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The Effect of Sputum Conversion Time ≤ 2 Months on The Outcome of Drug Resistant TB Patients: A Propensity Score Matching Analysis

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Abstract

Background: Sputum conversion time has long been used as a biomarker predictor of early success in DR-TB treatment, but the results of the existing studies are mostly observational cohort studies. Observational studies are inherently subject to possible bias due to non-randomization. To reduce this potential for bias, we used the Propensity score matching (PSM) approach, which is a statistical method that can be used to reduce the bias caused by unrandomization in an observational study.

Aim: To see the relationship between sputum conversion time ≤ 2 months and the final outcome of TB treatment RO with an estimated Average Treatment on The Treated (ATT) value.

Methods: Observational cohort study using the PSM approach. Data analysis was carried out in two stages, first by using the Partial Least Square – Structural Equation Modeling (PLS-SEM) approach to see variables that have the potential to cofound the final treatment outcome. Secondly, the data was then processed using the PSM approach with the final result in the form of an estimated ATT value at Sputum Conversion time ≤ 2 months against the final treatment outcome

Results: Analysis using the PLS-SEM approach showed that the final treatment outcome was significantly influenced directly by age, Diabetes Mellitus (DM) baseline status, sputum conversion time and treatment side effects. In further data analysis using the PSM approach, it was found that the main confounding for the final treatment outcome was the sputum conversion time. With an estimated ATT value when sputum conversion ≤ 2 months is 0.6882 (SE 0.091, p 0.000).

Conclusion: Sputum conversion time ≤ 2 months has a 68.2% greater chance of achieving the expected treatment results, compared to those who have sputum conversion time > 2 months.

Keywords: Time to Sputum Conversion, DR TB, Propensity score, PLS-SEM

Introduction

Drug-resistant tuberculosis (DR-TB) remains a significant global health burden. According to the World Health Organization (WHO) 2020 report, the worldwide success rate of DR-TB treatment is still low, at around 56%, with Indonesia ranked fifth out of 27 countries for the highest-burden of DR-TB.1,2

Based on existing studies, sputum conversion time is believed to be one of the factors affecting DR-TB patients' outcomes and may also be an early biomarker predictor for treatment success.3-7 However, the majority of study reports on this subject are purely observational study reports, which are inherently biased due to the lack of randomization process. To address this issue, we applied a

Propensity Score Matching (PSM) in our study, which is a statistical method that can be used to lessen potential bias in purely observational studies.8-11 By estimating the Average Treatment on The Treated (ATT) value, the goal of this study was to determine if sputum conversion time ≤ 2 months has an impact on the result of DR-TB treatment.

Methods

This study was designed with an analytic retrospective cohort using the PSM approach to reduce the bias that can emerge due to the lack randomization of subjects. The research aims to analyze the value of Average Treatment on the Treated (ATT) sputum conversion time on the final treatment result of patients with DR-TB. We carried out this study by analyzing the data from the National Tuberculosis Information System (SITB) and medical records of DR-TB patients at Saiful Anwar Hospital (RSSA) East Java, Indonesia.

The data will first be analyzed using a nonmatching method with the Partial Least Square - Structural Equation Modelling (PLS-SEM) approach to examine the relationship between demographic-comorbid factors, treatment regimen, sputum culture conversion time, and treatment side effects on the treatment success of patients with DR-TB. The same data will then be subjected to the Matching process and analyzed using the PSM approach to determine whether there is a difference between the nonmatching treatment and the matching analysis.

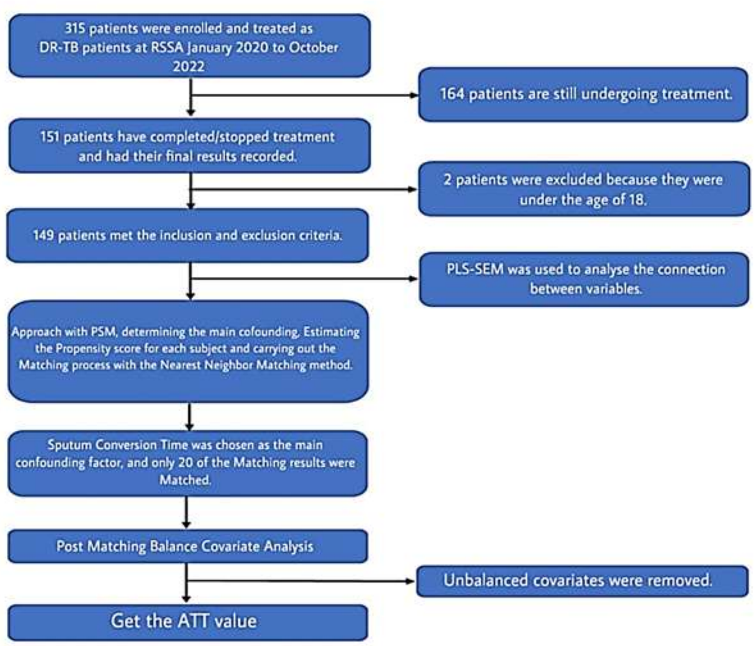
Results

Research Subject Characteristics

From January 2020 to October 2022, 315 DR-TB patients were enrolled at RSSA, with 151 patients having completed/stopped treatment and achieving final treatment results while 161 of them still in the treatment process. Two patients were excluded from the 151 who had final treatment results because they were under 18 years old. As a result, the total number of patients met the inclusion and exclusion criteria for the research was 149 patients.

The subjects' mean age was 42.12 years, with 27.5% of patients aged 46-55 years (early elderly). The gender breakdown was 55.7% male patients and 44.3% female patients. The average patient's BMI (Body Mass Index) was 19.04, with underweight (50.3%) being the most common BMI group and norm weight (3.6%). Furthermore, for the type of resistance, 67.8% were classified as RR, 14.1% as MDR, 12.8% as pre-XDR, 4.7% as XDR, and 0.7% as Poliresistant. Of the 149 patient samples, 30.2% had DM, 2% were HIV positive, and 6.7% had other comorbidities.

Figure 1. Flow of Research Results



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In total, 35.6% of patients received short-term treatment, and 64.4% received long-term treatment with the final results of treatment, 54.4% of patients had the favourable outcome.

In the initial CXR findings, 1.3% had atelectasis, 1.3% with pleural effusion, 29.5% fibrosis, 1.3% granuloma, 35.6% cavities, 2.0% consolidation, 26.8% moderately advanced, 0.7% with nodules, 0.7% normal, and 0.7% with pneumothorax. While in sputum conversion time, out of 149 patient samples, 8.7% had a sputum conversion time of 0 months, 52.3% for one month, 6.7% for two months, 3.4% for three months, 0.7% for four months, and 28.2% had no conversion. A total of 47.0% experienced side effects, with 32.9% experiencing gastrointestinal disorders, 4.7% experiencing psychiatric disorders, 14.1% experiencing skin disorders, 25.5% experiencing neuromusculoskeletal disorders, 8.1% experiencing cardiac disorders, 0.7% experiencing hearing disorders, 1.3% experienced liver disorders, 2.0% experienced kidney disorders, 3.4% experienced Visual impairment, 5.4% experienced blood disorders, 0.7% experienced endocrine disorders, and 3.4% experienced electrolyte disorders.

Table 1. Research Subject Characteristics

Baseline characteristic	Frequency	Percentage (%)
Age (years) (mean±SD)	42.12	±14.05
17-25 years old (late teenagers)	25	16.8%
26-35 years old (early adulthood)	27	18.1%
36-45 years old (late adulthood)	25	16.8%
46-55 years old (early elderly)	41	27.5%
56-65 years old (late elderly)	25	16.8%
>65 years old (seniors)	6	4.0%
Gender		
M	83	55.7%
F	66	44.3%
BMI (Body Mass Index) (mean±SD)	19.04	±3.72
Underweight	75	50.3%
Normoweight	50	33.6%
Overweight	15	10.1%
Obesity I	8	5.4%
Obesity II	1	0.7%
Resistance Type		
polyresistance	1	0.7%
RR	101	67.8%
MDR	21	14.1%
Pre-XDR	19	12.8%
XDR	7	4.7%

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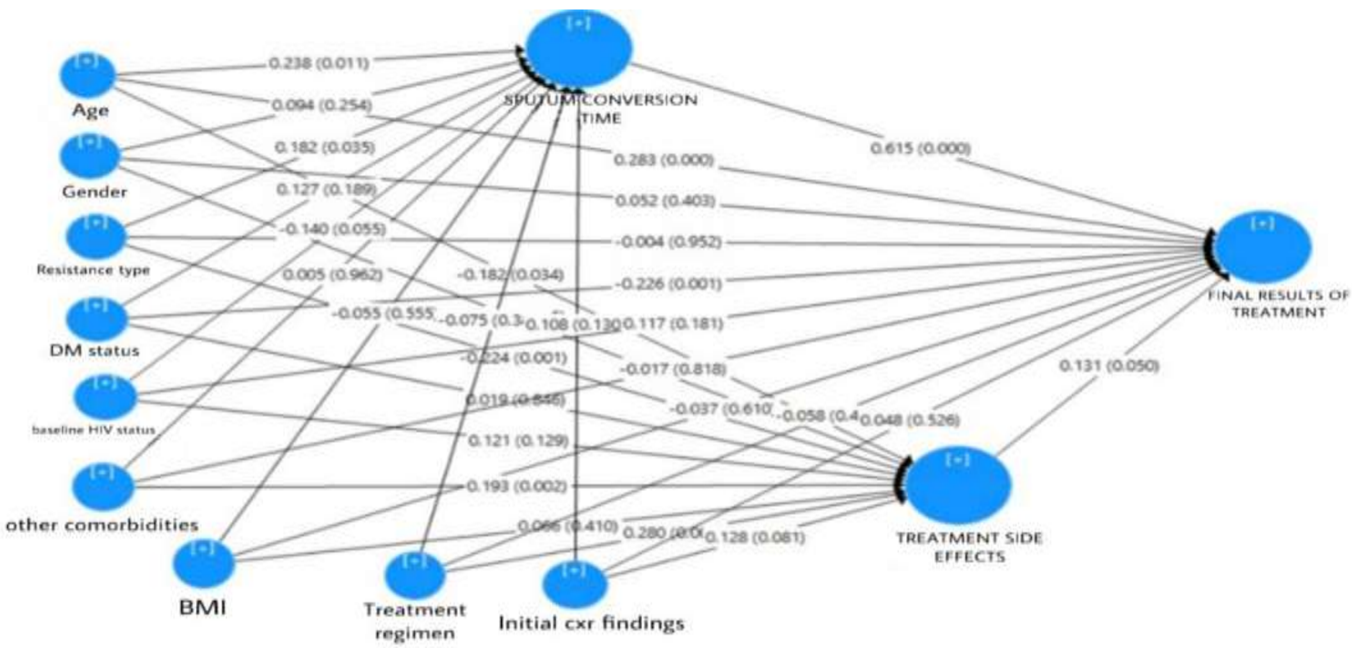
Baseline DM Status		
No	104	69.8%
Yes	45	30.2%
Baseline HIV Status		
HIV negative	146	98.0%
HIV positive	3	2.0%
Other comorbidities		
No	139	93.3%
Yes	10	6.7%
Treatment Regimen		
Short-term Regiment	53	35.6%
Long-term Regiment	96	64.4%
Final Treatment Results		
Loss to follow-up	28	18.8%
Failed	13	8.7%
Died	27	18.1%
Complete Treatment	37	24.8%
Healed	44	29.5%
Final Treatment Results		
Favourable outcome	81	54.4%
Unfavorable outcome	68	45.6%
Initial CXR findings		
Atelectasis	2	1.3%
Pleural Effusion	2	1.3%
Fibrosis	44	29.5%
granuloma	2	1.3%
Cavities	53	35.6%
Consolidation	3	2.0%
Moderately advanced	40	26.8%
Nodules	1	0.7%
Normal	1	0.7%
Pneumothorax	1	0.7%
Sputum Conversion Times		
0 month	13	8.7%

1 month	78	52.3%
2 months	10	6.7%
3 months	5	3.4%
4 months	1	0.7%
No Conversion	42	28.2%
Side Effects		
None	79	53.0%
Yes	70	47.0%
Gastrointestinal Disorders	49	32.9%
Psychiatric Disorders	7	4.7%
Skin Disorders	21	14.1%
neuromusculoskeletal disorders	38	25.5%
cardiac disorders	12	8.1%
Hearing Disorders	1	0.7%
Liver Disorders	2	1.3%
Kidney disorders	3	2.0%
Visual impairment	5	3.4%
Blood disorders	8	5.4%
Endocrine disorders	1	0.7%
Electrolyte disorders	5	3.4%

Figure 2. Flowchart of structural model path coefficients and P-values between various variables analyzed on sputum conversion time, treatment side effects and treatment results



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Phase I Data Analysis (Non-Matching Multivariate Analysis with PLS-SEM approach).

Figure 2 shows the output of the PLS-SEM structural model (inner model) after 500x bootstrapping. The Q2 value in PLS-SEM can be used to determine the Goodness of fit test. In regression analysis, the Q2 value has the same meaning as the coefficient of determination (R-square / R2), where the higher R2, the statistical mmodel used is said to be fitter and in accordance with the data. A Q-Square value greater than 0 (zero) implies that the statistical model used has predictive relevance, whereas a Q-Square value less than 0 (zero) shows that the model lacks predictive relevance. Based on data processing with PLS-SEM, the resulting coefficient of determination (R-square) value in this research is as follows: Sputum conversion time (0.149), Treatment side effects (0.200), Treatment final outcome (0.497). so the Q2 value in the above modeling is: Q2 value = 1 - (1 - R21) (1-R22) (1 - R23) ... (1 - R 2n) = 1- (1-0.149) (1-0.200)(1-0.497) = 1- 0.3426 = 0.6574.

The Q-square value generated in the overall model equation above is 65.74%, indicating that the structural model above has good enough predictive relevance to be used. Figure 2 also shows several variables that directly impact the final treatment results, which are also summarized in Table 2. PLS-SEM data analysis discovered that the following variables directly affected DR-TB treatment results: patient age, baseline DM status, presence or absence of treatment side effects, and sputum conversion time.

Table 2. Significance value of direct effect on DR-TB Treatment Outcome

Direct Effect	Coefficient Path	Standard Deviation	P Values
Age -> Treatment Results	0.283	0.077	**0.000**
TREATMENT SIDE EFFECTS -> TREATMENT RESULTS	0.131	0.066	**0.049**
SPUTUM CONVERSION TIME -> TREATMENT RESULTS	0.615	0.063	**0.000**
Baseline DM status -> TREATMENT RESULTS	-0.226	0.068	**0.001**

Phase II Data Analysis (Matching Analysis using PSM approach).

On this phase, the analysis begins with the selection of confounding variables, which are variables that are connected to the independent and dependent variables but are not intermediate variables. These variables have a partial or complete relationship with the exposure and outcome in the third factor. Some of the variables we used such as age (X1), gender (X2), DM status (X3), treatment regimen (X4), sputum conversion time (X5), and treatment side effects (X6). The selection of these variables as potential confounding variables was based on the results of previous analysis utilizing the PLS-SEM approach, in addition to the literature on factors affecting the outcomes of DR-TB treatment.

The major confounding variable is chosen based on the test's findings of the relationship between potential confounder variables and the final treatment outcome status variable (Y). The following hypotheses were employed:

H0: There is no significant relationship between variables that have the potential as confounding Xm and variable Y; m = 1, 2, 3, 4, 5, 6.

H1: There is a significant relationship between variables that have the potential as confounding Xm and variable Y; m = 1, 2, 3, 4, 5, 6

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Table 3. Testing the Relationship of Potential Variables as Confounding and Treatment Results Status (Y)

Variable	χ 2	*p-value*	Decision
Y*X1	9.908	0.001	Reject H_0**
Y*X2	0.387	0.533	Failed to Reject H_0
Y*X3	0.027	0.868	Failed to Reject H_0
Y*X_4	0.077	0.780	Failed to Reject H_0
Y*X_5	5.512	0.000	Reject H_0**
Y*X_6	0.0003	0.985	Failed to Reject H_0

According to Table 3, using the chi-square test statistic at a significance level of α = 5%, the variables that can potentially be significant confounding variables are patient age and sputum conversion time, both of which have a significant relationship with the final treatment results status. However, the sputum conversion time variable (X5) had the smallest p-value of the two variables; hence it was chosen as the main confounding variable.

The propensity score is symbolized by e(xi), while the logistic regression model is symbolized by π(xi). For each pair (xi,zi) with ductal conversion time (z) as a confounding variable, the probability distribution function is f(z)=e(xi)z (1-e(xi))1-z. Table 4 displays the results of estimating propensity score values for all research subjects (subjects 1 through 149).

Table 4. Value Estimation of the Propersity Score for each subject

Data to	**1**	**2**	**3**	**4**	**5**	**6**
1-6	0.673	0.488	0.837	0.550	0.720	0.767
7-12	0.837	0.753	0.720	0.508	0.837	0.753
13-18	0.655	0.837	0.380	0.837	0.616	0.488
19-24	0.885	0.761	0.761	0.923	0.720	0.923
25-30	0.885	0.761	0.950	0.923	0.791	0.923
31-36	0.616	0.923	0.616	0.605	0.925	0.655
37-42	0.925	0.753	0.753	0.925	0.923	0.837
43-48	0.885	0.655	0.761	0.837	0.837	0.720
49-54	0.923	0.616	0.950	0.925	0.950	0.753
55-60	0.753	0.662	0.655	0..837	0.950	0.925
61-66	0.655	0.950	0.605	0.605	0.623	0.380
67-72	0.795	0.837	0.767	0.496	0.906	0.862
73-78	0.862	0.623	0.623	0.623	0.623	0.605
79-84	0.508	0.496	0.623	0.605	0.605	0.623
85-90	0.623	0.673	0.655	0.720	0.508	0.616
91-96	0.623	0.662	0.753	0.673	0.655	0.862

97-102	0.862	0.508	0.858	0.795	0.496	0.605
103-108	0.906	0.862	0.795	0.858	0.623	0.761
109-114	0.655	0.488	0.720	0.488	0.488	0.720
115-120	0.508	0.616	0.605	0.616	0.837	0.837
121-126	0.906	0.496	0.623	0.488	0.605	0.720
127-132	0.720	0.923	0.858	0.623	0.616	0.380
133-138	0.862	0.380	0.616	0.655	0.623	0.837
139-142	0.767	0.795	0.720	0.720	0.761	0.655
143-148	0.761	0.655	0.720	0.616	0.753	0.655
149	0.923					

The nearest neighbour matching method was used in the matching analysis. Matching process frequently reduces the control group subject that does not have a matching partner from the treatment group; therefore, some data are not used. The propensity score value will be used to match data from the treatment group (the group with a sputum conversion time ≤ 2 months) with data from the control group (the group with a sputum conversion time > 2 months). The matching analysis results of 149 DR-TB patients yielded only 20 patients who could be matched and included in the further analysis; patient data from the treatment and control groups were paired based on the closest propensity score value.

An evaluation of the matching process was then conducted by testing the covariates' balance after matching. This evaluation was used to check the balance of covariates on confounding variables between the affected group and the unaffected (control group). Covariate balance testing is divided into two stages: before and after matching. Table 5a demonstrates that after performing propensity score matching analysis with binary logistic regression, the variables DM status (X3), treatment regimen (X4), and treatment side effects (X6) are unbalanced. As a result, it may be stated that these three variables cannot be utilized to determine ATT results since they are unbalanced. Meanwhile, based on the same table, it is possible to conclude that the variables Age (X1) and Gender (X2) remain balanced after post-matching analysis.

Table 5a. Balance Testing Results

Variable	Balance	P-value
X_1	Before	0.67
	After	0.57
X_2	Before	0.01
	After	0.32
X_3	Before	0.48
	After	0.00
X_4	Before	0.63
	After	0.00
X_6	Before	0.00

	After	0.00

Table 5b. ATT Estimation Results and Standard Error

Variables	ATT	SE	p-value
X_1, X_2, X_3, X_4, X_6	0.738	0.093	0.000
X_1, X_2	0.682	0.091	0.000

The ATT value is estimated to determine how much influence the time of sputum conversion has on the final treatment outcome after the effect of other variables (covariates) that are out of balance has been reduced. The balance testing findings show that the variables Age (X1) and Gender (X2) are balanced variables, but the other variables are not. Hence it is necessary to re-conduct PSM with binary logistic regression by only including only the two balanced variables. It aims to see the smallest significance value for ATT estimation. The estimated value and standard error of ATT for each equation are shown in Table 5b.

Table 5b shows that each model provides different results, with the conclusion that duct conversion time (Z) has a significant effect on treatment results in drug-resistant TB patients after DM Status (X3), Treatment Regimen (X4), and Treatment side effects (X6) are excluded from the model. According to Table 5, the effect of ATT estimation results for sputum conversion time ≤ 2 months is 0.682, which means that the chance of drug-resistant TB patients with sputum conversion time ≤ 2 months receiving the favourable outcome is 68.2% higher than patients with sputum conversion time > 2 months.

Discussion

Rosenbaum and Rubin introduced the propensity score in 1983 as a method to control confounding factors in observational research. It is a statistical adjustment method for balancing or matching research subjects in order to reduce bias owing to non-randomized treatment. Bias due to non-randomization is reduced when the comparison between the control and treatment groups is performed at nearly the same or as close to the same ratio as possible. The Propensity Score method is the conditional probability of receiving a treatment based on pre-treatment characteristics.8–11

We also used a nonmatching method as the first approach on this study using the PLS-SEM to see whether there are differences in the results or not compare to the matching method approach that we did afterwards. SEM (Structural Equation Model) is a form of multivariate analysis in the field of statistical studies that can test a series of relationships that are typically difficult to measure simultaneously, combining factor analysis and regression analysis (correlation) to test the relationship between variables in a model, both between indicators and constructs and between constructs. Meanwhile, PLS (Partial Least Square) is an SEM structural equation model based on components or variants. PLS is an alternate approach that shifts from a covariance-based to a variant-based SEM approach. Partial least square is a multivariate statistical technique that can handle numerous response and explanatory variables at the same time. This analysis is a good alternative to multiple regression and principal component regression analysis methods because this method is more robust. Robust indicates that the model parameters do not change significantly when new samples are acquired from the total population.12

Based on the age range of patients in this research, it was discovered that the majority of patients were less than 45 years old, with the mean age of patients being 42.12, and the majority were male. This is in accordance with research conducted by Soeroto et al., Yihunie et al., and Prasetya et al., Putri et al., Assamie et al., Mulu et al., where each of these studies found that many patients with DR-TB were under the age of 45 years old and were male.13–17

The number of patients with DR-TB under the age of 45 who are male will almost surely raise the socioeconomic burden of a region/country with a large number of DR-TB patients because this age is still considered productive. In 2016, Van deh Hof S et al. examined the economic burden of three countries with a high number of DR-TB patients: Ethiopia, Indonesia, and Kazakhstan. The study discovered that the total cost of diagnosing and treating patients with DR-TB in Indonesia is approximately 2342 USD/patient (approximately IDR 35,293,940 at a dollar exchange rate of IDR 15070), which was estimated in 2016 to be 9.3-24.9 times the total monthly household income of patients with DR-TB. Importantly, the study reported that 38-92% of patients with DR-TB lost their income, and 26-76% lost their jobs as a result of the DR-TB. Of course, this adds to the economic burden of a country with a high number of DR-TB patients.18

In our study, we found that the average BMI in DR-TB patients in our study was 19.04, where 50.3% of the patients were in the underweight category. Although in our study, we did not find a significant relationship between BMI and the final results of treatment or sputum conversion time, in the study conducted by Putri et al., it was concluded that DR-TB patients with underweight BMI have a slower sputum conversion time risk.19 Apart from this, the poor nutritional status of most of the research subjects can pose a separate socio-economic burden because malnutrition is believed to be a comorbidity of many other diseases.

Many of our subjects' poor nutritional status may be due to treatment side effects experienced by patients with DR-TB; in our research, 47% of 149 patients suffered side effects, the majority of which (32.9%) were gastrointestinal disorders (nausea, vomiting, loss of appetite). It aligns with the findings of several other studies, as reported by Yang et al., Edriyenti et al., and Prasad et al. The side effects of OAT might range from moderate symptoms, such as ordinary nausea, to severe symptoms, such as severe nausea and vomiting. In addition to gastrointestinal symptoms, OAT side effects may appear in other organ systems, including hepatotoxicity, hematological disorders to psychiatric disorders. Therefore, there must be special attention in the future to pay attention to this and efforts to prevent the emergence of treatment side effects.6,20,21

Regarding sputum conversion time, we discovered that 67.7% of patients had a conversion time of less than or equal to 2 months, whereas the rest had a conversion time of more than two months or no conversion. The sputum conversion time of ≤ 2 months has long been used to predict treatment efficacy in DR-TB patients.22 Patients with a sputum conversion time of ≤ 2 months are thought to have a better chance of obtaining the desired treatment results, which is what we studied in our research and will discuss in the next section. Despite the relatively high frequency of sputum conversion time ≤ 2 months in our study (67.7%), the number of patients who had a successful treatment outcome in our study was only 54.4%, which is lower than the WHO target of 85%. It could be because treatment outcome is not only influenced by sputum conversion time but also by other factors. We also discovered an essential finding regarding sputum conversion time, with roughly 28.2% of patients not converting at all. According to our investigation, this could be due to the high Loss to Follow-Up rate and death, totaling 36.9% (i.e., 18.8% loss to follow-up and 18.1% died).

In our study, PLS-SEM was used as the first approach prior to the matching process because we wanted to find out what factors affected both the final treatment outcome as well as treatment side effects and sputum conversion time due to the fact that the PLS-SEM approach can be used to predict a relationship between variables even when the structural model utilized for describing that relationship is complex and contains a number of constructs, as shown in Figure 2.

In our study, we noted that LTR was the most common regimen and that the mean patient age was 42.12 years. The LTR regimen itself, from several study reports, is associated with a greater number of side effects and loss to follow-up rate, whilst aged is known to be associated with a decreased immune system and high loss to follow-up.23,24 It will certainly affect patient adherence to treatment, as Gebreweld et al. reported, which may lead to a decrease in the expected treatment outcome.25

In their study, Torres et al. concluded that factors influencing the outcome of DR-TB treatment included age, gender, history of alcoholism, smoking history, HIV co-infection, and sputum conversion time of more than two months. In contrast, Panford et al. reported that factors influencing the outcome of DR-TB patients included gender, age, education level, baseline BMI status, and previous history of TB. Slightly different but similar results were found

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by Soeroto et al., where in their study of patients with LTR, it was found that the factors affecting the final treatment results were age, gender, BMI, previous history of Tb, and sputum conversion time.15,26-28 Although the results of these three studies are not totally comparable (due to the different subjects and epidemiology), we may see parallels in the variables that determine the final results, especially age and sputum conversion time.

Calculation of the ATT score for sputum conversion time ≤ 2 months in DR-TB patients at RSSA is 0.682, meaning that DR-TB patients with sputum conversion time ≤ 2 months have a 68.2% greater chance of achieving a Favorable Outcome compared to those who have sputum conversion time > 2 months. This finding is quite interesting because we found that age and sputum conversion time were also significantly related to influencing the final results of DR-TB treatment in other studies.26, 28 And sputum conversion time ≤ 2 months has long been used as a cutoff point to determine prognosis and DR-TB treatment duration.7,22,29

Based on our review, no study has attempted to calculate the ATT value of sputum conversion time in the subjects studied. Hence, we are interested in attempting to analyze the calculation of ATT calculation of sputum conversion time to assess how much it is likely to affect the final treatment outcome, with the cutoff point being ≤ 2 months, as in previous literature. And we discovered that a conversion time of ≤ 2 months was related to a higher likelihood of treatment success. Patients with a sputum conversion time of ≤ 2 months had a 68.2% higher chance of treatment success.

Our findings are also in line with findings from other studies such as that conducted by LV et al., where they found that the sensitivity and specificity of sputum culture conversion time ≤ 2 months to determine the prognosis of patients with DR-TB were 67.6% (95% CI: 50.2-82.0) and 76.4% (95% CI: 63.0-86.8).30 The study conducted by Kubartova et al. also found that sputum conversion time ≤ 2 months can be a reliable marker used in assessing the prognosis of patients with DR-TB.7 We hope this study will provide more information on the role of sputum conversion time in determining DR-TB prognosis.

Limitation

Basically, our research is a non-experimental study, so even though efforts have been made to reduce bias by matching the subjects using the PSM approach, the potential for bias still exists and is difficult to eliminate. The process of matching subjects using the matching method with the PSM approach as seen in our study will greatly reduce the subjects that can be processed for further analysis (in our study out of 149 subjects only 20 could be matched), so that in the future if the matching method is to be used like this, we recommend using a larger sample so that the results can better describe the actual situation. The difficulty is in studies that use secondary data like our study, even though the sampling technique uses the all population sampling technique, due to the limited population, the samples obtained are also limited.

Conclusion

According to analysis utilizing the PLS-SEM approach, age, DM status, sputum conversion time, and treatment side effects all significantly influenced treatment results. However, the results of subsequent data analysis using the PSM approach and the Matching method show that age and Sputum Conversion Time are the methods that have an essential effect on the final results of DR-TB treatment in RSSA. Treatment side effects and DM status, meanwhile, showed no discernible effect.

The result of the calculation of the ATT value of Sputum Conversion Time on the final results of DR-TB treatment (with a cutoff point ≤ 2 months as in the existing literature) is 0.682, meaning that DR-TB patients with a sputum conversion time ≤ 2 months have a 68.2% greater chance of achieving a Favorable Outcome than those with a sputum conversion time > 2 months. Sputum conversion time was selected as the main confounding factor because it had the smallest p-value (0.000).

Reference

1. Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P, et al. Global Tuberculosis Report 2020 – Reflections on the Global TB burden, treatment and prevention efforts. International Journal of Infectious Diseases. 2021 Dec 1;113:S7–12.
2. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit Kementerian Kesehatan Republik Indonesia D. PENATALAKSANAAN

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TUBERKULOSIS RESISTAN OBAT DI INDONESIA. 2020.
3. Ahmad N, Javaid A, Basit A, Afridi AK, Khan MA, Ahmad I, et al. Management and treatment outcomes of MDR-TB: Results froma setting with high rates of drug resistance. International Journal of Tuberculosis and Lung Disease. 2015 Sep 1;19(9):1109–14.
4. Girum T. Survival Status and Treatment Outcome of Multidrug Resistant Tuberculosis (MDR-TB) among Patients Treated in Treatment Initiation Centers (TIC) in South Ethiopia: A Retrospective Cohort Study. 2017.
5. Lan Z, Ahmad N, Baghaei P, Barkane L, Benedetti A, Brode SK, et al. Drug-associated adverse events in the treatment of multidrug-resistant tuberculosis: an individual patient data meta-analysis. Lancet Respir Med. 2020 Apr 1;8(4):383–94.
6. Prasad R, Singh A, Gupta N. Adverse drug reactions in tuberculosis and management. Vol. 66, Indian Journal of Tuberculosis. Tuberculosis Association of India; 2019. p. 520–32.
7. Kurbatova E V., Cegielski JP, Lienhardt C, Akksilp R, Bayona J, Becerra MC, et al. Sputum culture conversion as a prognostic marker for end-of-treatment outcome in patients with multidrug-resistant tuberculosis: A secondary analysis of data from two observational cohort studies. Lancet Respir Med. 2015 Mar 1;3(3):201–9.
8. Austin PC, Fine JP. Propensity-score matching with competing risks in survival analysis. Stat Med. 2019 Feb 28;38(5):751–77.
9. Widjanarko B, Purhadi O, Mahdalena. PROPENSITY SCORE UNTUK DATA KESEHATAN. Mojokerto; 2019 Nov.
10. Kane LT, Fang T, Galetta MS, Goyal DKC, Nicholson KJ, Kepler CK, et al. Propensity Score Matching A Statistical Method [Internet]. 2020. Available from: www.clinicalspinesurgery.com
11. Fu EL, Groenwold RHH, Zoccali C, Jager KJ, Van Diepen M, Dekker FW. Merits and caveats of propensity scores to adjust for confounding. Nephrology Dialysis Transplantation. 2019 Oct 1;34(10):1629–35.
12. Hair Jr JF, Hult GTM, Ringle CM, Sarstedt M, Danks NP, Ray S. Classroom Companion: Business Partial Least Squares Structural Equation Modeling (PLS-SEM) Using R [Internet]. 2021. Available from: http://www.
13. Assemie MA, Alene M, Petrucka P, Leshargie CT, Ketema DB. Time to sputum culture conversion and its associated factors among multidrug-resistant tuberculosis patients in Eastern Africa: A systematic review and meta-analysis. International Journal of Infectious Diseases. 2020 Sep 1;98:230–6.
14. Mulu W, Mekonnen D, Yimer M, Admassu A, Abera B. Risk factors for multidrug resistant tuberculosis patients in amhara national regional state. Afr Health Sci. 2015;15(2):368–77.
15. Soeroto AY, Nurhayati RD, Purwiga A, Lestari BW, Pratiwi C, Santoso P, et al. Factors associated with treatment outcome of MDR/RR-TB patients treated with shorter injectable based regimen in West Java Indonesia. PLoS One. 2022 Jan 1;17(1 January).
16. Prasetya FA, Sugiri YJ, Sartono TR, Al Rasyid H. Factors Affecting the Treatment Success of Short-Term Regimen for Drug Resistant Tuberculosis (DR TB) Patients at Dr. Saiful Anwar General Hospital Malang. Jurnal Respirologi Indonesia. 2022 Jul 11;42(3):192–200.
17. Yihunie Akalu T, Fentahun Muchie K, Alemu Gelaye K. Time to sputum culture conversion and its determinants among Multi-drug resistant Tuberculosis patients at public hospitals of the Amhara Regional State: A multicenter retrospective follow up study. PLoS One. 2018 Jun 1;13(6).
18. van den Hof S, Collins D, Hafidz F, Beyene D, Tursynbayeva A, Tiemersma E. The socioeconomic impact of multidrug resistant tuberculosis on patients: Results from Ethiopia, Indonesia and Kazakhstan. BMC Infect Dis. 2016 Sep 5;16(1).
19. Putri FA, Burhan E, Nawas A, Soepandi PZ, Sutoyo DK, Agustin H, et al. Body mass index predictive of sputum culture conversion among MDR-TB patients in Indonesia. International Journal of Tuberculosis and Lung Disease. 2014 May 1;18(5).
20. Yang TW, Park HO, Jang HN, Yang JH, Kim SH, Moon SH, et al. Side effects associated with the treatment of multidrug-resistant

tuberculosis at a tuberculosis referral hospital in South Korea. Medicine (United States). 2017 Jul 1;96(28).

21. Edriyenti EM, Medison I, Ermayanti S, Fitrina DW. FAKTOR RISIKO KEJADIAN EFEK SAMPING OBAT PADA PASIEN TB MDR DI SUMATERA BARAT TESIS. Padang; 2020.
22. Wallis RS, Doherty TM, Onyebujoh P, Vahedi M, Laang H, Olesen O, et al. Biomarkers for tuberculosis disease activity, cure, and relapse. Vol. 9, The Lancet Infectious Diseases. 2009. p. 162–72.
23. Abidi S, Achar J, Assao Neino MM, Bang D, Benedetti A, Brode S, et al. Standardised shorter regimens versus individualised longer regimens for rifampin- or multidrug-resistant tuberculosis. European Respiratory Journal. 2020 Mar 1;55(3).
24. Tack I, Dumicho A, Ohler L, Shigayeva A, Bulti AB, White K, et al. Safety and Effectiveness of an All-Oral, Bedaquiline-Based, Shorter Treatment Regimen for Rifampicin-Resistant Tuberculosis in High Human Immunodeficiency Virus (HIV) Burden Rural South Africa: A Retrospective Cohort Analysis. Clinical Infectious Diseases. 2021 Nov 1;73(9):E3563–71.
25. Gebreweld FH, Kifle MM, Gebremicheal FE, Simel LL, Gezae MM, Ghebreyesus SS, et al. Factors influencing adherence to tuberculosis treatment in Asmara, Eritrea: A qualitative study. J Health Popul Nutr. 2018 Jan 5;37(1).
26. Torres NMC, Rodríguez JJQ, Andrade PSP, Arriaga MB, Netto EM. Factors predictive of the success of tuberculosis treatment: A systematic review with meta-analysis. PLoS One. 2019 Dec 1;14(12).
27. Panford V, Kumah E, Kokuro C, Adoma PO, Baidoo MA, Fusheini A, et al. Treatment outcomes and associated factors among patients with multidrug-resistant tuberculosis in Ashanti Region, Ghana: a retrospective, cross-sectional study. BMJ Open. 2022 Jul 1;12(7).
28. Soeroto AY, Pratiwi C, Santoso P, Lestari BW. Factors affecting outcome of longer regimen multidrug-resistant tuberculosis treatment in West Java Indonesia: A retrospective cohort study. PLoS One. 2021 Feb 1;16(2 February).
29. D. A. Mitchison. Correspondence ASSESSMENT OF NEW STERILIZING DRUGS FOR TREATING PULMONARY TUBERCULOSIS BY CULTURE AT 2 MONTHS.
30. Lv L, Li T, Xu K, Shi P, He B, Kong W, et al. Sputum bacteriology conversion and treatment outcome of patients with multidrug-resistant tuberculosis. Infect Drug Resist. 2018;11:147–54.

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