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FACTORS INFLUENCING TREATMENT OUTCOMES OF DRUG-SENSITIVE TUBERCULOSIS PATIENTS: STUDY IN R.A. KARTINI HOSPITAL, JEPARA, INDONESIA

Bambang Hariyana[1,2]*, Soeharyo Hadisaputro[3], Amin Husni[4], Winarto Winarto[5], Endang Mahati[6], Ari Budi Himawan[2]

[1]Doctoral Study Program in Medical & Health Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[2]Department of Public Health Science - Preventive Medicine, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[3]Department of Internal Medicine, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[4]Department of Neurology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[5]Department of Microbiology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
[6]Department of Pharmacology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

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Corresponding Author:
E-mail: hariyana671@gmail.com

ABSTRACT

Background: Tuberculosis (TB) is an infectious and chronic disease, has become the second-ranked worldwide for the highest estimated new TB cases in Indonesia. The TB treatment success rate (TSR) in Central Java Province stands at 87% (below the target of 90%). **Objective:** To provide the factors that influence the results of pulmonary TB therapy at R.A. Kartini Hospital. **Methods:** This study was descriptive-analytical with a cross-sectional approach, using secondary data from R.A. Kartini Hospital along one year in 2023. Data were processed and analyzed using SPSS. **Results:** The average age of subjects was 39.26 ± 19.36, of which the majority were male (58.5%). Data showed that 58.1% of subjects had jobs, and the majority of subjects had no history of diabetes mellitus (DM) or human immunodeficiency virus (HIV) (86.6% and 96.7%, respectively). All subjects received TB treatment; most recovered (76.4%). Based on body mass index (BMI), 50.8% had a normal nutritional status. Chi-square test analysis showed a significant relationship between age and employment status with the success rate of TB treatment. However, age was significantly related to TB treatment outcomes with an odds ratio (OR) of 1.033 (p = 0.000). Employment status revealed significant results; working subjects were 2.261 times more likely to experience suboptimal treatment outcomes (p = 0.013). Moreover, HIV history showed a significant relationship with TB treatment outcomes after adjusting for age. **Conclusion:** Several factors were related to TB treatment outcomes, such as age, employment status, and TB-HIV co-infection.

INTRODUCTION

Tuberculosis (TB) is one of the infectious and chronic diseases with the third highest mortality rate. Although TB can be cured with proper treatment, this disease remains a significant public health problem, with a high number of cases and extensive socio-economic impacts.[1,2] Moreover, tuberculosis becomes the leading cause of death after ischemic heart disease and cerebrovascular disease. Data showed that the death rate from tuberculosis was 40/100,000 population (without TB-HIV co-infection) and 3.6 per 100,000 population (including TB-HIV co-infection) in 2017.[3]

Based on the Global TB Report (2023), Indonesia is the second-ranked in the world with the highest estimated new TB cases after India (reported 1,060,000 cases, or 385 per 100,000 population), with a death rate reaching 134,000 per year. This condition is higher compared to previous years. More than 724,309 new TB cases were found in 2022, which increased to 792,404 cases in 2023. Interestingly, this number is higher than cases before the pandemic,

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averaging less than 600,000 per year. Therefore, it is a new challenge for Indonesia, which is targeting to eliminate TB by 2030.[4] The World Health Organization (WHO) has launched the 'End Tuberculosis' strategy, which is part of the Sustainable Development Goals, to end the tuberculosis epidemic worldwide. The vision of the end TB strategy is a "TB-free world," namely, zero deaths, disease, and suffering due to TB, to end the TB epidemic in the world.[2]

TB patients' treatment success rate (TSR) is the number of all TB cases that are cured and complete treatment among all TB cases treated and reported. However, the TSR in the Central Java Province is 87 percent, below the target of 90 percent (62,513 cases found in 2022: around 17,695 cases cured and 44,818 cases completed treatment).[3] Various studies showed that many factors influence the success rate of TB treatment, such as age, gender, medication adherence, comorbidities, and others.[6]

R.A. Kartini Hospital, as one of the Regional Technical Implementation Units of the Jepara Regency Health Service, has provided services to tuberculosis patients through a lung clinic and documented them in the TB information system. This study aims to provide an overview of the characteristics of TB patients at R.A. Kartini Hospital based on TB information system data and analyze several factors that influence the results of TB treatment, especially pulmonary TB.

METHODS

This study employed a descriptive-analytical approach with a cross-sectional design, utilizing the Tuberculosis Information System at R.A. Kartini Hospital from January 2023 to December 2023. We included adult patients aged 18 years and older who were diagnosed with drug-sensitive pulmonary TB through a molecular rapid test. Data collected included demographic information (age, gender, occupation), body weight (BW), and body mass index (BMI) before treatment, treatment status (according to the standard or not), as well as a history of comorbidities (human immunodeficiency virus [HIV] and diabetes mellitus [DM]). According to the National Guidelines for Tuberculosis Management Medical Services, treatment outcome criteria were classified as cured, completed treatment, died, discontinued, or not evaluated. In this study, cured and completed treatment criteria were considered optimal outcomes, while the others were classified as suboptimal. Data were processed and analyzed using SPSS software. We presented the characteristics of respondents in the form of frequency distributions and percentages. The bivariate test was employed to analyze the effect of independent variables on dependent variables (TB therapy results) categorized using Chi-square and Fisher's exact test, as well as Mann-Whitney test just for age analysis. In contrast, logistic regression was used to identify which variable most influenced TB treatment outcomes.

RESULTS

A total of 246 subjects met the inclusion criteria, with the characteristics described in Table 1. The average age of the subjects is 39.26 ± 19.36, with the majority being male (58.5%); 58.1% of the subjects are employed, while the others are unemployed. Most subjects did not have a history of DM or HIV, or their history was unknown, at 86.6% and 96.7%, respectively. All subjects received TB treatment without any loss to follow-up. Most subjects (76.4%) completed treatment with cured results, while 23.6% experienced drug withdrawal, death, or treatment failure. Our results indicate that 90.7% underwent standard therapy, and 78.9% had a drug supervisor (PMO). The use of drug forms was dominated by fixed-dose combinations (FDCs) at 84.6%. Based on BMI results, 50.8% of subjects are normal, while the rest experience malnutrition (underweight, overweight, or obese).

Table 1. Characteristics of Subjects

Characteristics	N (%) (n = 246)
Age	39.26 ± 19.36
Gender	
Male	144 (58.5%)
Female	102 (41.5%)
Employment Status	
Not working	103 (41.9)
Working	143 (58.1)
History of DM	
No or not known	213 (86.6)
Yes	33 (13.4%)
History of HIV	
No or not known	238 (96.7%)
Yes	8 (3.3%)

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Follow-up of treatment	
Treated	246 (100%)
Lost to follow up	0 (0%)
Treatment outcomes	
Cured and completed treatment	188 (76.4%)
Died, discontinued, or not evaluated	58 (23.6%)
Treatment status	
According to the standard	233 (90.7%)
Not	23 (9.3%)
Presence of a medication supervisor	
Yes	194 (78.9%)
No	52 (21.1%)
Type of drugs	
Fixed drug combinations (FDCs)	208 (84.6%)
Separate medicine	38 (15.4%)
BMI criteria	
Normal	125 (50.8%)
Malnutrition (Underweight, overweight, and obesity)	121 (49.2%)

Chi-square test analysis revealed a significant relationship between age and employment status concerning the success of TB treatment.

Table 2 shows that there was a significant relationship between age and the success of TB treatment, where the age in the group with suboptimal results was significantly higher (47.41 ± 14.95 years) than the optimal group (36.74 ± 19.9) with $p < 0.001$. Employment status also showed a significant relationship, where subjects who worked had a higher proportion in the suboptimal group ($p = 0.012$). Meanwhile, other variables such as gender, history of DM, history of HIV, treatment status, presence of drug supervisors, type of drugs, and BMI criteria did not show a significant relationship ($p>0.05$) with TB treatment outcomes.

Table 2. Relationship between subject characteristics (risk factors) and success of TB treatment

Variables	TB therapy results		*p*
	Optimal n = 188 (76.4%)	Suboptimal n = 58 (23.6%)	
Age	36.74 ± 19.9	47.41 ± 14.95	0.000*,a
Gender			
Male	105 (55.9%)	39 (67.2%)	0.124 b
Female	83 (44.1%)	19 (32.8%)	
Employment Status			
Not working	87 (46.3%)	16 (27.6%)	0.012*,b
Working	101 (53.7%)	42 (72.4%)	
History of DM			
No	162 (86.2%)	51 (87.9%)	0.731 b
Yes	26 (13.8%)	7 (12.1%)	
History of HIV			
No	184 (97.9%)	54 (93.1%)	0.073 b
Yes	4 (2.1%)	4 (6.9%)	
Treatment outcomes			
Cured and completed treatment	188 (100%)	0 (0%)	0.000*,c
Died, discontinued, or not evaluated	0 (0%)	58 (100%)	
Treatment Status			
According to the standard	173 (92%)	50 (86.2)	0.184 b
Not	15 (8%)	8 (13.8%)	
Presence of a medication supervisor			
Yes	145 (77.1%)	49 (84.5%)	0.230 b
No	43 (22.9%)	9 (15.5%)	
Type of drugs			
Fixed drug combinations (FDCs)	161 (85.6%)	47 (81.0%)	0.396 b
Separate medicine	27 (14.4%)	11 (19.0%)	

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BMI criteria			
Normal	91 (48.4%)	34 (58.6%)	0.174 [b]
Malnutrition (Underweight, overweight, and obesity)	97 (51.6%)	24 (41.4%)	

∗significant, p < 0.05 using [a] Mann-Whitney test; [b] Chi-square test; and [c]Fischer's exact test

Bivariate logistic regression analysis showed a significant relationship between age and employment status with the success of TB treatment.

Table 3 shows the results of the bivariate logistic regression analysis, indicating that age was significantly associated with TB treatment outcomes, yielding an odds ratio (OR) of 1.033 (p = 0.000). Additionally, employment status was also statistically significant, as working individuals are 2.261 times more likely to experience suboptimal treatment outcomes than those who did not work (p = 0.013). Other variables, including gender, history of DM, history of HIV, treatment status, presence of a medication supervisor, type of drugs, and BMI criteria, did not show a statistically significant relationship in the bivariate model.

Table 3. Relationship between risk factors and TB category outcomes

Variable	OR	95% CI	*p*
Age	1.033	-	0.000*,[a]
Gender			
Female	Ref		
Male	1.623	0.873-3.014	0.126
Employment Status			
Not working	Ref		
Working	2.261	1.188-4.302	0.013*,[b]
History of DM			
No or not known	Ref		
Yes	0.855	0.351-2.087	0.731
History of HIV			
No or not known	Ref		
Yes	3.407	0.825-14.079	0.090
Treatment Status			
According to the standard	Ref		
Not	1.845	0.740-4.603	0.189
Presence of a medication supervisor			
Yes	Ref		
No	0.619	0.282-1.362	0.233
Type of drugs			
Fixed drug combinations (FDCs)	Ref		
Separate medicine	1.396	0.644-3.022	0.398
BMI criteria			
Normal	Ref		
Malnutrition (Underweight, overweight, and obesity)	0.662	0.365-1.201	0.175

∗significant, p < 0.05 using [a] Mann-Whitney test and [b] Chi-square test

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Table 4 shows that only HIV history showed a significant relationship to TB treatment outcomes after adjusting for age (Model 2: OR = 5.316; 95% CI: 1.091–24.172; p = 0.038). The employment variable approached significance in both models but did not reach a *p-value* < 0.05 (Model 1: p = 0.058; Model 2: p = 0.073). Other variables such as gender, history of DM, treatment status, presence of a medication supervisor, type of drugs, and BMI criteria did not show a significant relationship in both multivariate logistic regression models.

Table 4. Multivariate logistic regression analysis (Model 1 and Model 2)

Variable	Model 1			Model 2		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Gender						
Female	Ref			Ref		
Male	1.283	0.605-2.721	0.516	1.018	0.454-2.283	0.966
Employment Status						
Not working	Ref			Ref		
Working	2.097	0.975-4.513	0.058	2.121	0.933-4.821	0.073
History of DM						
No or not known	Ref			Ref		
Yes	0.915	0.357-2.345	0.854	0.690	0.266-1.790	0.445
History of HIV						
No or not known	Ref			Ref		
Yes	4.196	0.945-18.643	0.059	5.316	1.091-24.172	0.038*
Treatment Status						
According to the standard	Ref			Ref		
Not	2.205	0.569-8.542	0.252	1.870	0.475-7.345	0.370
Presence of a medication supervisor						
Yes	Ref			Ref		
No	0.601	0.262-1.378	0.229	0.678	0.289-1.588	0.371
Type of drugs						
Fixed drug combinations (FDCs)	Ref			Ref		
Separate medicine	0.910	0.290-2.860	0.872	0.806	0.253-2.569	0.716
BMI criteria						
Normal	Ref			Ref		
Malnutrition (Underweight, overweight, and obesity)	0.660	0.349-1.248	0.201	0.820	0.426-1.578	0.552

Model: 1 (Unadjusted) and 2 (adjusted for age); ∗significant, p < 0.05 using Chi-square test

DISCUSSION

The characteristics of this study followed previous results of six articles from different countries, which proved that most subjects were male. In the productive age range, male patients had a higher risk of experiencing TB treatment failure than female patients.[4] In contrast to the results obtained in this study, gender was not significantly related to treatment outcomes. The high possibility of TB treatment failure in male patients is due to higher activity levels not accompanied by sufficient rest and high rates of smoking, as well as being associated with lower compliance than women.[7,8] These findings supported gender-specific TB education and messaging.

Moreover, one factor that can affect the completion of TB treatment is age. A review analysis of six articles found that older age was a risk factor for TB treatment failure.[6,8,9] Research in Bekasi found an OR value of 3.81, which means that new cases of pulmonary tuberculosis patients of productive age have a 3.81-fold greater chance of successful

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treatment than patients of non-productive age.[10] Research conducted by Pauline et al. stated that age factors affect the success rate of TB treatment, especially in the elderly, who have a lower rate. Many physiological changes are associated with aging, such as decreased lung elasticity and decreased strength of the respiratory muscles. Malnutrition, which is also common in the elderly, can cause sarcopenia and affect the effectiveness of the therapy. The immunosenescence will increase oxidative stress, decrease the phagocytic capacity of neutrophils and macrophages, and play an essential role in M. tuberculosis surviving in cells.[11]

Sociological changes make the elderly less autonomous and more dependent on their surroundings. Another reason that can affect the success of treatment in the elderly is long-term TB treatment, which can be an extra obstacle to treatment compliance.[11] Compliance with TB treatment is a fundamental problem related to treatment outcomes. Lack of strict compliance with treatment, however, will increase the risk of therapy failure and the emergence of resistance to anti-tuberculosis drugs.[9]

Besides that, another factor that influences the success of SO TB treatment at R.A. Kartini Hospital is the employment status of TB patients. The odds ratio value of the employment status variable in this study was 2.261, which means that unemployed respondents tended to be 2.261 times more successful in TB treatment compared to active employment status. The results of this study differ from the study by Rizky et al., which stated that employment status was not related to the success rate of TB treatment at the Tapos Health Center.[12]

Employment status affects behaviour or compliance with taking medication. People who are overworking will make it difficult for TB patients to undergo regular treatment therapy; in other words, the level of compliance will be low. This is in accordance with Sherly's research, which stated that someone actively working tends to have lower compliance due to less time to think about their health. Someone with unemployed status generally has more free time or more time at home, so they have the opportunity to arrange the time to take medication.[13]

The multivariate logistic regression analysis in Table 4 showed that only HIV history had a significant relationship to TB treatment outcomes after adjusting for age. TB-HIV co-infection increased the risk of TB treatment failure by 5.3 times. A study in Colombia found that TB treatment failure was 1.69 times more likely.[14] This is supported by Keng Tok's study, which stated that patients with positive HIV infection had a four times higher risk of experiencing TB treatment failure than patients without HIV. In addition, another study in Nigeria also found the same pattern, where the HIV prevalence rate was 28.7% (from 268 TB cases). More than two-thirds (78.4%) of HIV-negative patients were successfully treated compared to 68.9% of HIV-positive patients who were successfully treated. Seventy-seven patients with HIV co-infection revealed 10.4% failed, 14.2% died, and 6.5% failed treatment, while HIV-negative patients showed 15.2% failed, 4.8% died, and 1.6% failed treatment. TB/HIV co-infection is significantly associated with poor treatment outcomes[15] because there is a disruption of the local immune response, which will reduce the ability of the granuloma to withstand the multiplication and spread of the tubercle bacillus.[16]

WHO has advocated and emphasized providing integrated TB and HIV services, as well as providing guidelines for TB-HIV activities with collaboration between national programs and stakeholders. One strategy that can be used to improve the success of treatment is to receive voluntary HIV counseling. Education by health workers to patients during counseling and HIV testing will provide better information to patients so that they can increase their interest in undergoing treatment. Therefore, it is important to provide clear and easy-to-understand information regarding the reasons and goals of treatment and well-coordinated management between TB and HIV to ensure optimal treatment outcomes in overcoming cases of co-infection. In addition, prevention of TB-HIV co-infection needs to be improved, such as conducting routine screening of vulnerable groups.[4]

However, the limitation of this study is the non-availability of several variables, such as socio-economic factors, including weight gain, type of work, and income, because we conducted it retrospectively using secondary data.

CONCLUSION

In conclusion, we found factors related to the success of TB treatment, such as age, employment status, and TB-HIV. We suggest that efforts are needed to address risk factors for reducing TB

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treatment failure, such as treatment assistance, especially for elderly patients; collaboration of smoking cessation services in standard TB case management practices; and prevention of TB-HIV co-infection by screening vulnerable groups.

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ETHICAL APPROVAL

Ethical approval was obtained with a research permit from the Ethics Review Board of the Faculty of Medicine, Diponegoro University, with the number 406/EC/KEPK/FK-UNDIP/VIII/2024.

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AUTHOR CONTRIBUTION

BH conceptualized the study, collected the data, and validated the data. WI, EM, and ABH analyzed and interpreted the data. BH wrote the original draft manuscript. SH, AH, WI, EM, and ABH reviewed and revised the manuscript. SH, EM and AH were supervisors. All authors have read and approved the final version of the manuscript.

CONFLICT OF INTEREST

We declare no conflict of interests in this study.

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