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Unsuccessful Drug-Resistant TB Treatment Outcomes among Patients with Short-Term Regimen in Central Java, Indonesia

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Abstract

Tuberculosis which shows resistance to various types of drugs poses a significant burden in efforts to prevent and control tuberculosis globally. Since 2020, guidelines from the WHO have recommended a shorter treatment with an all-oral regimen for Drug-Resistant Tuberculosis (DR-TB), with the inclusion of bedaquiline instead of an injectable agent. However, the treatment success rate for DR-TB in Indonesia is still low. This study aimed to determine factors contributing to unsuccessful DR-TB treatment using STR in Central Java. This was a nested case-control study of 412 DR-TB patients enrolled with a Short-Term Regimen, registered in 2021 to 2023 who had treatment results in a subset of the Tuberculosis Information System cohort data. Independent variables analyzed included age, gender, patient employment status, history of previous TB treatment, DM status, HIV status, resistance pattern, initial sputum examination results, drug side effects, treatment initiation interval, body mass index, and BPJS ownership status. Statistical analysis was done using SPSS version 22 software, with logistic regression analysis to identify the determinants. The determinant of unsuccessful treatment outcome in Central Java Province which is 51.04% was the positive results of initial sputum examination of treatment (aOR=10.501; 95%CI=5.056-21.807), drug side effects (aOR=1.853; 95%CI=1,000-3.436), obesity (aOR=3.115; 95%CI=1.188-8.166) and BPJS non-possession status (aOR=2.213; 95%CI=0.932-5.255). More strategies are needed to improve the success of treatment with STR.

Introduction

Drug-resistant tuberculosis (DR-TB) is defined as tuberculosis infection caused by bacteria that is resistant to treatment with at least two first-line antitubercular medications, namely rifampicin, or isoniazid and rifampicin. DR-TB can be transmitted through primary infection or treatment failure, the combination of drugs, co-infection, previous use of antitubercular medications, inadequate drug absorption, underlying disease, and non-adherence to antitubercular medications (World Health Organization, 2021). A research report at Rotinsulu Lung Hospital in Bandung, Indonesia found that a history of TB treatment significantly increased the risk of MDR-TB with an odds ratio of 56.84 (Nugrahaeni and Zaqiya, 2019). A study in Surakarta General Hospital, Central Java, Indonesia (2016-2017) reported that patients' knowledge about TB

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and its treatment influences adherence and treatment success rates (Sutanto, Sutanto and Harti, 2021).

Based on the WHO global report in 2019, there were around 465,000 cases of DR-TB globally, with a proportion of 3.3% new TB patients and 18% patients with previous TB treatment. In 2017, there were 558,000 cases of DR-TB, and around 8.5% of DR-TB cases became Extensively Drug Resistance TB (XDR-TB) (World Health Organization, 2019). In Southeast Asia, the incidence of TB has reached 4,340,000 cases, of which 171,000 are DR-TB cases (WHO, 2020). The estimated DR-TB in Indonesia is 2.4% of all new TB patients and 13% of previously treated TB patients with a total estimated incidence of DR-TB cases of 24,000 or 8.8/100,000 population. In 2019, around 11,500 DR-TB patients were discovered and reported, and around 48% of patients started second-line TB treatment, with a treatment success rate of 45% (WHO, 2020). Based on the level of distribution, in this case, Central Java Province ranks second (80,264 cases) with the highest number of TB infection cases in Indonesia after West Java Province (189,886 cases). Among them, 985 cases of DR-TB were notified and treated (Kemenkes, 2021).

WHO recommends identifying factors influencing treatment duration and outcomes as a research priority, particularly in high-burden countries (World Health Organization, 2019). WHO recommends 3 DR-TB treatment options: BPaL/BPaLM, Short Term Regimen (STR), and Long-Term Regimen/Individual Regimen. Short Term Regimen (STR) is a short all-oral regimen for 9 months consisting of: 6 Bedaquiline (Bdq) with 4-6 Levofloxacin (Lfx)/Moxifloxacin (Mfx)-Clofazimin (Cfz)-Pyrazinamide (Z)-Ethambutol (E)-Isoniazid (H) high dose-Etionamide (Eto)/5 Levofloxacin/Moxifloxacin-Clofazimin-Pyrazinamide-Ethambutol (World Health Organization, 2022; Conradie *et al.*, 2020, 2022; Sangsayunh *et al.*, 2024). A comparative prospective cohort study in DR-TB patients with alloy Long Term and Short Term in Pakistan showed that short-term treatment (73.8%) was as effective as long-term treatment (75.6%), with the added benefit of fewer side effects (Munir *et al.*, 2024).

The shorter TB regimen is based on observational studies in several countries that have implemented it previously, including Bangladesh, Benin, Burkina Faso, Burundi, Cameroon, Central Africa, Congo, Niger, Swaziland and Uzbekistan. The results show that the success rate of short-term treatment is higher than that of long-term treatment (Das and Ganguly, 2020; Trubnikov *et al.*, 2021; Wahid *et al.*, 2021; Soeroto *et al.*, 2022). Many studies show that the success rate of treatment with short-term regimens varies, between 44.3% – 83.7% (Das and Ganguly, 2020; Trubnikov *et al.*, 2021; Wahid *et al.*, 2021; Soeroto *et al.*, 2022). Considering the varying success rates, this study aims to identify the determining factors for the failure of treatment for drug-resistant tuberculosis in patients with shorter regimens in Central Java.

Method

This research uses data integrated into the Tuberculosis Information System (SITB) through the TB-03 form at the Central Java provincial level. This system records TB patient data and treatment monitoring carried out by DR-TB officers at health facilities. Research data was taken from the TB patients registered in 2021 to 2023. Respondents registered in the 2021-2023 SITB cohort totaled 509 DR-TB patients, but only 412 had DR-TB treatment results. The dependent variable is the success status of short-term DR-TB regimen treatment which is categorized as successful (cured and complete treatment) and unsuccessful (patients who died, failed treatment, and lost-to-follow-up) (Olayanju *et al.*, 2018; Oelofse *et al.*, 2021).

Independent variables that are potentially related to failure of short-term DR-TB regimen treatment are age which is categorized as 0-65 years, and age ≥ 65 years, gender, patient employment status which is categorized as working and not working, history of Previous TB treatment was categorized as a new case patient, and re-treatment, DM status was categorized into patients who had DM, and did not have DM, HIV status was categorized into non-reactive, reactive, and unknown. Resistance patterns were categorized into Mono-resistant, Rifampicin-resistant, Poli-resistant, MDR, Pre-XDR, and XDR. Resistance patterns are categorized into Mono-resistant,

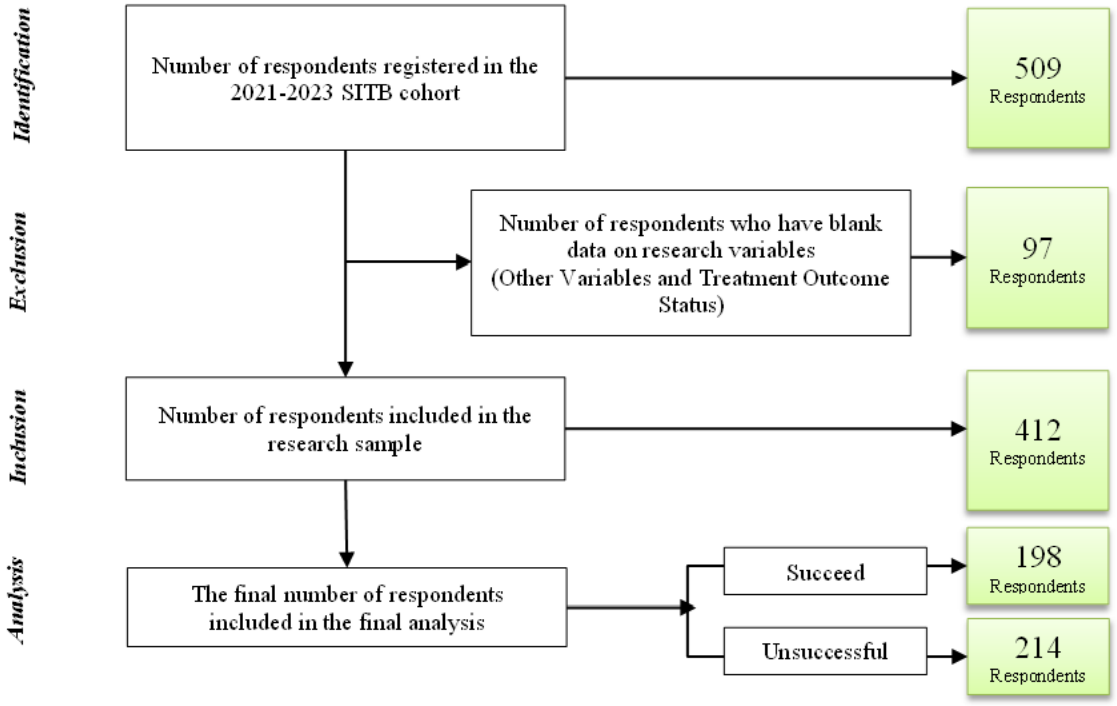

Figure 1. Sample Selection Chart

Rifampicin-resistant, Poli-resistant, MDR, Pre-XDR, and XDR. High Dose Isoniazid Resistance, Isoniazid-resistant, Levofloxacin-resistant, High Dose Moxifloxacin-resistant, and Moxifloxacin-resistant which are all categorized into sensitive, resistant, indeterminate, and unknown, examination results s Initial results are categorized into results negative, positive, and unknown, drug side effect status was categorized into none and there are drug side effects, treatment initiation interval was categorized into ≤ 7 days, and > 7 days, Body Mass Index (BMI) was categorized into Normal BMI (BMI 18, 5-25.0 kg/), Thin (BMI <18.5 kg/), and Obese (BMI >25 kg/), BPJS ownership status is categorized as having and not having BPJS.

Data are presented in frequencies and percentages based on variable categories. Bivariate analysis was used to identify risk factors associated with the failure of short-term DR-TB treatment regimens. All variables without collinearity were included in the logistic regression model using a stepwise method to determine associated variables (p 0.05). The odds ratio (OR) with 95% confidence interval (CI) was calculated as a measure of association. All analyses were performed by SPSS 22.0 (IBM Corporation, NY, USA). This research has received ethical approval from the Health Research Ethics Commission, Faculty of Health Sciences University of Jenderal Soedirman. Research ethical permission number 1481/EC/KEPK/VI/2024. No further ethical permission is required for the analysis of secondary data.

Result And Discussion

The distribution of 412 respondents was spread across 42 Programmatic Management of Drug-Resistant TB (PMDT) health facilities consisting of 3 community health centers and 39 hospitals, with the Ministry of Health owning 6 health facilities, non-profit organizations, 4 health facilities, 27 Regency/City Government health facilities, 2 Provincial Government health facilities, 1 company health facility, and 2 TNI health facilities. In the Prevalence of treatment for DR-TB patients in Central Java Province

Table 1. Characteristics of Respondents

Variable	Frequency	Percent
Treatment Results		
Succeed	198	48.06
Healed	192	46.60
Complete Treatment	6	1.46
Unsuccessful	214	51.94
Treatment Failure	26	12.15
Failed Due to Change in Diagnosis	91	42.52
Died	38	17.76
Lost-to-follow-up	150	27.57
Age		
0-65 Years	377	91.50
≥ 65 Years	35	8.50
Gender		
Man	230	55.83
Woman	182	44.17
Patient Employment Status		
Work	330	80.10
Doesn't work	82	19.90
History of Previous TB Treatment		
New Case	219	53.16
Retreatment	193	46.84
DM Status		
No DM	336	81.55
DM	76	18.45
HIV Status		
Non Reactive	272	66.02
Reactive	5	1.21
Not known	135	32.77
Resistance Patterns		
Monoresistens	0	0
RR	220	53.40
Poliresisten	4	0.97
MDR	178	43.20
Pre-XDR	8	1.94
XDR	2	0.49
High Dose Isoniazid Resistance		
Sensitive	125	30.34
Resist	174	42.23
Not Known	113	27.43
Isoniazid Resistance		
Sensitive	49	11.89
Resist	104	25.24
Not Known	259	62.86

Variable	Frequency	Percent
Levofloxacin Resistance		
Sensitive	291	70.63
Resist	10	2.43
Indeterminate	18	4.37
Not Known	93	22.57
High Dose Moxifloxacin Resistance		
Sensitive	291	70.63
Resist	10	2.43
Indeterminate	18	4.37
Not Known	93	22.57
Moxifloxacin Resistance		
Sensitive	294	71.36
Resist	8	1.94
Indeterminate	17	4.13
Not Known	93	22.57
Initial Sputum Examination Results		
Negative	219	53.16
Positive	97	23.54
Not known	96	23.30
Drug Side Effects		
No Drug Side Effects	74	17.96
There are drug side effects	338	82.04
Treatment Initiation Interval		
≤ 7 days	78	18.93
> 7 days	334	81.07
Body Mass Index (BMI)		
Normal	169	41.02
Thin	210	50.97
Obesity	33	8.01
BPJS status		
BPJS	41	9.95
Non BPJS	371	90.05

with combinations of Short-Term Regimens only 48.96% were declared successful, while 51.94% were unsuccessful. The prevalence of success was higher than research conducted in India, only 48%. (Kumar *et al.*, 2024).

Based on Table 1, the results of treatment of DR-TB patients in Central Java Province with combination Short-Term Regimen only 48.96% were declared successful, consisting of 192 recovered patients (46.60%), complete treatment was 6 patients (1.46%), while 51.94% were unsuccessful with the category consisting of 26 patients who failed treatment (12.15%), failed due to change in diagnosis in 91 patients (42.52%), died in 38 patients (17.76%), lost-to-follow-up 150 patients (27.57%). The characteristics of the majority of patients (91.50%) were aged between 0 and 65 years, 55.83% of patients were male and 44.17% were female. 80.10% of patients were working, 53.16% were new case patients, the majority of patients (81.55%) did not have DM,

Table 2. Determinants of Treatment Failure Short-Term Regimen in Drug-Resistant Tuberculosis Patients in Central Java Province

Variable	Succeed		Not successful		OR	CI 95		p-value
	n	%	n	%		Lower	Upper	
Age								0.040
0-65 Years	187	50.27	190	51.08	1 (Ref)	–	–	
≥ 65 Years	11	31.43	24	68.57	2.147	1.023	4.508	
Gender								0.090
Man	102	44.35	128	55.65	1 (Ref)	–	–	
Woman	96	52.75	86	47.25	0.714	0.483	1.055	
Patient Employment Status								0.114
Work	165	50.00	165	50.00	1 (Ref)	–	–	
Doesn't work	33	40.24	49	59.76	1.485	0.908	2.427	
History of previous TB treatment								0.587
New Case	108	49.32	111	50.68	1 (Ref)	–	–	
Retreatment	90	46.63	103	53.37	1.114	0.756	1.641	
Status DM								0.015
No DM	171	50.89	165	49.11	1 (Ref)	–	–	
DM	27	35.53	49	64.47	1.881	1.122	3.151	
Status HIV								0.532
Non Reactive	135	49.63	137	50.37	1 (Ref)	–	–	
Reactive	3	60.00	2	40.00	0.657	0.108	3.994	
Not known	60	44.44	75	55.56	1.232	0.814	1.864	
Resistance Patterns								0.000
RR	133	60.45	87	39.55	1 (Ref)	–	–	
Poliresisten	1	25.00	3	75.00	4.586	0.469	44.804	
MDR	60	33.71	118	66.29	3.007	1.992	4.539	
Pre-XDR	3	37.50	5	62.50	2.548	0.594	10.934	
XDR	1	50.00	1	50.00	1.529	0.094	24.764	
High Dose Isoniazid Resistance								0.000
Sensitive	69	55.20	56	44.80		–	–	
Resist	58	33.33	116	66.67	2.464	1.536	3.954	
Not Known	71	62.83	42	37.17	0.729	0.434	1.225	
Isoniazid Resistance								0.000
Sensitive	22	44.90	27	55.10	1 (Ref)	–	–	
Resist	25	24.04	79	75.96	2.575	1.253	5.293	
Not Known	151	58.30	108	41.70	0.583	0.315	1.078	
Levofloxacin Resistance								0.008
Sensitive	126	43.30	165	56.70	1 (Ref)	–	–	
Resist	4	40.00	6	60.00	1.145	0.317	4.146	
Indeterminate	9	50.00	9	50.00	0.764	0.295	1.980	
Not Known	59	63.44	34	36.56	0.440	0.272	0.712	

Variable	Succeed		Not successful		OR	CI 95		p-value
	n	%	n	%		Lower	Upper	
High Dose Moxifloxacin Resistance								0.008
Sensitive	126	43.30	165	56.70	1 (Ref)	–	–	
Resist	4	40.00	6	60.00	1.145	0.317	4.146	
Indeterminate	9	50.00	9	50.00	0.764	0.295	1.980	
Not Known	59	63.44	34	36.56	0.440	0.272	0.712	
Moxifloxacin Resistance								0.007
Sensitive	126	42.86	168	57.14	1 (Ref)	–	–	
Resist	4	50.00	4	50.00	0.750	0.184	3.057	
Indeterminate	9	52.94	8	47.06	0.667	0.250	1.776	
Not Known	59	63.44	34	36.56	0.432	0.267	0.699	
Initial Sputum Examination Results								0.000
Negative	132	60.27	87	39.73	1 (Ref)	–	–	
Positive	49	50.52	48	49.48	1.486	0.918	2.405	
Not Known	17	17.71	79	82.29	7.051	3.909	12.717	
Drug Side Effects								0.000
No Drug Side Effects	17	22.97	57	77.03	1 (Ref)	–	–	
There are drug side effects	181	53.55	157	46.45	0.259	0.145	0.463	
Treatment Initiation Interval								0.032
≤ 7 days	46	58.97	32	41.03	1 (Ref)	–	–	
> 7 days	152	45.51	182	54.49	1.721	1.044	2.838	
Body Mass Index (BMI)								0.014
Normal	77	45.56	92	54.44	1 (Ref)	–	–	
Which ones	112	53.33	98	46.67	0.732	0.488	1.100	
Obesity	9	27.27	24	72.73	2.232	0.979	5.086	
BPJS status								0.157
BPJS	24	58.54	17	41.46	1 (Ref)	–	–	
Not BPJS	174	46.90	197	53.10	1.598	0.831	3.074	

66.02% were declared non-reactive to HIV, the resistance pattern of 53.40% of patients were Rifampicin-resistant, 53.16% of patients had negative initial sputum examination results, 82.04% experienced drug side effects during treatment, the treatment initiation interval was more than 7 days 81.07%, patients with a thin BMI were 50.97% and 90.05% did not have BPJS.

Table 2 shows the results of crosstabulation determinants of failure of short-term DR-TB regimen treatment are patients aged 65 years and over (OR=2.147; p-value <0.005), patients with DM (OR=1.881; p-value <0.005), patients with MDR resistance patterns (OR=3.007; p-value <0.005), has a higher risk of failure to treat DR-TB with a short-term regimen. Patients with resistance to high doses of isoniazid, isoniazid, levofloxacin, or moxifloxacin (p-value <0.005) have a higher risk of not being successful in treatment compared to patients who are sensitive to these drugs. Patients who started treatment more than 7 days after diagnosis had a higher risk of treatment failure (OR=1.721, P-value <0.005), as well as patients with obesity (OR=2.232, P-value <0.005), which was higher for less successful in treatment compared with patients with normal BMI. In line with research in India which stated that the main reasons for stopping treatment in DR-TB patients were busy schedules (29%), comorbidities (19.8%), feeling there was early improvement/no improvement (10.5%), and the presence of drug side effects (18.4%)

Table 3. Logistic Regression Determinants of Unsuccessful Drug-Resistant TB Treatment Outcomes Among Patients with Short-Term Regimen in Central Java

Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95 C.I.for EXP(B)	
							Lower	Upper
Isoniazid Resistance			18.64	2	0.000			
Resist	-1.268	0.447	8.04	1	0.005	0.281	0.117	0.676
Not Known	-1.252	0.343	13.36	1	0.000	0.286	0.146	0.559
Initial Sputum Examination Results			41.38	2	0.000			
Positive	2.351	0.373	39.77	1	0.000	10.501	5.056	21.807
Not Known	2.401	0.43	31.13	1	0.000	11.036	4.748	25.65
Drug Side Effects	-1.619	0.371	19.04	1	0.000	0.198	0.096	0.41
There are drug side effects	0.617	0.315	3.838	1	0.050	1.853	1.000	3.436
Body Mass Index (BMI)			8	2	0.018			
Thin	0.593	0.497	1.423	1	0.233	1.81	0.683	4.797
Obesity	1.136	0.492	5.341	1	0.021	3.115	1.188	8.166
Non BPJS	0.794	0.441	3.242	1	0.072	2.213	0.932	5.255
Constant	-1.333	0.568	5.505	1	0.019	0.264		

Notes. Model 5: Hosmer and Lemeshow test: $\chi 2$ = 9,847; P = 0.000, Nagelkerke R^2 = 41;

(Kumar *et al.*, 2024), although the results of this study showed that there was no significant relationship between drug side effects and treatment success, 73.36% of patients with drug side effects experienced treatment failure, a prospective study conducted on a cohort of Pre-XDR and XDR DR-TB patients in India resulted in a combination Short Term Regimen with bedaquiline achieved good treatment success, though bedaquiline and other antitubercular medications have the potential to prolong the QTc interval, the benefits outweigh the risks. Additionally, this regimen proved to be highly effective with rapid sputum culture conversion rates and good treatment outcomes. Giving a Short-Term Regimen requires cardiovascular and biochemical evaluation before treatment as a precautionary measure and appropriate patient selection for the use of bedaquiline safe and successful results (Barvaliya *et al.*, 2020).

Multivariate analysis showed positive initial sputum examination results (aOR=10,501; 95%CI=5,056-21,807), there were drug side effects (aOR=1,853; 95%CI=1,000-3,436), BMI (aOR=3,115; 95%CI= 1.188-8.166) and BPJS non-possession status (aOR=2.213; 95%CI=0.932-5.255) increase the chance of treatment failure. The results of this study highlight several main factors, namely positive initial sputum examination results, drug side effects, obesity and not having BPJS. The results of the same study in West Java showed that male gender was an independent factor that increased the chances of successful treatment, while a history of previous TB treatment, sputum conversion time >2 months, and malnutrition, especially underweight, reduced the chances of success for DR-patients. TB is treated with shorter regimens. (Soeroto *et al.*, 2022). Other studies have also identified several predictors of poor DR-TB treatment outcomes, including older age, being male, a history of resistance to ofloxacin and other second-line drugs, delayed conversion of sputum culture, positive BTA at diagnosis, and the presence of comorbidities (HIV, type 2 DM, malnutrition) (Tiwari, Kumar and Kapoor, 2012; Javaid *et al.*, 2018; Leveri *et al.*, 2019; Tola *et al.*, 2021), in addition to the results of crosstabulation. This study shows a significant relationship between age and treatment success, where patients aged 65 years and over have a significantly higher risk of not being successful in treatment compared to younger patients (OR=2.147; p-value <0.005). This is consistent with literature showing that factors related to the aging process, such as decreased immune function and comorbidities,

may worsen the prognosis of DR-TB (Zhao *et al.*, 2012; Demile *et al.*, 2018; Agustina, Maulida and Yovsyah, 2019; Tao *et al.*, 2021).

The presence of Diabetes Mellitus (DM) also plays an important role in the success of DR-TB treatment. Patients with DM have a higher risk of not being successful in treatment (OR=1.881; p-value <0.005). This is following previous findings showing that DM can influence the response to TB treatment through immune system disorders and pharmacological interactions between TB drugs and DM treatment. DM can interfere with the production of protective cytokines, such as type 1 and type 17 cytokines, which are important for the immune response to TB (Abbas *et al.*, 2022; Kumar and Babu, 2023). The pattern of TB drug resistance is also a critical factor influencing the success of treatment. Patients with MDR resistance patterns had a higher risk of treatment failure (OR=3.007; p-value <0.005). This shows the importance of rapid identification and treatment of drug resistance patterns to optimize DR-TB treatment outcomes.

Resistance to various types of TB drugs, such as high-dose isoniazid, isoniazid, levofloxacin, and moxifloxacin, was also shown to be a significant risk factor for treatment failure (p-value <0.005). Resistance to various types of TB drugs, such as high-dose isoniazid, isoniazid, levofloxacin, and moxifloxacin, is a significant risk factor for treatment failure (Migliori *et al.*, 2013). Drug resistance, particularly to rifampicin, isoniazid, and fluoroquinolones, has been identified as a major contributor to treatment failure and the emergence of multidrug-resistant (Pre-XDR) tuberculosis[30]. Appropriate drug sensitivity testing and adjustment of treatment regimens based on drug resistance are needed in treating DR-TB.

Delay in starting treatment also has a serious impact on DR-TB treatment outcomes. Patients who started treatment more than 7 days after diagnosis had a higher risk of treatment failure (OR=1.721; p-value <0.005) (Asres, Jerene, and Deressa, 2018; Tedla *et al.*, 2020). Early detection and immediate intervention in the management of DR-TB to avoid disease progression. This study also highlights that obese patients have a higher risk of treatment failure compared to patients with normal BMI (OR=2.232; p-value <0.005). This increased risk is due to several factors, including changes in the pharmacokinetics and pharmacodynamics of TB drugs in obese patients, which may lead to reduced drug exposure and efficacy. Additionally, obese patients may have a higher burden of comorbidities, such as diabetes, which may further complicate TB treatment and increase the risk of treatment failure (Longo *et al.*, 2013; Theofiles *et al.*, 2015; Conway *et al.*, 2016; Pinner *et al.*, 2021; Schell *et al.*, 2022).

Efforts that need to be made by health agencies to prevent the failure of DR-TB treatment with short-term regimens include several important strategies. These strategies encompass better management of DR-TB cases by prioritizing early detection through routine sputum examinations, surveillance, and intensive treatment of drug side effects to minimize negative impacts that could interfere with the success of treatment. Additionally, expanding access to BPJS or other health insurance programs for TB patients is crucial so that they can receive adequate treatment without being hampered by financial problems.

Conclusion

The results showed that the initial sputum examination was positive (aOR=10,501; 95%CI=5,056-21,807), drug side effects (aOR=1,853; 95%CI=1,000-3,436), BMI (aOR=3,115; 95%CI=1,188 -8.166) and BPJS non-possession status (aOR=2.213; 95%CI=0.932-5.255) are predictors of failure to achieve short-term DR-TB treatment. This study provides helpful insights into the determinants of unsuccessful DR-TB treatment outcomes and has implications for enhancing treatment success in tuberculosis control programs. Strategies to prevent failure of DR-TB treatment with short-term regimens in this population must include good management of DR-TB cases. It is important to control risk factors for treatment failure to reduce the burden of DR-TB, both internally and externally to prevent it. This research only covers one area of Central Java Province, so it cannot represent other areas that have different characteristics. Further research needs to be conducted to

overcome these limitations. Further research needs to be carried out regarding the success of the DR-TB treatment regimen in the form of BPaL/M (Bedaquiline, Pretomanid, Linezolid, and/or Moxifloxacin) which will begin to be implemented comprehensively in Central Java Province in 2024 as a comparison with the results of this study. Clinical-based research on DR-TB treatment and the risk factors associated with it should also be conducted for comparison with the results of these community-based studies.

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