	19	3,4
Distance to Health Care Facility		
Q1 (<1 km-14,50 km)	498	88,1
Q2 (14,51 km-29,50 km)	38	6,7
Q3 (29,51 km-44,50 km)	18	3,2
Q4 (44,51 km-60 km)	11	1,9
Ratio of doctors per 100,000 Population		
Q1 (2,8-4,3)	136	24,1
Q2 (4,4-8,8)	92	16,3
Q3 (8,9-21,5)	174	30,8
Q4 (21,6-54,5)	163	28,8
Category of TB		
Pulmonary	519	91,9
Extra pulmonary	46	8,1

Characteristic	Frequency (n = 565)	Percentage (%)
Type of TB		
BTA-positive pulmonary TB	316	55,9
BTA-negative pulmonary TB	203	35,9
Extrapulmonary TB	46	8,1
Type of TB Diagnosis		
Bacteriologically	316	55,9
Clinically	249	44,1
Microscopic Test Status at Diagnosis		
Performed	226	40,0
Not performed	339	60,0
Treatment Status		
Standardized	552	97,7
Not standardize	13	2,3
OAT Combination		
Category 1	527	93,3
Child category	38	6,7
Duration of Treatment		
Q1 (0-2 months 14 days)	110	19,5
Q2 (2 months 15 days-4 months 26 days)	64	11,3
Q3 (4 months 27 days-7 months 10 days)	379	67,1
Q4 (7 months 11 days-12 months)	12	2,1
Microscopic Test Results at the End of Second Month		
BTA negative	241	42,7
Not tested	304	53,8
BTA positive	20	3,5

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Table 2. Bivariate Analysis of Determinants of Successful Treatment among New TB Patients in Brebes Regency (N=565)

Determinant	TB Treatment Outcome		p-value	PR (95%CI)
	Successful Treatment	Unsuccessful Treatment		
	n (%)	n (%)		
Sex				
Female	164 (65,3)	87 (34,7)	0,99	1,01 (0,72-1,44)
Male	204 (65,0)	110 (35,0)		
Age				
<15	30 (66,7)	15 (33,3)	0,55	1,22 (0,63-2,36)
15-24	67 (72,0)	26 (28,0)	0,10	1,57 (0,95-2,60)
25-34	68 (68,0)	32 (32,0)	0,33	1,29 (0,80-2,09)
≥35	203 (62,1)	127 (37,9)	-	Ref
Working Status				
Working	189 (65,4)	100 (34,6)	0,96	1,00 (0,72-1,45)
Not working	179 (64,9)	97 (35,1)		
Type of Residence Place				
Urban	311 (66,9)	154 (33,1)	0.08	1,52 (0,98-2,37)
Rural	57 (57,0)	43 (43,0)		
Health Insurance Coverage				
Yes	93 (66,4)	47 (33,6)	0,78	1,08 (0,72-1,62)
No	275 (64,7)	150 (35,3)		
Pregnancy Status				
Not pregnant	366 (65,1)	196 (34,9)	1,00	0,94 (0,08-10,36)
Pregnant	2 (66,7)	1 (33,3)		
DM Status				
No	359 (66,0)	185 (34,0)	0,04*	2,59 (1,07-6,25)
Yes	9 (42,9)	12 (57,1)		
HIV Status				
No	366 (65,2)	195 (34,8)	0,61	1,88 (0,26-13,43)
Yes	2 (50,0)	2 (50,0)		
Type of Health Care Facility				
Primary health care	240 (69,2)	107 (30,8)	0,76	1,30 (0,50-3,41)
Hospital	116 (58,3)	83 (41,7)	0,86	0,81 (0,31-2,16)
Clinic	12 (63,2)	7 (36,8)	-	Ref
Distance to Health Care Facility				
Q1 (<1 km-14,50 km)	328 (65,9)	170 (34,1)	0,28	0,43 (0,09-2,01)
Q2 (14,51 km-29,50 km)	25 (65,8)	13 (34,2)	0,31	0,43 (0,08-2,27)
Q3 (29,51 km-44,50 km)	6 (33,2)	12 (66,7)	0,01*	0,11 (0,02-0,69)
Q4 (44,51 km-60 km)	9 (81,8)	2 (18,2)	-	Ref
Ratio of doctors per 100,000 Population				
Q1 (2,8-4,3)	93 (68,4)	43 (31,6)	-	Ref
Q2 (4,4-8,8)	53 (57,6)	39 (42,4)	0,12	0,62 (0,36-1,08)
Q3 (8,9-21,5)	108 (62,1)	66 (37,9)	0,30	0,76 (0,47-1,21)
Q4 (21,6-54,5)	114 (69,9)	49 (30,1)	0,87	1,07 (0,65-1,76)
Category of TB				
Pulmonary	331 (63,8)	188 (36,2)	0,03*	0,43 (0,20-0,90)
Extra pulmonary	37 (80,4)	9 (19,6)		
Type of TB				
BTA positive pulmonary TB	203 (64,2)	113(35,8)	0,04*	0,44 (0,20-0,94)
BTA negative pulmonary TB	128 (63,1)	75 (36,9)	0,03*	0,41 (0,19-0,90)
Extra pulmonary TB	37 (80,4)	9 (19,4)	-	Ref
Type of TB Diagnosis				
Bacteriologically	203 (64,2)	113 (35,8)	0,68	0,92 (0,65-1,29)
Clinically	165 (66,3)	84 (33,7)		

Determinant	TB Treatment Outcome		p-value	PR (95%CI)
	Successful Treatment	Unsuccessful Treatment		
	n (%)	n (%)		
Microscopic Test Status at Diagnosis				
Performed	182 (80,5)	44 (19,5)	<0,001**	3,40 (2,29-5,03)
Not performed	186 (54,9)	153 (45,1)		
Treatment Status				
Standardized	359 (65,0)	193 (35,0)	1,00	0,83 (0,25-2,72)
Not standardize	9 (69,2)	4 (30,8)		
OAT Combination				
Category 1	344 (65,3)	183 (34,7)	0,93	1,09 (0,55-2,17)
Child category	24 (63,2)	14 (36,8)		
Duration of Treatment				
Q1 (0-2 months 14 days)	9 (8,2)	101 (91,8)	<0,001**	0,45 (0,01-0,18)
Q2 (2 months 15 days-4 months 26 days)	7 (10,9)	57 (89,1)	<0,001**	0,06 (0,01-0,26)
Q3 (4 months 27 days-7 months 10 days)	344 (90,8)	5 (9,2)	0,01*	4,91 (1,40-17,14)
Q4 (7 months 11 days-12 months)	8 (66,7)	4 (33,3)	-	Ref
Microscopic Test Results at the End of Second Month				
BTA negative	196 (81,3)	45 (18,7)	0,09	2,34 (0,89-6,21)
Not tested	159 (52,3)	145 (47,7)	0,38	0,59 (0,23-1,52)
BTA positive	13 (65,0)	7 (35,0)	-	Ref

In bivariate analysis (Table 2), TB treatment success was significantly associated with the absence of DM status (PR: 2.59; 95% CI: 1.07-6.25) and distance from residence to health care facility of 29.51 km-44.50 km (PR: 0.11; 95% CI: 0.02-0.69). Respondents with pulmonary TB category (PR: 0.43; 95% CI: 0.20-0.90), BTA positive pulmonary TB (PR: 0.44; 95% CI: 0.20-0.95) and BTA negative (PR: 0.41; 95% CI: 0.19-0.89); microscopic test performed at diagnosis (PR: 3.40; 95% CI: 2.29-5.03), BTA-negative microscopy test result at the end of the second month after treatment initiation (PR: 2.34; 95% CI: 0.89-6.21) and length of TB treatment significantly influenced the successful treatment. In contrast to these results, age, gender, employment status, place of residence, health insurance coverage, pregnancy status, HIV status, type of health care facility, treatment status, and OAT combination were not significantly associated with successful TB treatment.

Based on the DM status variable, it shows that new TB patients who do not have DM comorbidities are 2.59 times more likely to succeed in TB treatment. These results are in line with previous research in Bandung, Indonesia which explains that treatment failure and death of TB patients tend to increase especially in those with comorbidities such as DM (Lestari et al., 2020; Mohammed et al., 2017; Vrieling et al., 2018). DM increases TB treatment failure due to impaired immune system, impaired renal function, risk of drug toxicity, including risk of liver toxicity (Gadallah et al., 2016; Reis-Santos et al., 2013). Elevated blood sugar worsens the clinical manifestations of TB, and TB can worsen blood sugar control. Complications in diabetes can potentially lead to side effects of antituberculosis drugs, significant impairment of renal function, and peripheral neuropathy (Riza et al., 2014). Patients with DM are also susceptible to infections such as decreased leukocyte function, especially phagocytosis, which can lead to increased sensitivity to Mycobacterium tuberculosis (Restrepo, 2016).

The variables of distance to health care facility (Q3), category of TB disease in the lungs, type of TB BTA positive and negative, and duration of TB treatment (Q1 and Q2) had smaller PR values than the variable of DM status. The status of having microscopic test done at diagnosis, BTA negative microscopic test result at the second month after treatment initiation, and duration of TB treatment (Q3) had a greater PR value than not having DM

status.

Furthermore, variables with a p-value <0.25 were analyzed using logistic regression test to determine variables that have a strong contribution in association with successful treatment of new TB patients. Based on Table 2, there were 10 suitable variables, namely age, place of residence place, DM status, distance to health care facility, ratio of doctors per 100,000 population, category of TB, type of TB, microscopic test status at diagnosis, duration of treatment, and microscopic test results at the end of second month.

Table 3. Multivariable Analysis of Determinants of Successful Treatment among New TB Patients in Brebes Regency (N=565)

Variable	B	SE	Wald	p-value	AdjOR (CI 95%)
Category of TB	-1,30	0,59	4,94	0,03	0,27 (0,08-0,85)
Ratio of doctors per 100,000 Population					
Q2 (4,4-8,8)	-0,92	0,39	5,35	0,02	0,39 (0,18-0,87)
Microscopic Test Status at Diagnosis	0,74	0,34	4,82	0,03	2,09 (1,08-4,06)
Duration of Treatment					
Q1 (0-2 months 14 days)	-2,49	0,84	8,63	<0,001	0,08 (0,01-0,43)
Q2 (2 months 15 days-4 months 26 days)	-2,91	0,87	11,05	<0,001	0,05 (0,01-0,30)
Q3 (4 months 27 days-7 months 10 days)	2,83	0,78	8,47	<0,001	9,80 (2,10-45,57)
Microscopic Test Results at the End of Second Month					
BTA negative	2,24	0,40	31,06	<0,001	9,40 (4,27-20,69)

Based on the results of multivariable analysis of logistic regression models, 5 variables significantly continue to affect the successful treatment of new TB patients, namely pulmonary TB category (AdjOR: 0.27; 95% CI: 0.08-0.85; p=0.03), the ratio of doctors (Q2) (AdjOR: 0.39; 95% CI: 1.18-0.87; p=0.02, comparison: ratio of 2.8-4.3 doctors per 100,000 population (Q1)); microscopic test status at diagnosis (AdjOR: 2.09; 95% CI: 1.08-4.06; p=0.28) compared to no test; duration of treatment (Q1,Q2,Q3) compared to 7 months 11 days-12 months (Q4), and negative BTA microscopic test results at the end of second month after treatment initiation (AdjOR: 9.40; 95% CI: 4.27-20.69; p<0.001, comparison: BTA positive microscopy test result) (Table 3).

In this study, new TB patients categorized as pulmonary TB were 0.27 times more likely to have successful TB treatment than new TB patients categorized as extrapulmonary. The pulmonary TB patient category consisted of patients with positive and negative bacteriologic examinations. Patients with a positive bacteriologic examination are closely associated with the presence of a cavity at the time of the diagnostic test of the thoracic photograph. Patients with cavity lesions on chest X-ray have a lower likelihood of treatment success (Ralph et al., 2014; Soeroto et al., 2022). Bilateral cavities are associated with prolonged culture conversion and TB treatment failure. This is due to the presence of damaged lung parenchyma, which limits drug penetration into the tissue (Dheda et al., 2017). study conducted by Kurbatova et al. showed cavities on chest X-ray were associated with treatment failure (Kurbatova et al., 2012). The morphology of cavities varies and the majority of cavities are located in the apical or posterior lobes. Thicker cavity walls are associated with higher concentrations of Mycobacterium tuberculosis (Urbanowski et al., 2020). The results in this study are in line with previous research which shows that TB patients with anatomical location of the disease in the lungs have increased treatment success due to higher cure rates than extra-pulmonary (Terefe & Gebrewold, 2018). The risk of death in patients with extra-pulmonary TB is 5.58 times higher than in patients with pulmonary TB because most organs involved in extra-pulmonary TB are lymph nodes (52.79%), pleura (22.22%), bones (13.89%) skin (5.55%) and meninges

(5.55%) (Rahmanian et al., 2018).

Ratio of doctors of 4.4-8.8 per 100,000 population in the patient's area increased the probability of successful treatment of new TB patients by 0.39 times compared to new TB patients in area that had a smaller ratio of doctors per 100,000 population. Ratio of doctors per 100,000 population indicates the burden of health resources in delivering health services to the community. The greater the number of doctors in an area, it can be said that the coverage of services to the community can be more evenly distributed and optimal (Agustina et al., 2019). Appropriate management of TB cases is essential in eliminating TB and health care providers play an important role in its diagnosis and management (Lestari et al., 2020). This not only includes 6-8 months of treatment with anti-tuberculosis drugs but also involves counseling on the disease process and treatment adherence. Treatment adherence shows a significant relationship with TB treatment (Chusna & Fauzi, 2021). Non-adherence to treatment is a complex view of the patient's personality and attitude as well as the ability of health services, especially in Indonesia where the quality of health services is uneven (Lestari et al., 2020). Failure of health resources to monitor patient treatment adherence and lack of patient knowledge or motivation can cause TB patients to not complete their treatment, and increase the risk of TB multi-drugs resistance (Izudi et al., 2020; Rahayu et al., 2021). From the perspective of TB patients, boredom with treatment, negative perceptions and stigma towards their condition, lack of knowledge regarding the effects, and duration of treatment lead to low treatment adherence. For this reason, access to health workers aims to support and educate TB patients can help minimize the problem of unsuccessful treatment (Pradipta et al., 2021). Besides prescribing medication, health workers also play an important role in helping patients overcome individual challenges to complete treatment (Alipanah et al., 2018).

The accuracy of TB diagnosis determines the success of treatment and control of TB infection. In this study, microscopic testing at diagnosis showed a treatment success rate 2.09 times greater than that of new patients who were not diagnosed with microscopic testing. However, microscopic testing at diagnosis is not the gold standard due to the low sensitivity of microscopic testing. The low sensitivity will miss many patients who are truly TB positive, increasing the number of "false negatives". Microscopic examination to detect acid-resistant bacilli in clinical specimens is a rapid and inexpensive test, but previous studies have shown that the sensitivity of microscopic testing was 54% in respiratory samples and 50% in non-respiratory samples (Afsar et al., 2018). RMT is a sensitive and rapid method when compared to other methods, RMT was shown to be more sensitive than microscopic tests in both respiratory (100% vs 54%) and non-respiratory (87% vs 50%) specimens. In addition, live bacteria should not be taken as specimens in treated patients. Since live and dead bacilli cannot be distinguished by PCR methods, it is known that false positive results can be seen in patients with a history of MTB (Bilgin et al., 2016). In high prevalence TB infection, it was found that the sensitivity value of sputum microscopic examination was lower than other diagnostic tools, such as GeneXpert (RMT) (9.3% vs. 16.7%) (Geleta et al., 2015).

The length of treatment for TB patients must be under the standard, which is 6 months consisting of intensive (2 months) and continued (4 months) treatment phases, if the sputum test results are still positive at the end of second month, it will be emphasized on the recommendation to extend the intensive phase (Silva et al., 2020). Extending the treatment period may lead to the risk of drug resistance and may cause treatment failure (Lee et al., 2020). Our study showed that new TB patients with treatment duration of 4 months 26.5 days to 7 months 9.5 days showed the most significant association with successful TB treatment rate. The AdjOR value for this length of treatment was 9.8, which increased the probability of successful treatment 9.8 times compared to new TB patients who underwent treatment for longer than this period. The WHO currently recommends at least 6 months of treatment for active TB and 12 months for latent TB. These long treatment periods can be difficult for patients to adhere to, especially once they are well and need to return to work. Poor

adherence can lead to relapse and even death in individuals and increased transmission and development of drug resistance (Tesema et al., 2020).

Negative BTA microscopic test results at the end of second month after treatment initiation showed a significant association with treatment success of new TB patients. The AdjOR value showed that a negative BTA microscopic test at the end of second month increased treatment success by 9.4 times compared to those without the test. Sputum smear conversion in the second month of previous treatment was associated with treatment success (Do Socorro Nantua Evangelista et al., 2018). In line with previous research, BTA positive at second months of TB treatment was found to be the strongest predictor of treatment failure (Koo et al., 2020). This is also consistent with the findings of Soeroto et al in West Java and Liu et al in China (Liu et al., 2018; Soeroto et al., 2022). Treatment of sputum specimens for microscopic testing is recommended at monthly intervals until two consecutive specimens are negative. A meta-analysis confirmed that a negative sputum smear at two months of treatment is a predictor of successful TB treatment (Torres et al., 2019). Sputum microscopic is a low-cost test and can be used by TB programs to identify those at risk for early intervention. The first two months of TB treatment is when there is rapid killing of actively dividing bacilli and semi-dormant bacilli and the majority of BTA-positive patients turn negative during this period (Izudi et al., 2020). A positive sputum smear at two months may be due to primary or alternative drug resistance, leading to MDR TB and treatment failure, especially in the context of poor adherence, so if the result is still BTA-positive the recommendation to extend the intensive phase is emphasized (Gadoev et al., 2015).

A weakness of this study is not included variables strongly associated with TB treatment outcomes such as contact history, patient clinical symptoms, lung X-ray examination, and length of treatment delay. This is due to the accessibility of variables located on other forms in SITB.

CONCLUSION

This study showed that pulmonary TB category, doctor ratio of 4.4-8.8 per 100,000 population, microscopic test status at diagnosis, treatment duration of less than 7 months 11 days-12 months, and BTA negative microscopic test result at the end of the second month after the treatment initiation are determinants of successful treatment of new TB patients. Improved patient-focused integrated care and prevention efforts, proper early diagnosis through increased coverage of bacteriological tests according to the gold standard, increased and equitable distribution of the number of health workers, increased coverage of microscopic tests at the end of the second month after treatment initiation, carried out treatment according to standards, increased efforts to monitor compliance and completeness of treatment, and increased the reporting cases in TB surveillance system, can be reduced the risk of unsuccessful treatment of new TB patients.

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