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Risk Factors for Pulmonary Tuberculosis in Patients with HIV : A Systematic Literature Review

Putu Ayu Sawitri[1*]

[1]Magister Of Public Health,Faculty Of Public Health, Halu Oleo University, Kendari, Indonesia

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Abstract

Coinfection of tuberculosis (TB) and human immunodeficiency virus (HIV) is a significant global health problem, especially in developing countries. In 2023, an estimated 10.8 million people fell ill with TB worldwide, about 161 000 people died of HIV-associated TB. The percentage of notified TB patients who had a documented HIV test result in 2023 was 80%. HIV weakens the immune system, increasing susceptibility to TB, which is the leading cause of death in patients with HIV. This study aimed to identify and analyze various risk factors that contribute to the occurrence of pulmonary tuberculosis in HIV patients. This study is a literature review with a systematic approach to fifty journals published between 2020 until 2025, search on various scientific databases such as Google Scholar, PubMed, and Garuda Ristekbrin portals. The main risk factors for pulmonary TB in HIV patients include CD4 levels <200 cells/mm^3, advanced clinical stage of HIV, low socioeconomic status, low education levels. In addition, environmental factors such as household air pollution and a history of contact with TB people also increase the risk. Behavioral variables such as substance use and delays in antiretroviral therapy also aggravate the patients condition. In conclusion, patients with HIV have a high risk factor for developing TB, so it is necessary to increase active screening, strengthening patient education, and strengthen social support. Appropriate risk-based interventions will improve treatment success and lower coinfection mortality.

Correspondence Address:
Jl. KS Tubun, Baruga, Kencari City, Southeast Sulawesi, Indonesia
E-mail: putu19ayu99@mail.com

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Introduction

Tuberculosis (TB) is one of the infectious diseases that is still a global public health problem, especially in developing countries. The risk of TB is significantly increased in individuals with Human Immunodeficiency Virus (HIV), as a decrease in the body's immunity leads to activation of latent infections into active TB (Winter et al., 2020).

In 2023, an estimated 10.8 million people fell ill with TB worldwide, including 6.0 million men, 3.6 million women and 1.3 million children. A total of 1.25 million people died from tuberculosis (TB) in 2023 (including 161 000 people with HIV). The percentage of notified TB patients who had a documented HIV test result in 2023 was 80%, this was the same level as in 2022, but up from 76% in 2021. Worldwide, TB has probably returned to being the world's leading cause of death from a single infectious agent. It was also the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance. (WHO, 2024).

Indonesia ranks second in the world in terms of the number of TB cases, with 845,000 TB cases and 19,000 TB-HIV co-infection patients in 2019. Meanwhile, out of 271 million people, an estimated 543,100 are living with HIV, and an estimated 4,700 TB-HIV patients have died from approximately 96,000 TB-related deaths (Kemenkes RI, 2021).

In Indonesia, this condition is increasingly complex because the incidence of TB is still high which is influenced by environmental factors such as housing density and poor ventilation (Salwa Salsabila Deliananda & R. Azizah, 2022).

TB-HIV coinfection is known to increase morbidity and mortality rates, especially in patients with very low CD4 levels. Meta-analyses showed that the risk of death increased sharply in patients with CD4

<200 cells/µL, even greater in CD4 <100 and <50 cells/µL (Sari et al., 2022). Research in China and Ethiopia has also shown that low CD4 and advanced clinical stage of HIV are important determinants in poor clinical outcomes of TB-HIV patients (Moges & Lajore, 2024).

In addition to immunological aspects, socioeconomic and demographic factors also play an important role in the risk of TB in HIV patients. Patients with low economic status, limited education, and informal employment were found to have higher susceptibility to TB, as shown in studies in Papua and Bogor (Anggraeni et al., 2024). Residential environments that do not meet health standards, including poor ventilation and densely populated homes, have also been shown to increase the risk of TB infection (Wang et al., 2025).

Behavioral factors such as smoking habits and a history of contact with people with TB are also important predictors. In Malang and Aceh Besar Regencies, these two factors showed a significant relationship with the incidence of TB-HIV coinfection (Nisak et al., 2024). On the other hand, family involvement and the role of health workers in medication monitoring (PMO) have been shown to improve patient adherence to treatment, which is key to the success of therapy (Botutihe et al., 2024).

Challenges in the management of TB-HIV are also exacerbated by the lack of optimal integration of TB and HIV services, delayed diagnosis, and the burden of dual therapy between anti-tuberculosis drugs (OAT) and antiretroviral drugs (ARVs). This problem creates a physical and psychological burden on the patient, which can lead to medication discontinuation or therapy failure (Rosfita, et al., 2023). Therefore, a comprehensive understanding of the various risk factors for pulmonary TB in HIV patients is indispensable in efforts to formulate more effective and integrated risk-based intervention strategies.

Methods

This study used a literature review method to examine various risk factors that contribute to the incidence of pulmonary tuberculosis in patients with Human Immunodeficiency Virus (HIV). Data collection was carried out through literature search on various scientific databases such as Google Scholar, PubMed, and accredited national journals available through the PERPUSNAS and Garuda Ristekbrin portals. Keywords used in searches included: "risk factors for pulmonary tuberculosis in HIV", "TB-HIV coinfection", "HIV/AIDS and pulmonary TB", and "clinical and social factors of HIV TB".

From the initial search results, fifty journals relevant to the topic of tuberculosis in HIV patients were obtained. The selection process is then carried out based on inclusion and exclusion criteria. Inclusion criteria include: 1. journals published in the last five years (2020–2025), 2. discuss HIV patients with pulmonary TB infection, and 3. explicitly describe the risk factors for TB in HIV patients from clinical, social, environmental, and behavioral aspects. The exclusion criteria include: 1. articles in the form of opinions or editorials, 2. journals that only discuss TB or HIV separately without linking the two, and, 3. journals that focus on pediatric TB or non-pulmonary TB.

After the selection process, fifteen main journals that met the criteria were obtained and used as a source of analysis in this study. The journals were thematically analyzed to identify and classify the dominant risk factors, both in terms of individuals (low CD4, advanced stages of HIV), environment (pollution, poor ventilation), and social factors (low education, informal employment), in order to provide a comprehensive understanding of the susceptibility of HIV patients to pulmonary TB.

The following is the result of the literature search and analysis conducted by the researcher, presented in a flowchart using the PRISMA 2020 diagram.

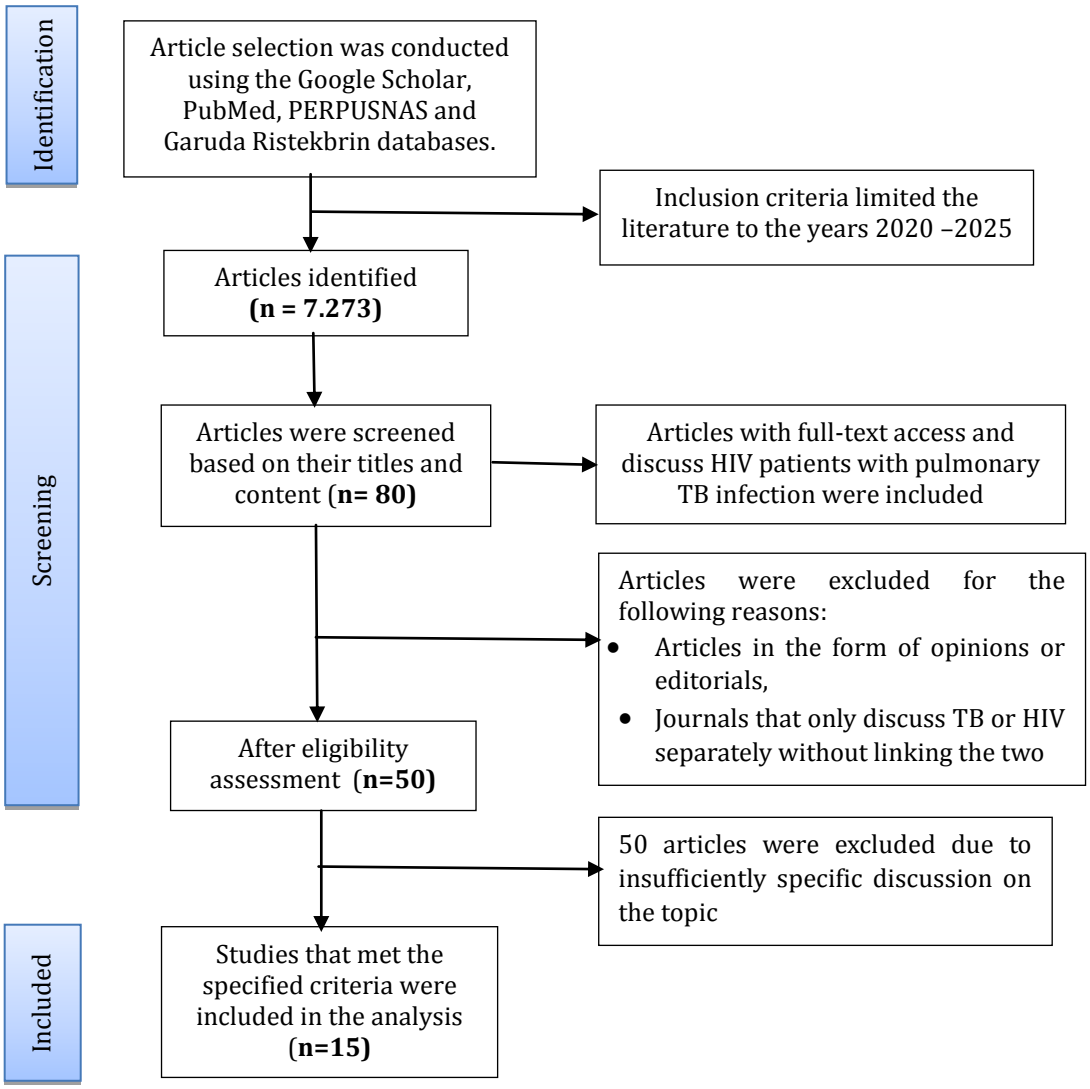

Figure 1. PRISMA 2020 Flow Diagram

Results

Based on the results of the literature review, it was found that the risk of pulmonary tuberculosis (TB) in patients with Human Immunodeficiency Virus (HIV) is influenced by various complex factors, including immunological status, environmental conditions, access to health services, and socioeconomic status. Of the fifty journals analyzed, as many as fifteen journals that were most relevant and met the inclusion criteria were selected for further analysis in this study.

Table 1. Systematic Review

No.	Autor / Year	Title	Location	Methods	Results
1.	Nuniek Anggraeni, Titik Nuryastuti, and Arief Nurrochmad/ 2024	Overview of the Output of Antituberculosis Therapy in HIV Coinfected TB Patients at Abepura Jayapura Hospital, Papua	Jayapura, Papua, Indonesia.	Descriptive design with a retrospective cohort design, a sample of 32 HIV coinfected TB patients.	Most patients develop pulmonary TB with RHZE OAT therapy and combipak preparations. Therapy outcomes showed that 21.88% of patients were declared cured, 40.62% completed complete treatment, and 37.5% discontinued, with patient adherence being an important factor in the success of therapy.
2.	Virana Putri A. Botutihe, Herlina Jusuf,	Analysis of Factors Related to the Level of	Gorontalo City, Gorontalo	An observational analysis with a	Age, economic status, role of health workers, and family support were significantly

No.	Autor / Year	Title	Location	Methods	Results
	and Nikmatisni/ 2024	Medication Compliance of Co-Infected TB-HIV Patients in Gorontalo City	Province, Indonesia.	cross-sectional approach, involving a total of 30 TB-HIV co-infection respondents.	related to medication adherence levels, while gender, CD4 test results, smoking history, and education level were not significantly related.
3.	Indah Rismarwati, Fitria Diniah Janah Sayekti/2024	Overview of molecular rapid test results and risk factors for pulmonary tuberculosis in patients human immunodeficiency virus	Cilegon City, Banten Province, Indonesia.	Descriptive method with a quantitative approach and involved 34 HIV patients as respondents.	The number of HIV patients with TB coinfection is 36 people. A total of 35 patients (97.22%) had CD4 values <200 cells/mm^3, which means that their immunity was very low. Most of the patients were 20 – 60 years old and male (83.33%). As many as 58.33% of patients experienced TB coinfection less than one month after being diagnosed with HIV.
4.	Lilik N. Widyaningrum, Dwi W. Indriati, Diyantoro, Aliyah Siti Sundari/2022	Profile of HIV/AIDS Patients Coinfected with Tuberculosis in Ibnu Sina District Hospital, Gresik, East Java, Indonesia	Gresik, East Java, Indonesia.	Descriptive observational design with a cross-sectional approach, using secondary data from 643 medical records of HIV/AIDS patients.	A total of 76 HIV/AIDS patients (11.8%) experienced TB coinfection, the majority were male, aged 15–35 years, had a high school/college education, worked, and had PMO. Most have risk factors for transmission through sexual intercourse, CD4 <200 cells/mm^3, body weight <55 kg, and are in the clinical stage of advanced HIV.
5.	Patrick D.M.C. Katoto and colleagues/2024	Household air pollution and risk of pulmonary tuberculosis in HIV-Infected adults	Bukavu, South Kivu Province, Democratic Republic of the Congo.	The study used a case-control design with 1,277 HIV adults, consisting of 435 cases of pulmonary TB and 842 controls.	Results showed that high exposure to household air pollution, including long cooking times and high CO levels, significantly increased the risk of pulmonary TB in individuals with HIV. The risk increases proportionally to the level of CO exposure, with the highest odds ratio of 4.64 in the highest quintile of CO exposure compared to the lowest.
6.	Yinfa Zhou, Tao Li, Shufang Lin, and colleagues/2023	Characteristics and treatment outcomes of coinfected tuberculosis patients with human immunodeficiency virus in Southeast China, 2012–2021	Fujian Province, Southeast China.	This observational study used data from the China National TB Surveillance System during 2012–2021.	Of the 160,309 TB cases reported, 347 of them were HIV co-infections. The success rate of TB treatment in TB-HIV patients was 83.8%, while 16.2% experienced treatment failure, death, or discontinuation. In addition, TB-HIV patients also showed higher rates of drug resistance to rifampicin and isoniazid.
7.	Jinou Chen, Ling Li, Tao	Predicting the risk of active	Yunnan Province,	A cross-sectional study	This nomogram has been shown to be superior to the

No.	Autor / Year	Title	Location	Methods	Results
	Chen, and colleagues/ 2022	pulmonary tuberculosis in people living with HIV: development and validation of a nomogram	China.	that develops and validates a TB prediction nomogram in HIV patients using the LASSO method.	WHO W4SS algorithm and the XPHACTOR model in detecting active TB in HIV patients, and shows high clinical benefits, especially in health facilities with limited resources.
8.	Misutarno, Siti Nur Hasina, M. Shodiq, Khamida, and Rahmadaniar Aditya Putri/2024	The Relationship Between HIV Human Immunodeficiency Virus and the Incidence of Tuberculosis (TB)	Surabaya, East Java, Indonesia.	Analytical observational design with a cross-sectional approach. The sample consisted of 40 HIV patients who were hospitalized during March–April 2024.	As many as 70% of HIV patients in this study experienced TB coinfection, with the highest incidence in advanced HIV stages (stages III–IV). Factors such as young age, male gender, employment in the informal sector, and risky sexual behaviors contribute to an increased risk of TB in HIV patients.
9.	Victoria Husadani Permata Sari, Setyo Sri Rahardjo, and Bhisma Murti/2022	Mortality of TB-HIV Co-Infection Patients Based on CD4 Level: Meta-Analysis	Multi-country studies in Europe and Latin America.	PRISMA-based meta-analysis design with the PICO approach and analyzed using the Review Manager (RevMan) 5.3 application.	The results showed that the risk of death increased with a decrease in CD4 levels. Patients with CD4 <200 cells/μL had a 2-fold higher risk of death (aHR=2.00), CD4 <100 cells/μL 2.4 times (aHR=2.40), and CD4 <50 cells/μL 3.12 times (aHR=3.12) compared to patients with CD4 ≥200 cells/μL, with all statistically significant outcomes ($p<0.001$).
10.	Alfy Rizka Silfa Rosfita, Rie Dahniar Marissa Marpaung, and Rojwa Azka Syakira/2023	Unraveling the Complexity of Managing Tuberculosis Coinfection in Patients with Human Immunodeficiency Virus (HIV): Current Challenges and Solutions	Does not focus on one specific location, but discusses global and national issues in Indonesia.	Narrative review method by reviewing various current literature from relevant national and international journals on TB-HIV management.	The results of the review show that the main challenges in the management of TB-HIV coinfection include the complexity of therapy, the lack of integration of TB and HIV services, and the limitations of early detection; while suggested solutions include active screening, service integration, TB prevention therapy, and ongoing education for health workers.
11.	Fitri Amelia Rizkia, Irvan Medison, and Fenty Anggrainya/2025	Diagnosis and Management of Pulmonary Tuberculosis in HIV with Severe Immunodeficiency	Padang, Indonesia.	This study was a descriptive-analytical case report in a 33-year-old male with pulmonary TB.	Results showed significant clinical improvement after 9-month OAT therapy and ART started 2 weeks after OAT; patients experienced weight gain, improvement in respiratory symptoms, and negative sputum test results without the onset of IRIS.
12.	Putri Immi Rizky Budiyani,	Factors Associated with Successful Drug	DKI Jakarta Province,	This study used a cross-	As many as 73.29% of TB-HIV patients in DKI Jakarta successfully underwent

No.	Autor / Year	Title	Location	Methods	Results
	Ratna Djuwita, Renti Mahkota, Dwi Handayani/2024	Susceptible Tuberculosis Treatment among Tuberculosis – Human Immunodeficiency Virus Patients in DKI Jakarta Province 2020–2022	Indonesia.	sectional design and analyzed secondary data from SITB.	treatment, and success was higher in patients who were treated at health centers and received ART. TB treatment (aOR 6.16).
13.	Sivaporn Gatechompol, Jiratchaya Sophonphan, Sasiwimol Ubolyam, Anchalee Avihingsanon, Frank van Leth, Frank Cobelens, and Stephen J. Kerr/2020	Incidence and Factors Associated with Active Tuberculosis Among People Living with HIV After Long-Term Antiretroviral Therapy in Thailand: A Competing Risk Model	Bangkok, Thailand.	long-term prospective cohort analysis using a competing risk regression model, involving 2,636 people with HIV.	During 24,229 person-years, there were 113 cases of TB incidence with an incidence rate of 4.66 per 1000 PY. Significant risk factors included CD4 < 50 cells/mm^3 (aSHR 18.23), BMI < 18 kg/m^2 (aSHR 8.21), and substance use history (aSHR 6.03); The incidence of TB decreases after long-term ART, but remains higher than that of the general Thai population.
14	Leni Haryani, Nur Rizky Ramadhani, Rizky Fajar Meirawan, and Bram Burmanajaya/2023	Overview of Risk Factors for HIV Patients with Tuberculosis at Bogor City Hospital	Bogor City, Indonesia.	This study was a descriptive study with a cross-sectional design.	The results showed that 71.7% of HIV patients also had TB. The three variables that had a significant relationship with the incidence of TB in HIV patients were gender (men are more at risk, PR=2,858), clinical stage of HIV (stage 3–4, PR=2,313), and socioeconomic status (underprivileged, PR=2,993).
15	Nurin Marfidhotul Iftitah, Sapto Adi, and Rara Warih Gayatri / 2020	Factors Affecting the Co-Occurrence of Tuberculosis Co-Infection in HIV/AIDS Patients in Malang Regency	Malang Regency, East Java Province, Indonesia.	This study is an observational analytical study with a retrospective case control design.	Results showed that contact with TB patients (p=0.000; OR=2.092), advanced clinical stage (p=0.000; OR=2.541), and low education (p=0.000; OR=1.822) is a significant risk factor for TB-HIV coinfection.

Discussion

Tuberculosis (TB) is one of the most common and deadliest opportunistic infections in patients with Human Immunodeficiency Virus (HIV). The combination of these two diseases creates a negative synergistic impact on the immune system, accelerating disease progression and increasing mortality (Misutarno, et al 2024). The significantly decreased CD4 levels due to HIV make the body very susceptible to the activation of latent TB into active TB, even with small amounts of exposure to germs (Rismarwati et al., 2024).

This condition is exacerbated by various other factors, such as low adherence to treatment, poor socioeconomic conditions, and high exposure to an unhealthy environment. Some studies also highlight that delayed diagnosis and lack of integration of TB-HIV services also increase the risk of complications and therapy failure (Anggraeni et al., 2024). Therefore, it is important to comprehensively identify the various risk factors that contribute to the incidence of pulmonary TB in HIV patients.

This discussion will systematically outline the findings of fifteen selected journals with a focus on the main risk factors divided into several categories, namely immunological and clinical, socioeconomic and demographic, environmental, behavioral, and health care systems.

Immunological and Clinical Factors

Low CD4 levels have consistently been a major risk factor in almost all studies. Patients with CD4 <200 cells/mm^3 have a higher susceptibility to pulmonary TB, as found in a study in Cilegon that reported that 97.22% of HIV-TB patients had CD4 <200 (Widyaningrum et al., 2022) Meta-analysis conducted by (Sari et al., 2022) also showed an increased risk of death with decreased CD4 levels, especially in the <50 cell/µL category. Similar things were reported by (Dwi Puspita Sari & Ella Nurlaella Hadi, 2023) who developed a risk prediction nomogram for active TB based on CD4 count and previous TB history.

In addition to CD4, the clinical stage of advanced HIV has also been shown to be significant. (Misutarno et al., 2024) suggests that stage III–IV has a strong correlation with TB incidence. These results are reinforced by (Marfidhotul Iftitah et al., 2020) and (Haryani et al., 2023) who found that patients with advanced HIV were more at risk of TB coinfection.

The model showed good performance with a C-index of 0.72 in the training data and 0.68 in the validation data. With a sensitivity of 93% and a specificity of 35% at the cutoff of a score of 100, this nomogram has been shown to be superior to the WHO W4SS algorithm and the XPHACTOR model in detecting active TB in HIV patients (Chen et al., 2022). This confirms that a clinical data-based prediction approach can improve early detection of TB, especially in resource-constrained areas.

Socio-Economic and Demographic Factors

Several socioeconomic characteristics, such as education and employment status, also affect risk. (Widyaningrum et al., 2022) It found that the majority of co-infected patients were men aged 15–35 years old with a secondary education background and working in the informal sector. Another study in Bogor showed that low socioeconomic status and male gender increased the risk of TB (Haryani et al., 2023).

Environmental Factors

Exposure to household air pollution is an important finding in the study (Katoto et al., 2024) They revealed that high carbon monoxide levels due to the use of biomass fuels and poor ventilation increased the risk of pulmonary TB by up to 4.64 times in the HIV population. This condition is an important highlight in developing countries with limited healthy housing infrastructure.

Adherence to Therapy

Patient adherence to treatment determines the success of TB-HIV therapy. (Botutihe et al., 2024) mentioned that family support and the active role of health workers were the main predictors of compliance, while economic and age factors also influenced. On the other hand, at Abepura Hospital, Jayapura, more than a third of TB-HIV patients have stopped taking medication, and this has a negative impact on therapy outcomes (Anggraeni et al., 2024).

Health Service Quality and Drug Resistance

The influence of service quality is reflected in the study (Budiyani et al., 2024) which states that the success of TB-HIV therapy is higher in patients who undergo treatment at health centers and receive ART. In China, (Zhou et al., 2023) found that HIV diagnosis after TB as well as non-local status were risk factors for therapy failure, followed by high rates of resistance to rifampicin and isoniazid.

Dual Burden of Therapy and Management Complexity

The complexity of HIV-TB co-infection treatment is a challenge for clinicians (Rosfita, et al., 2023) noted that the interaction between ARVs and OAT, delayed diagnosis, and lack of service integration are major barriers in the management of coinfection. This is confirmed by a case report from Padang that shows the success of long-term therapy when ART is administered in an integrated manner with OAT (Rizki, 2025).

Additional Factors: Body Mass Index

(Gatechompol et al., 2022) mentioned that in addition to CD4, body mass index <18 kg/m^2 and the use of addictive substances also significantly increased the incidence of TB in HIV patients undergoing long-term ART.

Conclusion

Pulmonary tuberculosis in patients with HIV is a complex and multifactorial co-infection condition, which significantly increases morbidity and mortality. Based on a review of 15 journals, it was found that the main risk factors that consistently appeared included CD4 levels <200 cells/mm^3, advanced clinical stage of HIV, and delayed diagnosis. Socio-economic factors such as low education levels, informal

employment status, and poor economic conditions also contribute to increased vulnerability to infection. In addition, environmental factors such as exposure to indoor air pollution, poor ventilation, and a history of contact with TB patients also have a significant contribution to the incidence of TB in HIV patients.

Adherence to treatment, both OAT and ART therapy, is an important factor that determines the success of therapy and the prevention of relapse. Family support, the role of health workers, and the quality of services in health facilities have been proven to play a role in improving patient clinical outcomes. These findings confirm the importance of a holistic and integrative approach to TB prevention and management in HIV patients, including CD4-based early detection and symptom screening, strengthening patient education, and effective integration of TB-HIV services.

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