# **Analysis of Pulmonary Tuberculosis Prevalence in HIV/AIDS Patients Based on Co-Infection Aspects**

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#### ABSTRACT

TB and HIV co-infection occurs when a person has active or latent TB and HIV infection. HIVpositive sufferers have a 30 times greater risk of getting TB than HIV-negative people. This study aimed to analyze the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on the co-infection aspect at the Southeast Sulawesi Health Office. This study used a design analytic observational with a crosssectional approach. The population in the study was all TB and HIV/AIDS patients who were recaptured at the Southeast Sulawesi Provincial Health Office. The sample size was 105 people. The results showed that CD4 levels significantly affected the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on coinfection at the Southeast Sulawesi Health Office. The clinical stage has a significant effect on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on co-infection at the Southeast Sulawesi Health Office; nutritional status has a significant effect on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on co-infection at the Sulawesi Health Office Southeast Sulawesi and Hb levels have a of significant effect on the prevalence pulmonary TB in HIV/AIDS patients based on co-infection at the Southeast Sulawesi Health Office.

*Keywords:* Prevalence, Tuberculosis, HIV/AIDS, co-infection

## **INTRODUCTION**

HIV/AIDS is an infectious disease that threatens many countries, including Indonesia (Makam & Matsa, 2021). Human Immunodeficiency Virus (HIV) is a virus that infects white blood cells, causing a decrease in human immunity. This infection also causes sufferers to experience decreased body resistance, making it very easy to be infected with various other diseases. Acquired Immune Deficiency Syndrome (AIDS) is a collection of disease symptoms from decreased immunity caused by HIV infection (Dafitri et al., 2020). According to the 2020 UNAIDS annual 38 million people live with report, HIV/AIDS around the world, of whom 1.7 million are newly infected with HIV/AIDS, and 690 thousand people die. The largest HIV-infected population in the world is on the African continent, with as many as 25.7 million people; Southeast Asia, as many as 3.8 million people; and America, as many as 3.5 million people. The lowest was in the West Pacific, with 1.9 million people. The high population of people infected with HIV in Southeast Asia requires Indonesia to be vigilant about the spread and more transmission of this virus (UNSAID, 2021). The development of HIV/AIDS in Indonesia tends to fluctuate. Data shows that over the last eleven years, the number of HIV cases in Indonesia peaked in 2019, namely 50,282 cases. The highest number of AIDS cases in

the last eleven years was in 2013, with 12,214 cases. While the number of people living with HIV was reported to be as many as 7,650 out of 810,846 people tested for HIV, and 6,762 people received ARV treatment (Kemenkes RI, 2018).

The number of HIV/AIDS cases in Southeast Sulawesi has reached 9,871 cases, for 2022 the number of HIV/AIDS cases is 162 cases spread across 17 Regencies/Cities, with the highest number of cases being in Kendari City, with a total of 59 cases, followed by South Konawe Regency with a total of 30 cases and Bau-Bau City with a total of 17 cases. It is estimated that the number of HIV/AIDS cases will continue to increase if preventive measures are not taken immediately (Dinkes Propinsi Sulawesi Tenggara, 2021).

HIV/AIDS is a disease that needs to be aware. HIV, which is a disease that causes a decrease in the body's immunity, will encourage patients to get other infections. The co-infection of the disease often experienced by HIV/AIDS patients is Tuberculosis (TB). WHO estimates that TB has become the cause of 13% death of people with AIDS. Even though the risk of being infected with TB drops by 70-90% in patients taking ART, TB is still the most common cause of death in people with HIV (Cahyati, 2019; Cui et al., 2017).

*Tuberculosis* is a direct infectious disease caused by Mycobacterium tuberculosis. TB and HIV coinfection occurs when a person has active or latent TB and HIV infection. People who are HIV positive have a 30 times greater risk of getting TB than people who are HIV negative. Each infection, both TB and HIV infection, will accelerate the process of worsening the other. HIV infection will speed up the process from latent TB to active TB, while TB bacterial infection will worsen the condition of people living with HIV (Dalbo & Tamiso, 2016; Damayati et al., 2018).

According to the UNAIDS report, in 2018, there were 10 million new cases of TB, and around 9% of them occurred in HIV patients. People living with HIV without TB symptoms require TB preventive therapy, which reduces the risk of developing TB and reduces the TB/HIV mortality rate by about 40%. Many cases of death from TB-HIV occur in countries with low to middle income, namely in Asia and Africa (UNSAID, 2021). As a country in Asia, Indonesia noted that in 2018, the number of tuberculosis cases was 569,899, with an estimated 35% that had not been reported. For TB-HIV cases, there were 10,174 people. Then it increased to 568,987 in 2019, with 12,015 people with TB-HIV cases (Dafitri et al., 2020).

*Tuberculosis* is the most common opportunistic infection found in Human Immunodeficiency Virus (HIV) infection and is the highest cause of death in people living with HIV/AIDS (PLWHA). The incidence of TB-HIV coinfection becomes a serious case which, if not treated immediately, will cause difficult-to-control problems. The risk of TB transmission is 26 to 31 times greater in people with HIV compared to people without HIV (Dalbo & Tamiso, 2016; Damayati et al., 2018).

Factors such as age, sex, CD4 level, haemoglobin level, nutritional status, and clinical stage influence **TB-HIV** coinfection. In their research, Iftitah et al. (2020) stated that the clinical stage of TB-HIV co-infected patients has a significant relationship and is a risk factor for TB coinfection in HIV patients in Malang Regency. Patients with symptoms and signs of clinical stage 3 or 4 usually have a severely weakened immune system and CD4 insufficient cells facilitate to opportunistic infections. Further research suggests several other biological mechanisms that could explain the results related to BMI: (1) HIV patients with low CD4 counts tend to lose weight, and (2) people with HIV are more likely to maintain their CD4 counts at higher levels, with a possible explanation of the protective effect of fat or adipose cells its selves (Friedman et al., 2018; Kim et al., 2016).

# **MATERIALS & METHODS**

This cross-sectional study was carried out at the Southeast Sulawesi Provincial Health Office from March to April 2023 which involved patient data at the Southeast Sulawesi Provincial Health Office who were diagnosed with HIV/AIDS for the 2019-2022 period, with a total of 9,871 patients but after being screened using the sample criteria, a total sample of 105 people was obtained.

The inclusion criteria include data on patients diagnosed with TB/HIV/AIDS registered at the Southeast Sulawesi Provincial Health Office for the 2019-2022 period, suffering from TB and being positive for HIV/AIDS without other comorbidities and having complete data regarding the history of the disease, such as clinical stage, nutritional status. , CD4 and HB levels. At the same time, patients suffering from TB with comorbidities other than HIV/AIDS.

The dependent variable in this study was the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on co-infection, and the independent variables were CD4 levels, clinical stage, nutritional status and haemoglobin levels. CD4 level is the number of markers of the immune system (CD4) examined in HIV testing in units of cells/mm3 when the patient is diagnosed with HIV/AIDS with objective criteria: Severe risk: If the patient with HIV/AIDS has a CD4 level <200 cells/mm, risk Moderate: If an HIV/AIDS patient has a CD4 level >200 cells/mm, Mild risk: If an HIV/AIDS patient has a CD4 level=200 cells/mm.

The Clinical variable stage is the severity of HIV based on the CD4 count <200 cells/mm and the symptoms the patient suffers. Clinical stages are divided into four stages with objective criteria: Advanced stage: If the HIV/AIDS patient is in stage III or IV; low stage: If the HIV/AIDS patient is in stage I or II

The variable Nutritional status is the nutritional state of the patient at the time of diagnosis of HIV/AIDS, which is

categorized based on BMI with objective criteria: Poor: If the HIV/AIDS patient has a BMI <18.5 kg/m2, Poor: If the HIV/AIDS patient has a BMI > 18.5 kg/m2, Good: If the HIV/AIDS patient has BMI = 18.5 kg/m2. Haemoglobin level is the value of the patient's blood haemoglobin level in g/dl when the patient is diagnosed with HIV/AIDS with objective criteria: High risk: If the HIV/AIDS patient has a Hb level <11 g/dl, Low risk: If the HIV/AIDS patient has a Hb level Hb > 11 g/dl, Not at risk: If an HIV/AIDS patient has a Hb level = 11 g/dl

Medical record data for all HIV/AIDS patients retrieved from the Southeast Sulawesi Provincial Health Office during 2019-2022. Data is input into SPSS ver.16.0, which is then verified. Data out using analysis was carried the prevalence and frequency distribution than the data was presented descriptively in the form of narration, text and tables. The second is the relative prevalence analysis and simple linear regression test.

## RESULT

The distribution of frequencies shown in a list, table, or diagram shows the frequency of the various events in a sample. This study presented data using tables for each variable (CD4, Clinical Stage, Nutritional Status, and Risk Hb Levels).

Table 1 Frequency	Distribution of Resea	rch variables

Variables	Frequency	%
CD4		
Severe	67	63,8
Moderate	11	10,5
Mild	27	25,7
Stadium klinis		
Advanced	73	69,5
Low	32	30,5
Status gizi		
Worst	47	44,8
Poor	31	29,5
Good	27	25,7
Kadar HB		
High	79	75,2
Low	21	20
No risk	5	4,8

Table 1 shows that the frequency distribution of CD4 levels in HIV/AIDS patients for severe risk is 67 people or 63.8%, moderate risk is 11 people or 10.5%,

and mild risk is 27 people or 25.7%. It can be concluded that 67 out of 105 HIV/AIDS patients, or 63.8% had CD4 levels <200 cells/mm.

The frequency distribution of clinical stages in HIV/AIDS patients for the advanced category was 73 people or 69.5%, and the low stage was 32 people or 30.5%. It can be concluded that as many as 73 people out of a total of 105 HIV/AIDS patients, or 69.5%, have reached stage III or IV.

The frequency distribution of nutritional status in HIV/AIDS patients for the bad category was 47 people or 44.8%, the poor category was 31 people or 29.5%, and the good category was 27 people or 25.7%. It can be concluded that the majority of HIV/AIDS patients had poor nutritional status, namely as many as 47 out of a total of 105 HIV/AIDS patients or 44.8% of whose nutritional status had a BMI <18.5 kg/m2.

The frequency distribution of Hb levels in HIV/AIDS patients for the high-risk category was 79 people or 75.2%, the low-risk category was 21 people or 20%, and no risk was five people or 4.8%. It can be concluded that the majority of HIV/AIDS patients who have high-risk Hb levels have Hb levels <11 g/dl, namely 79 people out of a total of 105 HIV/AIDS patients or 75.2%.

Table 2 Tuberculosis & HIV/AIDS Crosstabs

		HIV	HIV/AIDS	Total
Tuberculosis	Yes	73	32	105
	No	57	0	57
Total		130	32	162

After calculating the prevalence value, the PR value = 0.39 < 1. It can be concluded that both tuberculosis and HIV/AIDS are mild risk factors.

A simple linear regression test can be used to determine the effect of the independent and dependent variables, in this case, the effect of CD4 levels, clinical stage, nutritional status, and Hb levels on the prevalence of tuberculosis. This test uses the SPSS 25 application. The results of the analysis can be seen in the following table.

Table 3. Simple Linear Regression Test Results				
Variable (x)	RSquare (%)	Significance		
Kadar CD4	66,1 %	0,000		
Clinical stage	59,4 %	0,000		
Nutrition status	45,2 %	0,000		
Hb level	80 %	0,000		

Table 3 shows that the four variables have a significance value of 0.000 <0.05, which means that the four variables (CD4 levels. clinical stage, nutritional status, and Hb levels) influence the prevalence of tuberculosis. CD4 level has a correlation rate of 66.1% with the prevalence of tuberculosis, the clinical stage has a correlation rate of 59.4% with the prevalence of tuberculosis, nutritional status has a correlation rate of 45.2% with the prevalence of tuberculosis, and the Hb level has a correlation rate of 80% with the prevalence of tuberculosis.

# DISCUSSION

The first variable in this study was the CD4 level variable to analyze the effect of CD4 levels on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on the co-infection aspect at the Southeast Sulawesi Provincial Health Office. The number of CD4 cells in the blood is a reliable indicator to monitor the severity of immune damage caused by HIV. It facilitates us to make decisions about giving anti-retroviral treatment.

The frequency distribution of CD4 levels in HIV/AIDS patients for mild risk was 27 people or 25.7%, moderate risk was 11 people or 10.5%, and severe risk was 67 people or 63.8%. It can be concluded that 67 out of 105 HIV/AIDS patients, or 63.8% had CD4 levels <200 cells/mm. CD4 levels significantly affect tuberculosis's prevalence, with a value of 0.000 < 0.05. In line with a study conducted by Jamil (2014), which concluded that a decrease in CD4 levels indicates an increase in the incidence of pulmonary tuberculosis infection in people with HIV. However, patients with the same CD4 levels can still have different opportunistic infections. Further research was revealed by (Lima et al., 2016), which stated that the clinical characteristics of

patients showed that the majority of HIV/AIDS patients with TB co-infection had an advanced clinical stage (3 or 4) and a CD4 count <200 cells/mm3. The average CD4 count in HIV/AIDS patients with TB co-infection was lower, around 169 cells/mm3, compared to HIV/AIDS patients without TB co-infection, which was 377 cells/mm3.

CD4 count is a method for assessing the immune status of PLWHA. CD4 examination complements clinical examination to determine patients who need prophylactic OI treatment and ARV therapy. (TLC) cannot replace CD4 screening. A decrease in CD4 levels indicates an increased occurrence of opportunistic infections in people with HIV, although patients with the same CD4 levels can still have different opportunistic infections.

The second variable that was measured in the study was the clinical stage variable with the aim of analyzing the effect of clinical stage on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on the co-infection aspect at the Southeast Sulawesi Provincial Health Office. Clinical stage is a very influential indicator of disease occurrence. TB and HIV this is because the clinical stage directly affects the decrease in CD4 levels in the body.

The frequency distribution of clinical stages in HIV/AIDS patients for the mild category was 32 people or 30.5% and the severe risk was 73 people or 69.5%. It can be concluded that as many as 73 people out of a total of 105 HIV/AIDS patients or 69.5% have reached stage III or IV. Clinical stage has a significant effect on the prevalence of tuberculosis of 0.000. This is in line with research conducted by Cahyati (Cahyati, 2019) which stated that in the variable clinical stage of the case group the percentage of patients with clinical stages III and IV was 93.33% and clinical stages I and II were 6.6%. Whereas in the control group clinical stages III and IV were 0% and clinical stages I and II were 100%. Based on statistical tests using Fisher's test, a p value of 0.000 was obtained so that Ho was rejected. This means that it can be seen that there is a relationship between the clinical stage of HIV and the incidence of tuberculosis in PLHIV.

In advanced stages of HIV/AIDS (stage 3 and stage 4), there has been massive destruction of CD4+ cells, and even the intensity of CD4+ reaches below 200 cells/mm3. CD4+ cells are the main target of HIV, and the progressive destruction of these cells is a characteristic of all stages of HIV disease. Human immunodeficiency virus (HIV) can kill one by one or after giant cells and syncytium is formed. Singlecell killing occurs due to the accumulation of unintegrated viral DNA and inhibition of synthesis. cellular protein Svncvtium formation is induced by a virulent strain of HIV in a stepwise mechanism. CD4+ cells that express viral antigens on the surface will attract uninfected CD4+ cells, resulting in a fusion of the membranes that form a syncytium. One HIV-infected cell can damage hundreds of uninfected cells by forming a syncytium (Fajrunni'mah & Mirawati, 2022). In the group that experienced CD4 destruction, especially below 200 cells/mm3, the immune integrity of HIV patients was very low. It was characterized by a loss of immune system function in maintaining body health, so the risk of being exposed to and infected with TB bacteria became very high (Kim et al., 2016).

The third variable measured in the study was the nutritional status variable to analyze the effect of nutritional status on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on the coinfection aspect at the Southeast Sulawesi Provincial Health Office. In general, nutrients affect the immune system through a mechanism of regulation of cytokine excretion and production because the pattern of cytokine production is important in the response to infection. Poor nutritional conditions will affect a person to get an infectious disease because a good nutritional status will correlate with an increase in

immunity which functions as an antidote to the infection.

The frequency distribution of nutritional status in HIV/AIDS patients for the bad category was 47 people or 44.8%, the poor category was 31 people or 29.5%, and the good category was 27 people or 25.7%. It can be concluded that the majority of HIV/AIDS patients had poor nutritional status, namely as many as 47 out of a total of 105 HIV/AIDS patients or 44.8% of whose nutritional status had a BMI <18.5 kg/m2. Nutritional status has a significant effect on the prevalence of tuberculosis of 0.000. In line with research conducted by Janan (2019), which states that nutritional status significantly affects the prevalence of TB-HIV disease with a significant number of 0.00 <0.05. Monitoring the nutritional status of TB patients regularly during visits or taking medication at the Puskesmas/RS. Providing consultations to TB patients regarding drug side effects that can affect the patient's nutritional intake, such as nausea, vomiting or diarrhoea.

Malnutrition is a major risk factor for TB. HIV not only causes TB co-infection directly but also causes other infections, including gastrointestinal tract (GI tract) infection. Infection of the GI tract causes abnormal absorption of D-xylose and fat in the small intestine. In addition, GI tract infection will cause diarrhoea, resulting in dehydration. In addition, HIV drugs such as highly active antiretroviral (HAART) have several side effects, such as diarrhoea, which further exacerbate weight loss (Sitorus et al., 2022).

Lack of nutritional intakes, such as glucose in CD4 cells, will cause immune system cells to lose their function and main mechanism in eradicating TB bacilli. Research by Taha et al. (2007) also shows a correlation between low body weight and the development of TB. First, TB can cause malnutrition and anaemia through anorexia, increased metabolic rate, and malabsorption. On the other hand, malnutrition can exacerbate immune deficiency and increase the risk of active TB (Rubaihayo et al., 2016; Sekalala, 2017).

The fourth variable in this study was the HB level variable to analyze the effect of HB levels on the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on the co-infection aspect at the Southeast Sulawesi Provincial Health Office. Low haemoglobin levels can cause reduced oxygen in the lungs which can cause TB symptoms, one of which is shortness of breath. Anaemia, which means Hb levels are below the normal value, is a haematological disorder.

The frequency distribution of Hb levels in HIV/AIDS patients for the high-risk category was 79 people or 75.2%, the lowrisk category was 21 people or 20%, and no risk was five people or 4.8%. It can be concluded that the majority of HIV/AIDS patients who have high-risk Hb levels have Hb levels <11 g/dl, namely 79 people out of a total of 105 HIV/AIDS patients or 75.2%. Hb levels have a significant effect on the prevalence of tuberculosis of 0.000. In line with research conducted by Krisnahari & AAS (2018),which concluded that haemoglobin levels in patients with pulmonary tuberculosis in this study were in the abnormal category of 13 patients (54%) and normal category of 11 patients (46%). Tuberculosis sufferers get results with haemoglobin levels that are below normal or low due to other causes due as a weak immune system, consuming less nutritious food and consuming less iron-containing foods such as vegetables and fruit. Apart from this, side effects of drugs, such as nausea, can also affect the appetite of tuberculosis sufferers and symptoms of coughing up blood that occurs for a long time, causing blood vessels to burst. As for tuberculosis sufferers with normal haemoglobin levels, it is caused by a good immune system and awareness of the importance of maintaining a good health pattern by maintaining dietary nutrition, consuming iron regularly and getting enough rest.

The decrease in haemoglobin levels related to antiretroviral therapy in patients infected with HIV/AIDS most likely occurs due to three mechanisms, namely decreased red blood cell production, increased red blood cell destruction, and ineffective red blood production. Generally, the cell three mechanisms include bone marrow infiltration caused by neoplasm or infection, endogenous decreased erythropoietin, hemolytic anaemia, drug and use (Krisnahari & AAS, 2018; Soraya & Artika, 2016).

## CONCLUSION

CD4 levels, clinical stage, nutritional status and HB levels significantly affect the prevalence of pulmonary tuberculosis in HIV/AIDS patients based on co-infection at the Southeast Sulawesi Health Office.

## **Declaration by Authors**

**Ethical Approval:** This study obtained ethical feasibility under the Health Research Ethics Commission of the Halu Oleo University, Indonesia.

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