



**PREDICTORS OF PULMONARY TUBERCULOSIS CO-INFECTION  
AMONG HIV PATIENTS IN KHZ. MUSTHAFA HOSPITAL: A CROSS-  
SECTIONAL STUDY**

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## ABSTRACT

**Background:** Tuberculosis (TB) remains the leading cause of mortality among People Living with HIV (PLHIV), posing a significant public health challenge in high-burden settings like Indonesia. This study aimed to identify the significant predictors of pulmonary TB co-infection among HIV-positive patients at a regional referral hospital.

**Methods:** A retrospective cross-sectional study was conducted using medical records of 140 eligible HIV patients at KHZ Musthafa Hospital, Tasikmalaya, from 2022 to 2023. Bivariate and multiple logistic regression analyses were performed to identify determinant factors.

**Results:** The prevalence of pulmonary TB co-infection was alarmingly high at 59.2%. The final multivariate model identified three independent predictors: duration of antiretroviral therapy (ART) for less than 12 months (AOR=5.3, 95% CI 2.246–12.474), advanced WHO clinical stage (AOR=2.9, 95% CI 1.319–6.734), and the presence of other opportunistic infections (AOR=4.6, 95% CI 1.963–11.005).

**Conclusion:** The high prevalence and identified predictors underscore a critical need for intensified TB screening, particularly for patients who are new to ART, presenting in advanced clinical stages, or diagnosed with other opportunistic infections. Integrated TB-HIV services focusing on these specific high-risk groups are essential for improving clinical outcomes.

**Keywords:** risk factors, co-infection pulmonary TB, HIV patients

## ABSTRAK

**Latar Belakang:** Tuberkulosis (TB) masih menjadi penyebab utama kematian pada Orang dengan HIV (ODHIV), menjadi tantangan kesehatan masyarakat yang signifikan di negara dengan beban tinggi seperti Indonesia. Penelitian ini bertujuan untuk mengidentifikasi faktor prediktor utama koinfeksi TB paru pada pasien HIV positif di sebuah rumah sakit rujukan regional.

**Metode:** Sebuah studi potong lintang retrospektif dilakukan dengan menggunakan data rekam medis dari 140 pasien HIV yang memenuhi kriteria di **RS KHZ Musthafa**, Tasikmalaya, dari tahun 2022 hingga 2023. Analisis bivariat dan regresi logistik ganda digunakan untuk mengidentifikasi faktor-faktor determinan.

**Hasil:** Prevalensi koinfeksi TB paru ditemukan sangat tinggi, yaitu sebesar 59,2%. Model multivariat final mengidentifikasi tiga prediktor independen: durasi terapi antiretroviral (ART) kurang dari 12 bulan (AOR=5,3; 95% CI 2,246–12,474), stadium klinis WHO lanjut (AOR=2,9; 95% CI 1,319–6,734), dan adanya infeksi oportunistik lain (AOR=4,6; 95% CI 1,963–11,005).

**Kesimpulan:** Prevalensi yang tinggi dan faktor-faktor prediktor yang teridentifikasi menggarisbawahi adanya kebutuhan kritis untuk skrining TB yang lebih intensif, terutama bagi pasien yang baru memulai ART, berada pada stadium klinis lanjut, atau terdiagnosis dengan infeksi oportunistik lain. Pelayanan terintegrasi dan komprehensif pada TB Paru dan diagnosis HIV serta pengobatannya diperlukan untuk manajemen ko-infeksi TB/HIV yang lebih baik.

**Kata kunci:** faktor risiko, ko- infeksi TB Paru, pasien HIV

## INTRODUCTION

The syndemic of Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) constitutes one of the most significant global public health challenges, with TB remaining the leading cause of mortality among People Living with HIV (PLHIV) and accounting for nearly one-third of all AIDS-related deaths (WHO, 2023). This well-documented pathological synergy occurs as HIV-mediated depletion of CD4+ T-lymphocytes cripples the host's cell-mediated immunity, drastically increasing the risk of both acquiring a primary TB infection and reactivating latent *Mycobacterium tuberculosis* (Badje et al., 2017; Noursadeghi & CK Bell, 2018). This profound biological vulnerability, a critical concern in high-burden countries like Indonesia establishes the integration of TB and HIV services as an urgent global public health priority (Kementerian Kesehatan RI, 2023).

Globally, an estimated 10.6 million people fell ill with TB in 2022, and about 6.3% of these cases were among PLHIV. The WHO's End TB Strategy aims to reduce TB deaths by 95% and cut new cases by 90% between 2015 and 2035, with a critical component being the management of co-

morbidities like HIV (WHO, 2023; Windels et al., 2024). This includes achieving ambitious targets such as providing TB preventive treatment (TPT) to at least 90% of eligible PLHIV. Similarly, the UNAIDS 95-95-95 targets aim for 95% of all PLHIV to know their status, 95% of those diagnosed to receive sustained antiretroviral therapy (ART), and 95% of those on ART to have viral suppression, which indirectly reduces TB risk (UNAIDS, 2024). Despite these global frameworks, the burden of TB-HIV co-infection remains disproportionately high in many resource-limited settings.

Indonesia faces a particularly severe challenge, ranking second globally for TB burden and grappling with a concentrated HIV epidemic. National strategies emphasize integrated care, yet the vast heterogeneity of the archipelago necessitates localized data to guide effective implementation (Kementerian Kesehatan RI, 2023; Pertiwi et al., 2023). While international cohort studies have robustly identified universal predictors for TB co-infection—including severe immunosuppression (CD4 count  $<200$  cells/mm<sup>3</sup>), absence or short duration of antiretroviral therapy (ART), malnutrition, and smoking (Hoffmann et al., 2022; Sharma et al., 2016). The specific weight and interplay of these factors can vary significantly across different populations. Studies within various Indonesian contexts have highlighted the importance of local determinants, from nutritional status in urban settings to adherence challenges in rural areas (Karyadi, 2017; Kusumawati et al., 2021).

While numerous international studies have identified key predictors for TB co-infection among PLHIV, these factors can vary significantly by region. Established predictors include severe immunosuppression (CD4 count  $<200$  cells/mm<sup>3</sup>), poor adherence to ART, malnutrition, smoking, and a history of contact with TB patients (Eze et al., 2023; Nainggolan et al., 2023; Xiao et al., 2023). However, local socio-demographic characteristics, healthcare system capacities, and patient behaviors can modulate these risks. Data on the most dominant predictors within specific clinical settings in Indonesia, particularly outside of major metropolitan areas, remain scarce. KHZ.Musthafa Hospital, as a key healthcare provider in Tasikmalaya, serves a unique patient demographic whose specific risk profile for TB-HIV co-infection has not been thoroughly investigated. The lack of previous research on KHS. Musthafa and other research in the Tasikmalaya region is one of the reasons why this research is important. Therefore, this study aims to identify the significant predictors of pulmonary tuberculosis co-infection among HIV patients receiving care at KHZ.Musthafa Hospital. The findings are expected to provide crucial, evidence-based insights for clinicians and public health program managers to develop targeted screening protocols, optimize preventive strategies, and improve the clinical management of this vulnerable population, ultimately contributing to the reduction of TB-HIV-related morbidity and mortality in the region.

## **METHOD**

### *Participant characteristics and research design*

This study utilized a hospital-based, retrospective cross-sectional design. Data were extracted from the medical records of patients receiving care at the Voluntary Counseling and Testing (VCT) clinic of KHZ.Musthafa Hospital between January 2022 and December 2024. The hospital is a government-operated referral center for HIV care in the Tasikmalaya Regency, West Java, Indonesia.

### *Study Population and Selection Criteria*

A consecutive sampling technique was employed to include all patient records that met the eligibility criteria. The inclusion criteria were: (1) a confirmed HIV diagnosis, (2) aged 18 years or older, and (3) a medical record with complete data for all primary variables. Conversely, patients were excluded if their primary residence was documented as outside the Tasikmalaya Regency or if their records contained substantial missing data on the outcome or key predictor variables, which would preclude meaningful analysis. A total sampling technique, constituting a census of the accessible population,

was employed as the most rigorous approach for this study's context. This method maximized the sample size to N=140 and eliminated selection bias.

### *Variables and Measurements*

All variables were extracted directly from patient medical records.

- a. The dependent variable was the presence of pulmonary tuberculosis (TB) co-infection. A case was defined as a patient with a physician-confirmed diagnosis of pulmonary TB, supported by at least one positive result from an Acid-Fast Bacilli (AFB) smear test on a sputum sample.
- b. The independent variables were grouped into sociodemographic and clinical categories:
  1. Sociodemographic variables included: age (in years), gender (male/female), marital status (categorized as married vs. unmarried, which included single, divorced, or widowed), and highest level of education (categorized as primary school or lower, secondary school, and higher education).
  2. Clinical variables included:
    - a) WHO Clinical Stage: The most advanced stage of HIV disease recorded for the patient, categorized as early-stage (Stage 1 & 2) or advanced-stage (Stage 3 & 4).
    - b) Duration of ART: The length of time a patient had been on antiretroviral therapy, dichotomized as <12 months or ≥12 months.
    - c) Nutritional Status: Assessed using the Body Mass Index (BMI), calculated as kg/m<sup>2</sup> and categorized as underweight (<18.5) or normal/overweight (≥18.5).
    - d) Anemia Status: Determined from hemoglobin (Hb) levels, categorized as anemic (<13 g/dL for males, <12 g/dL for females) or not anemic.
    - e) Opportunistic Infections (OIs): The documented presence or absence of any other opportunistic infection besides TB during the study period.

### *Data analysis*

All data were coded and analyzed using IBM SPSS software version 23.0. Initially, descriptive analysis was performed to generate frequency distributions and percentages for all sociodemographic and clinical variables. For inferential analysis, the association between each independent variable and pulmonary TB co-infection was first assessed using the chi-square ( $\chi^2$ ) test; variables with a p-value ≤ 0.25 were selected as candidates for the multivariate model.

Subsequently, a multiple logistic regression analysis with a forward likelihood ratio (LR) method was conducted to identify significant independent predictors. The strength of association was measured using Adjusted Odds Ratios (AORs) with their corresponding 95% Confidence Intervals (CIs), and a p-value < 0.05 was considered statistically significant. The goodness-of-fit of the final model was assessed using the Hosmer-Lemeshow test. Finally, to confirm the adequacy of the sample size, a *post-hoc* power analysis was conducted. Based on the smallest significant effect size from the multivariate analysis (AOR = 2.9) at an alpha of 0.05, the study's statistical power was determined to be >0.95, confirming the findings are statistically robust.

## **RESULTS AND DISCUSSION**

A total of 140 HIV-positive patient records met the inclusion criteria. The majority were male (77.9%), with a mean age of 30.7 years (SD: 4.97). Most participants were married (75.9%), had low educational attainment, and were employed (69.3%). The prevalence of pulmonary TB co-infection was 59.3%. Regarding other opportunistic infections, oral candidiasis was the most common (20.0%). The overall prevalence of pulmonary TB co-infection within this cohort was alarmingly high at 59.3% (n=83).

**Table 1:** Socio-demographic characteristics of study participants in KHZ Mushafa Hospital (n=140)

Variables	Frequency	Percent (%)
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Sex		
Male	109	77.9
Female	31	22.1
Age	-	-
Mean: 30.7 yo		
SD: 4.97 yo		
Min: 18 yo		
Max: 59 yo		
Marital Status		
Married	63	75.9
Unmarried	20	24.1
Education Status		
Elementary	56	40.0
Junior high school	22	15.7
Senior high school	60	42.9
Undergraduate	1	0.7
Post-graduate	1	0.7
Opportunistic infection		
Oral candidiasis	20	20.0
Wasting syndrome	14	10.0
Condyloma acuminata	9	6.4
Toxoplasma cerebri	10	7.1
Seborrheic dermatitis	3	2.1
Pneumonia	9	6.4
Cryptosporidiosis	5	3.6
None	62	44.3
Job		
Employee	97	69.3
Unemployee	43	30.7
TB Paru co-infection		
Yes	83	59.3
No	57	40.7

In the initial bivariate analysis, several factors were found to be significantly associated with TB co-infection, including marital status, anemia, Body Mass Index (BMI), ART duration, WHO clinical stage, and the presence of other opportunistic infections (all  $p < 0.05$ ). The final multivariate logistic regression model identified three independent predictors as significantly associated with pulmonary TB co-infection. As detailed in Table 2, the most potent predictor was an antiretroviral therapy (ART) duration of less than 12 months (Adjusted Odds Ratio [AOR] = 5.3, 95% CI: 2.246–12.474;  $p < 0.001$ ). This was followed by the presence of other opportunistic infections (AOR = 4.6, 95% CI: 1.963–11.005;  $p < 0.001$ ) and an advanced WHO clinical stage (Stage 3 or 4) (AOR = 2.9, 95% CI: 1.319–6.734;  $p = 0.009$ ).

**Table 2:** Bivariate and multivariate association of TB/HIV co-infection and independent factors in KHZ Mushafa Hospital

	TB/HIV co-infected		COR (95%CI)	P-value	AOR (95%CI)	P-value
	Yes f (%)	No f (%)				
Age						
Productive age	82 (98.8)	54 (97.1)	4.55 (0.462-44.945)	0.304	-	-
Non-productive age	1 (1.2)	3 (2.9)				
Sex						
Male	66 (79.5)	43 (75.4)	1.26 (0.565-2.827)	0.716	-	-
Female	17 (20.5)	14 (24.6)				
Marital Status						
Married	63 (75.9)	31 (54.4)	2.642 (1.280-5.4510)	0.013	-	-
Unmarried	20 (24.1)	26 (45.6)				
Education level						
Low	82 (98.8)	56 (98.2)	1.46 (0.090-23.901)	1.000	-	-
High	1 (1.2)	1 (1.8)				

Anemia status							
Anemia	54 (65.1)	25 (43.8)	2.383 (1.194-4.756)	0.021	-	-	-
Non-anemia	29 (34.9)	32 (56.2)					
Lama terapi ARV							
≥12 months	55 (63.2)	21 (36.8)	3.367 (1.664-6.813)	0.001	5.294 (2.246-12.474)	<0.001	
< 12 months	28 (26.8)	36 (63.2)					
Opportunistic infection							
Yes	54 (65.1)	24 (42.1)	2.56 (1.281-5.119)	0.012	4.684 (1.963-11.005)	<0.001	
No	29 (34.9)	33 (57.9)					
Clinical stage WHO							
3 and 4	65 (78.3)	31 (54.3)	3.029 (1.448-6.317)	0.005	2.980 (1.319-6.734)	0.009	
1 and 2	18 (11.7)	26 (45.7)					
BMI							
Underweight	52 (63.8)	24 (42.1)	2.306 (1.158-4.592)	0.026	-	-	-
Normal	31 (36.2)	33 (57.9)					

This study provides critical, localized evidence on the predictors of TB-HIV co-infection from a regional referral hospital in Indonesia, a nation contending with the world's second-largest tuberculosis burden. Our analysis identified three powerful and independent predictors a short duration of ART, advanced WHO clinical stage, and the presence of other opportunistic infections which collectively delineate a high-risk clinical profile for co-infection.

The most potent predictor was an ART duration of less than one year. This finding is robustly supported by a vast body of international literature, which characterizes the initial year of ART as a period of profound immunological vulnerability. This vulnerability is primarily driven by delayed immune reconstitution, as patients new to therapy have not yet achieved the CD4+ T-cell recovery required to effectively control *M. tuberculosis* (Lawn et al., 2011; Suthar et al., 2013). A landmark prospective study in Côte d'Ivoire, published in *The Lancet Global Health*, definitively demonstrated that TB incidence peaked within the first six months of ART initiation (Badje et al., 2017). This global pattern is precisely mirrored in our findings and is consistent with research from Indonesia, which confirms that significant CD4 recovery is a time-dependent process, marking the initial year as a critical "window of risk" (Karyadi, 2017). This period is further complicated by the phenomenon of Immune Reconstitution Inflammatory Syndrome (IRIS), where a recovering immune system unmasks a previously subclinical TB infection (Noursadeghi & CK Bell, 2018; Pertiwi et al., 2023; Triwicaksana et al., 2022; Wong et al., 2020).

Advanced WHO clinical stage (3 or 4) emerged as the second powerful predictor. This logically reflects the core pathophysiology of the TB-HIV syndemic, where susceptibility to TB is a direct function of immunodeficiency (Gumilang et al., 2022; Swinkels et al., 2025). The WHO staging system serves as an indispensable clinical proxy for immunological failure, particularly where routine CD4 monitoring is inconsistent (WHO, 2005). Our results are strongly corroborated by a meta-analysis and large multi-country cohorts, which confirm a steep gradient of TB risk with advancing WHO stage (Anglaret et al., 2012; Suthar et al., 2013). This link has been consistently validated within the Indonesian context, where advanced clinical stage is tightly correlated with profoundly low CD4 counts, creating a permissive environment for opportunistic pathogens (Jayani et al., 2020; Kurniawati et al., 2022; Putri et al., 2023; Viyani & Kurniasari, 2024) (Nugraha et al., 2020; Rachmawati, 2018).

The presence of other opportunistic infections was the third independent predictor. This finding highlights the concept of a generalized state of immune collapse, where the diagnosis of an OI such as oral candidiasis serves as a sentinel event for profound immunodeficiency (Jayani et al., 2020; Sharma et al., 2016; Trisnashanti & Romdhoni, 2025). This aligns with epidemiological studies demonstrating the clustering of OIs in severely immunocompromised individuals, who face the worst prognoses (Meng et al., 2023). This underscores the need for an integrated diagnostic approach, where the identification of one OI should immediately trigger a high-suspicion screening for TB, a practice

supported by local Indonesian studies (Anindita, 2012; Asmarawati et al., 2018; Rosamarlina et al., 2016; Sutini et al., 2022).

A notable finding was that several variables significantly associated with TB in the bivariate analysis, particularly anemia and low BMI, did not retain significance in the final multivariate model. This does not diminish their clinical importance but rather clarifies their role within the causal pathway. International literature firmly establishes that both malnutrition and anemia are consequences of advanced HIV and active TB disease itself, creating a "vicious cycle" of worsening immunity and infection (Fuseini et al., 2021; Ghosh et al., 2024; Selimin et al., 2021). Their predictive power was likely absorbed by the more robust and composite variable of WHO clinical stage, which already encapsulates the clinical manifestations of wasting and severe illness. This suggests they are critical markers of disease progression rather than independent drivers.

## **LIMITATION OF THE STUDY**

Several limitations inherent to this study's design warrant consideration. As the findings are derived from a single institution, caution should be exercised when extrapolating the results to different healthcare settings or the general HIV population in Indonesia. The retrospective data collection also meant our analysis could not account for several potentially significant confounders, most notably viral load measurements and a detailed history of TB episodes before ART commencement. Furthermore, although the sample size provided adequate statistical power ( $>0.95$ ) to detect the strong associations reported, it may have lacked the sensitivity to identify weaker, yet potentially relevant, predictors. Future research, preferably through larger, multi-center prospective cohorts, is essential to confirm our results and explore a wider range of determinants with greater precision.

## **CONCLUSIONS AND SUGGESTIONS**

This study identifies a clear, high-risk clinical profile for pulmonary TB co-infection among HIV patients, characterized by three independent predictors: a short duration of antiretroviral therapy, an advanced WHO clinical stage, and the presence of other opportunistic infections. This evidence-based profile provides a powerful tool for risk stratification, enabling clinicians to prioritize intensified screening for the most vulnerable individuals.

These findings strongly support local health policies, such as the strategy mandated by the Tasikmalaya Health Offices, which calls for routine TB screening for all people living with HIV. By delineating who is most at risk within this population, our research offers a practical framework to implement this policy more effectively. Focusing diagnostic resources on patients matching this high-risk profile can optimize the efficiency of existing TB-HIV collaboration programs and accelerate early case detection, ultimately contributing to better patient outcomes in Tasikmalaya and similar high-burden settings.

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The authors did not receive support from any organization for the submitted work.

## Conflict of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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