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Factors Associated with Successful Drug Susceptible Tuberculosis Treatment among Tuberculosis – Human Immunodeficiency Virus Patients in DKI Jakarta Province 2020 – 2022

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ABSTRACT
Tuberculosis and HIV are serious health issues that can significantly impact an individual's immune system by evading immune monitoring functions. Research on TB-HIV treatment success, especially in DKI Jakarta province, is still limited. This study aims to assess the treatment success of tuberculosis patients who also have HIV co-infection through an analysis of the patient's sociodemographic and clinical characteristics. This cross-sectional study used secondary data from the Tuberculosis Information System (SITB) of the DKI Jakarta Provincial Health Office from 2020 to 2022. We conducted a chi-square bivariate test, and for multivariate analysis, we used the Cox Regression with constant time at risk to provide Prevalence Rasio (PR). Out of 1902 patients with TB-HIV, the TB treatment outcome was successful in 73.29% (cured and completed treatment) and unsuccessful in 26.71% (failed, died, or lost to follow-up). There was a higher chance that TB treatment would work for people who got it in primary care (aPR: 1.16; 95% CI: 1.04–1.29) and those who got ART (aPR: 3.72; 95% CI: 1.20–11.55). Most patients had a successful treatment outcome, although it was below the target of 90%. Therefore, ensuring that such patients get monitoring in their treatment, especially in hospitals, and also get ART is important. It is crucial to strengthen and provide holistic support to ensure compliance and the success of TB and HIV treatment.
Keywords: **TB-HIV, Treatment Success, Drug Susceptible.**

INTRODUCTION

Mycobacterium tuberculosis causes tuberculosis (TB), a direct infectious disease that remains a priority issue in the world as well as in Indonesia to control and combat (Burusie et al., 2024; Kumari et al., 2024; Li et al., 2022; Pradipta et al., 2024). The World Health Organization (WHO) has stated that TB will be the world's second-leading infectious disease cause of death,

after COVID-19. Tuberculosis is also the leading cause of mortality for people with the Human Immunodeficiency Virus (HIV) and is associated with antimicrobial resistance (Organization, 2023).

HIV is a retrovirus that spreads through body fluids and attacks the immune system. These viruses can weaken immunity and increase the individual's susceptibility to opportunistic infection (IO) (Oladimeji et al., 2011). TB is one of the IOs that can occur in HIV patients. The risk of developing active TB in people with HIV (ODHIV) is 20–37 times higher than in people without HIV (Romaino et al., 2022). Tuberculosis and HIV can significantly impact an individual's immune systems by evading immune monitoring functions; however, the exact mechanisms are not completely understood. Mycobacterium tuberculosis and HIV can accelerate immunological impairment and lead to premature death if not treated (Umayorubhagom & Baliga, 2023; Yang et al., 2022).

In its report entitled "WHO Global Tuberculosis Report 2023," an estimated 10.6 million cases of TB worldwide by 2022 and 7.5 million cases (60.3%) have been diagnosed and treated. The total number of cases of tuberculosis discovered in Indonesia was 724,309 cases, with an estimated 335,691 cases of unrecovered tuberculosis. This is what puts Indonesia at the moment in second place as the country with the most TB burden after India. The incidence of HIV tuberculosis globally was 671,000, with an estimated death rate of 167,000 cases. The prevalence of HIV among TB patients in Indonesia is around 2.4% (Ayuningtyas et al., 2022), with the proportion of HIV TB among TB cases in Jakarta DKI being 5% by 2022 (Kemenkes, 2023).

The treatment success rate of TB-HIV patients in Indonesia was 68%, compared to the overall treatment success rate of TB, which was 86%. Despite the availability of treatment for both infections, 6,500 people who suffered from TB and HIV died in Indonesia in 2021 (Organization, 2022a). In 2011–2013, the average success rate for TB-HIV patients in Adam Malik North Sumatra RSUP in 2011–2013 was 68.56% (Yusria et al., 2017), while the success of treatment for TB-HIV patients in Sulianti Saroso RSUP DKI Jakarta was 70% (Andayani et al., 2023).

Treatment of TB in HIV patients is the same as for HIV-negative TB patients for at least six months with a 2HRZE/4HR (category 1 regimen), but some cases take longer, about eight to twelve months (Cox et al., 2021; Jeong et al., 2022; Kumari et al., 2024). Patients with TB and HIV have a higher risk of death, treatment failure, and relapse (Bargaje et al., 2022; Fetensa et al., 2024). ART significantly improves the response to TB treatment and outcomes in individuals with HIV co-infection, highlighting its crucial role (Organization, 2022b).

Research on TB-HIV treatment success, especially in DKI Jakarta province, is still limited. This study needs to be carried out because Jakarta is a densely populated city with a high mobility rate and therefore has a wider potential for disease transmission. Socio-demographic factors, as well as the accessibility of health services can influence the spread and control of TB-HIV in DKI Jakarta.

The aim of this study is to assess the treatment success of tuberculosis patients who also have HIV co-infection through an analysis of the patient's sociodemographic and clinical characteristics. The findings of this study may also be utilized as an overview for developing more focused interventions, such as community-level educational and preventative initiatives. Consequently, this study possesses the capacity to enhance the efficacy of public health initiatives aimed at addressing tuberculosis and HIV.

RESEARCH METHODS

We conducted a cross-sectional study and utilized secondary data from the Tuberculosis Information System (SITB) of the DKI Jakarta Provincial Health Office. This information system is an individual-based and real-time reporting system used by all health care facilities, like puskesmas, clinics, and hospitals to report cases of tuberculosis found (Deviernur & Adnan, 2023).

The participants in this study were all TB patients who underwent treatment in 2020–2022, registered in the SITB, and met the inclusion criteria. The inclusion criteria for this study were TB-HIV patients aged 15 years or older who remained immobile during treatment and possessed the final outcome of TB treatment. The inability to meet these criteria was referred to as the exclusion criteria. Eligible samples that did not have a complete variable were also excluded from the study.

The minimum number of samples required for this study was estimated to be 1864 cases from previous studies (Oladimeji et al., 2013), related to the variable type of anti-tuberculosis drug (OAT). However, we utilised the entire dataset of 1.902 cases that satisfy the criteria of this study. Eligible samples that did not have a complete variable were also excluded from the study.

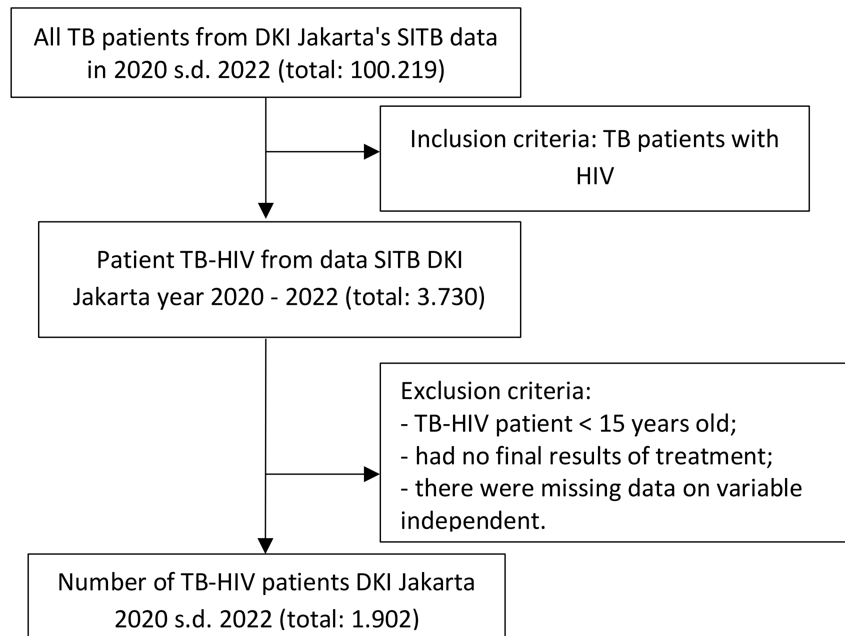

Figure 1.

The dependent variable or outcome of this study is the success of treatment for TB - HIV patients. The definition of treatment results in this study refers to module 4 (four) TB treatment by WHO, 2022. Successful tuberculosis treatment is achieved when the patient "has completed the treatment" and is "entirely cured," while unsuccessful treatment occurs if the patient fails to respond, dies, or lost to follow-up. Patients are considered recovered when they finish treatment following national policy guidelines and show no signs of treatment failure. Treatment is considered complete when patients finish treatment as advised by national policy, even if the outcome does not meet the criteria for healing or treatment failure.

In this study, the independent variables consist of clinical and sociodemographic characteristics. Sociodemographic factors include health facility types, age, gender, and employment status. Clinical characteristics include the type of diagnosis, anatomical site, treatment history, antituberculosis drug (OAT) combination, and use of antiretroviral therapy (ART).

The age variable is categorised as 15–44 years and 45 years and older (≥ 45); gender is separated into "male" and "female." Patients who are employed, including private entrepreneurs, are categorized as "working," while students, housewives, and social residents or inmates are categorised as "unemployed". The variable type of health facility is divided into “primary healthcare” and “hospital." Primary healthcare includes Puskesmas and clinic.

The clinical characteristic variables consist of two forms of diagnosis: "bacteriological confirmed" and "clinically diagnosed." Patients are considered bacteriologically confirmed TB patients if they test positive for TB through sputum tests using rapid molecular tests (TCM) or

microscopic examinations. Patients with TB symptoms supported by X-ray findings and mantoux are classified as clinically diagnosed. We categorize anatomical location variables based on the patient's TB illness location, specifically "lung TB" and "extra pulmonary TB."

Patients treatment histories are classified as new patients if they have not been treated for TB, and they are categorized as previously treated if they had received TB treatment but recurred, discontinued treatment, or previously failed treatment. OAT alloys are divided into category 1 (RHZE) and category 2, which are category 2 alloys plus streptomycin injections. The use of antiretroviral therapy (ART) is grouped into “yes” and “no”.

Stata 15 is used to analyse variables by doing a chi-square bivariate test to assess differences in proportions across several datasets and to measure the link between dependent and independent variables using the prevalence ratio (PR). Multivariate analysis is also done with the Cox Regression with constant time at risk to determine the most dominant independent variable against the dependent variable and produce the correct PR value in the cross-sectional study.

Generally, Cox regression is applied to time-to-event data, in which the response consists of the amount of time it takes an individual to deliver the desired outcome. The estimation of the hazard rate function, which describes the dependence of the hazard rate on a set of covariates, is performed using Cox regression. When all cohort members are assigned a constant risk period, the hazard rate ratio calculated using Cox regression is equivalent to the prevalence ratio in cross-sectional studies or the cumulative incidence ratio in longitudinal studies (Barros & Hirakata, 2003).

The DKI Jakarta Provincial Health Office has permitted data usage in this study under authorization number 427/HM.10.02. Respondents' names and population identities have been omitted to maintain patient confidentiality

RESULTS AND DISCUSSION

Table 1. Distribution of Treatment Results for TB - HIV Patients in DKI Jakarta 2020 - 2022

Variabel	Category	Frequency (N)	Proportion %
Treatment Outcome	**Success**	**1394**	**73.29%**
	Cured	270	19.37%
	Treatment completed	1124	80.63%
	Not Success	**508**	**26.71%**
	Failed	7	1.38%
	Died	179	35.24%
	Lost to follow up	322	63.39%

In this study, 73.29% of TB-HIV patients had successful treatment results, 80.63% of TB - HIV patients had completed treatment, and 19.37% had recovered. 26.71% of TB - HIV patients experienced treatment failure, primarily due to 63.39% of patients discontinuing therapy (lost to follow up).

Table 2. sociodemographic/clinical characteristics and treatment outcomes among TB – HIV patients in DKI Jakarta, 2020 - 2022

Variabel	Total (N)	Treatment Outcome		P - value	PR (95% CI)
		Success	Not Success		
Age (year)					
15 – 44	1565	1175 (75%)	390 (25%)	< 0.001	1.16 (1.06 – 1.26)
≥ 45	337	219 (65%)	118 (35%)		1
Sex					
Female	408	288 (71%)	120 (29%)	0,164	0.95 (0.89 - 1.02)
Male	1494	1106 (74%)	388 (26%)		1
Employment Status					
Work	1393	1004 (72%)	389 (28%)	0.047	0.94 (0.89 - 0.99)
Unemployed	509	390 (77%)	119 (23%)		1
Type of Health Facilities					
Primary Healthcare	639	514 (80%)	125 (20%)	< 0.001	1.15 (1.09-1.21)
Hospital	1263	880 (70%)	383 (30%)		1
Type of Diagnosis					
Bacteriological confirmed	659	505 (77%)	154 (23%)	0.016	1.07 (1.01 - 1.13)
Clinically diagnosed.	1243	889 (72%)	354 (28%)		1
TB Location					
Pulmonary	1674	1226 (73%)	448 (27%)	0,886	0.99 (0.91 - 1.08)
Extra pulmonary	228	168 (74%)	60 (26%)		1
Treatment history					
New patient	1738	1282 (74%)	456 (26%)	0,13	1.08 (0.97 - 1.20)
Previously treated	164	112 (68%)	52 (32%)		1
Regimen					

Category 1	1394	1335 (96%)	472 (4%)	0,01	1.19 (1.01 - 1.39)
Category 2	95	59 (62%)	36 (38%)		1
on ART					
Yes	1887	1391 (74%)	496 (26%)	< 0.001	3.68 (1.34 - 10.14)
No	15	3 (20%)	12 (80%)		1

Table 2 shows the success of treatment for patients with TB - HIV in DKI Jakarta in 2020–2022. More cases were found in patients aged 15–44 years (75%), male (74%), not working (77%), and treated in Primary Healthcare (80%).

From the clinical characteristics of patients, the success of treatment for TB – HIV patients was higher in bacteriologically confirmed patients (77%), in patients with extrapulmonary TB (74%), who had never had a history of TB treatment before (74%), receiving category 1 therapy (96%), and in patients receiving ART (74%).

Table 3. Bivariate and Multivariate analysis of factors associated to the success treatment of TB – HIV Patients

Variabel	Bivariate Analysis			Multivariat Analysis		
	PR	95% CI	p - value	adj.PR	95% CI	p - value
Age (year)						
15 – 44	1.16	1.06 – 1.26	< 0.001			
≥ 45	1	-				
Sex						
Female	0.95	0.89 – 1.02	0.164			
Male	1	-				
Employment status						
Work	0.94	0.89 – 0.99	0.047			
Unemployed	1	-				
Type of Health Facilities						
Primary healthcare	1.15	1.09 – 1.21	< 0.001	1.16	1.04 – 1.29	0.009*
Hospital	1	-		1	-	
Type of Diagnosis						
Bacteriological confirmed	1.07	1.01 – 1.13	0.016			
Clinically diagnosed.	1	-				
TB Location						

Pulmonary	0.99	0.91 – 1.08	0.886			
Extra pulmonary	1	-				
Treatment History						
New patient	1.08	0.97 – 1.20	0.130			
Previously treated	1	-				
Regimen						
Category 1	1.19	1.01 – 1.39	0.011			
Category 2	1	-				
on ART						
Yes	3.68	1.34 – 10.14	< 0.001	3.72	1.20 – 11.55	0.023*
No	1	-		1	-	

* significant at p-value < 0.05

In the bivariate analysis, patients aged 15 - 44 years have a 1.16 times higher chance of successful treatment than those aged ≥ 45 years (p = < 0.001). Patients who worked were 0.94 times more likely to have a successful treatment outcome than those who did not work (p = 0.047). Treatment success rates for tuberculosis and HIV patients in primary care were 1.15 times higher than in hospital (p = < 0.001).

Patients who tested bacteriologically for TB had a 1.07 times greater treatment success rate than those diagnosed with TB based on clinical symptoms (p = 0.016). Patients treated with category 1 TB drugs were 1.19 times more successful than with category 2 drugs (p 0.011) and patients on ART were 3.68 times more successful than those who were not. Meanwhile, other variables, which were sex, TB Location and TB Treatment history were found to have an insignificant association with TB treatment success among TB/HIV co-infection in DKI Jakarta. In the multivariable analysis, predictors of successful tuberculosis treatment outcome were patients who treated in primary healthcare and got ART. Patients who treated at primary healthcare 1.2 times higher odds of having successful TB treatment outcome (aPR:1.16, 95% CI: 1.04–1.29, p=0.009). Patients with ART treatment had 3.7 times higher odds of having successful TB treatment outcome (aPR: 3.72, 95% CI: 1.20–11.55, p=0.023).

Discussion

Patients treated in primary healthcare and receiving ART were predictors of successful tuberculosis treatment outcomes in the multivariable analysis. Patients treated in primary healthcare had 1.2 times higher odds of achieving a successful TB treatment outcome (aPR: 1.16, 95% CI: 1.04–1.29, p 0.009). The study revealed that the success rate of TB-HIV treatment in primary healthcare was 80%, compared to 70% in the hospital. In 2015, the successful treatment rate for tuberculosis at 30 primary health care facilities in Bekasi City was 85.2%. The majority of successful cases involved new patients with pulmonary tuberculosis, totaling 265 individuals (Amalia et al., 2022).

This study also found Patients treated for TB at primary healthcare 1.2 had a greater success rate in their therapy compared to those treated at the hospital. Research in Semarang, Indonesia, found that patients treated at Puskesmas were 3.7 times more successful than those treated in the hospital (p = 0.000) (Rakhmawati et al., 2023). In 2015, the successful treatment rate for tuberculosis at 30 primary health care facilities in Bekasi City was 85.2%. The majority of successful cases involved new patients with pulmonary tuberculosis, totaling 265 patients.

Individuals receiving antiretroviral therapy (ART) showed more favourable tuberculosis treatment results in comparison to those not receiving ART (aPR: 3.72, 95% CI: 1.20–11.55, p 0.023). A study in Malawi found that 38% of TB - HIV patients were treated with ART. Patients who received antiretroviral therapy (ART) had a higher success rate compared to those who did not receive ART (Tweya et al., 2013).

The study conducted in Sichuan, China, also demonstrated that patients who did not receive ART had 1.4 times higher odds of unfavourable results compared to those who started antiretroviral medication [4], similar to the study conducted in Kuala Lumpur – Malaysia, patients who did not receive antiretroviral therapy were more likely to have unsuccessful treatment for their tuberculosis and HIV co-infection (p = 0.017) (Selimin et al., 2021).

Both HIV and ART status had a significant impact on TB treatment results. HIV-infected individuals had lower treatment success rates and were twice as likely to die compared to HIV-negative individuals. Tuberculosis patients with HIV receiving antiretroviral therapy (ART) were more likely to have successful treatment results than those not receiving ART. ART boosts the immunological response in TB - HIV patients, resulting in increased survival rates (Tweya et al., 2013).

CONCLUSION

The study revealed that the percentage of TB-HIV patients who successfully completed their treatments at DKI Jakarta between 2020 and 2022 was 73.29%, falling short of the Ministry of Health of the Republic of Indonesia's target of 90%. The multivariate analysis in this study indicates that patients receiving treatment in primary health care institutions and undergoing ART therapy are factors associated with the success of TB-HIV treatment.

Thus, we recommend that it be necessary to strengthen medical supervision of patients taking medication in hospitals by ensuring that patients take medication on a regular basis, conducting surveillance and monitoring of side effects experienced by patients, and providing counselling. In addition, it is necessary to educate and strengthen patients to be able to follow ART therapy alongside TBC treatment consistently, and officials are obliged to carry out records and reporting related to TBC and ART therapies. Holistic support to ensure compliance and the success of TB and HIV treatment is imperative.

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