

# Demographic and Clinical Risk Factors for Tuberculosis Co-Infection in HIV patients: A Literature Review

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## Abstract

Tuberculosis (TB) is an opportunistic infectious disease that is most often found in HIV infection. HIV-TB coinfection is currently the main cause of mortality in the world due to this infectious agent. The aim of this study was to analyze factors in HIV co-infection with Tuberculosis demographically and clinically. The research design in this article is a literature review, by searching several literature sources in the form of research journals and determining the risk of Nataru HIV co-infection with Tuberculosis in the journal. The selected research journal summarizes the research design, research description, variables and research results. Based on research results from several journals, it is known that there are many cases of co-infection between HIV patients and Tuberculosis cases, because tuberculosis is an opportunistic disease that easily infects people with low immune systems. In the studies that have been reviewed it can also be said that the key to the increase Tuberculosis cases are people who have low CD4 or a vulnerable immune system.

Keywords: Co-Infection, PLHIV, Tuberculosis, HIV-TB Co-Infection

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## 1. Introduction

Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system. Infection with this virus can reduce the ability of human immunity to fight foreign objects in the body, which in the terminal stage of infection can cause Acquired Immunodeficiency syndrome (AIDS). HIV is a virus that attacks the white blood cells in the body (lymphocytes) resulting in a decrease in human immunity. A person with HIV in their blood may appear healthy and not necessarily need treatment. However, they can transmit the virus to others if they have risky sex and share injecting equipment with others (Nurlinda et al., 2021).

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Since 1975 more than 75 million people have been infected with the HIV virus and approximately 32 million people have died from HIV. Globally, 36.9 million (32.7-44.0 million) people were living with HIV at the end of 2018. An estimated 0.8% (0.6-0.9%) of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic continues to vary widely between countries and regions. The WHO region of Africa remains hardest hit, with nearly 1 in every 25 adults (3.9%) living with HIV and accounting for nearly two-thirds of people living with HIV worldwide (Nurlinda et al., 2021).

Globally, 1.3 million (1.0-1.7 million) people will be infected with HIV by 2022. Since 2010, the number of people infected with HIV has decreased by 38%, from 2.1 million (1.6-2.8 million). There will be 130,000 (90,000-210,000) children infected with HIV by 2022 (2). By 2022, 630,000 [480,000-880,000] people will die from HIV-related diseases globally. Since 2010, HIV-related deaths have been reduced by 51%, from 1.3 million (970,000-1.8 million). The global HIV epidemic will claim 69% fewer lives by 2022 since its peak in 2004. And 84,000 (56,000-120,000) children will die from HIV-related causes by 2022. HIV continues to be a major global public health problem, having so far claimed 40.4 million [32.9-51.3 million] lives (WHO, 2023).

WHO treatment data show that 29.8 million people living with HIV are receiving antiretroviral therapy globally. Of people living with HIV in 2022, 86% [73->98%] know their status, 76% [65-89%] are receiving treatment and 71% [60-83%] have suppressed viral load (WHO, 2023). In the African region, the WHO estimates that 25.6 million (21.6-30.0 million) people will be living with HIV by 2022, with 90% (76 to >98%) knowing their status, 82% (69-96%) receiving treatment and 76% (64-89%) having suppressed viral load. An estimated 20.9 million people are receiving antiretroviral therapy in 2022. An estimated 660,000 (480,000-920,000) people are infected with HIV in 2022; and the number of people infected with HIV across all ages declines to 0.57 (0.41-0.8) per 1000 uninfected population in 2022 from 1.75 [1.24-2.44] in 2010. 380,000 (300,000-540,000) deaths attributable to HIV-related causes by 2022, a decrease of 56% from 2010 (WHO, 2023).

In Southeast Asia, the WHO estimates that 3.9 million (3.4-4.6 million) people will be living with HIV by 2022, of which 81 per cent (70-94 per cent) will know their status, 65 per cent (57-76 per cent) will be on treatment and 61 per cent (53-71 per cent) will have reduced viral load. An estimated 2.6 million people received antiretroviral therapy in 2022. An estimated 110,000 (85,000-160,000) people are infected with HIV in 2022; and the number of people infected with HIV across all ages declines to 0.06 (0.04-0.08) per 1000 uninfected population in 2022 from 0.12 (0.09-0.16) in 2010. 85,000 (62,000-120,000) deaths attributable to HIV-related causes by 2022, a decrease of 63.4% from 2010 (WHO, 2023).

In the 2015 Belay study of 287 pulmonary TB suspects tested for HIV, 82 (28.6%) were HIV positive. A significantly higher proportion of bacteriologically confirmed pulmonary TB patients [40 (40.4%)] were HIV co-infected compared to patients without bacteriological evidence for pulmonary TB [42 (22.3%)]. However, among Afar ethnic pastoralists, HIV infection in BTA and/or culture negative pulmonary TB suspects [7 (7.6%)] and bacteriologically confirmed pulmonary TB patients [4 (11.8%)] is comparable Tuberculosis (TB) is the most common opportunistic infectious disease in HIV infection. HIV-TB co-infection is now the leading cause of mortality worldwide due to these infectious agents (Mulungeta et al., 2015).

## 2. Method

This literature review was made by collecting, reviewing, and citing related journals. The journals were obtained through searches from Google Scholar and Pubmed search engines. The keywords used in the search included "Tuberculosis Co-Infection", "HIV Patient". The journals used were published between 2015-2023. From the search results, 15 journals were obtained and reviewed.

### 3. Result

The literature search through the data base obtained 15 articles that will be reviewed in this study. A summary of the articles reviewed in this study can be seen in Table 1.

Tabel 1. Summary of reviewed articles

No.	Title	Author	Objective	Design	Sampling	Main Findings
1.	Analysis of tuberculosis/hiv co-infection trends in Ukraine in 2008-2017	Tetiana V. Stepanova, Olga P. Nedospasova, Mykhailo V. Golubchikov (2019)	To conduct a comprehensive analysis of the epidemic situation regarding tuberculosis/HIV co-infection in Ukraine according to selected epidemiological and clinical characteristics.	Retrospective Epidemiological Study	8000 secondary data from the Ministry of Health 2008-2017	It was found that the incidence of newly diagnosed active tuberculosis associated with HIV in Ukraine increased by 89.4% - from 6.1 per 100,000 population in 2008 to 11.6 per 100,000 population in 2017, against the background of a gradual decrease in the incidence of active tuberculosis by 36.5% over the same period. The TB/HIV comorbidity rate increased 2.8-fold from 7.9% to 20.3%. The incidence rate of TB/HIV co-infection was highest among people aged 25-44 years, men, urban residents, and in the southern regions of Ukraine.
2.	Systematic or Test-Guided Treatment for Tuberculosis in HIV-Infected Adults	Fracois-Xavier Blanc et al, (2020)	Conduct a randomised clinical trial to compare the benefits and risks of a tuberculosis screening strategy involving a combination of ancillary investigations (urine LAM test, Xpert MTB/RIF test, and chest radiography) and targeted treatment with a systematic empirical strategy of tuberculosis treatment in HIV-infected patients with severe immunosuppression.	Pseudo-Experiment	522 patients in the systematic treatment group and 525 patients in the guided treatment group were involved	It was found that at week 24, the death rate from any cause or invasive bacterial disease (calculated as the number of first events per 100 patient-years) was 19.4 with systematic treatment and 20.3 with guided treatment (adjusted hazard ratio, 0.95; 95% confidence interval.) [CI], 0.63 to 1.44). At week 48, the corresponding figures were 12.8 and 13.3 (adjusted hazard ratio, 0.97 [95% CI, 0.67 to 1.40]). At week 24, the odds of tuberculosis were lower with systematic treatment than with guided treatment (3.0% vs. 17.9%; adjusted hazard ratio, 0.15; 95% CI, 0.09 to 0.26), but the odds of grade 3 or 4 drug-related adverse events were higher with systematic treatment (17.4% vs. 7.2%; adjusted hazard ratio 2.57; 95% CI, 1.75 to 3.78). Serious adverse events were more common with systematic treatment.
3.	Genetic polymorphism of toll-like receptors in HIV-I infected patients with and without tuberculosis co-infection	Gaurav Kaushi et al (2022)	Identify differences in Toll-like receptor genetic polymorphisms in HIV-I infected patients with and without tuberculosis co-infection	Prospektif Cross-sectional (potong lintang)	223 HIV positive patients, 150 HIV positive patients with latent tuberculosis (TB) infection, 150 HIV positive	It was found that there were statistically significant differences observed in TLR4 allelic frequencies between healthy subjects and HIV+ TB patients ( $P < 0.001$ ), healthy subjects, and Category-I pulmonary TB (PTB) patients ( $P < 0.01$ ) and between healthy subjects and HIV+ TB patients ( $P < 0.001$ ). TLR4 genotype frequencies were also significantly different between healthy subjects and PTB Cat I patients ( $P < 0.001$ ) as well as HIV+ and HIV+TB patients ( $P < 0.01$ ).

					patients with active TB, 200 HIV negative patients newly diagnosed with sputum BTA positive pulmonary TB, and 205 healthy subjects.	Statistically significant differences were also observed between HIV+ and PTB Cat I patients ( $P = 0.04$ ), HIV+ LTBI and HIV+ TB patients ( $P = 0.01$ ), and between HIV+ TB and PTB Cat I patients ( $P < 0.01$ ).
4.	Prevalence and associated factors of HIV-TB co-infection among HIV patients: a retrospective Study	Melakamu A Zeru (2021)	This study was designed to assess the prevalence of TB/HIV co-infection and determine the underlying factors.	Retrospective Study	514 HIV patients on ARVs	Five hundred and fourteen patients were enrolled in this study. Of these, 187 (37.4%) had TB. Bivariate logistic analysis showed that HIV patients based on marital status [AOR = 2.6; 95%CI = 1.19-2.89], educational status [AOR = 3.74; 95%CI = 2.47-5.66], weight less than 50kg [AOR = 2.54; 95%CI = 1.35 - 4.81], CD4 count < 200 cells/mm <sup>3</sup> [AOR = 4.57; 95%CI = 2.38 - 6.86] and patients in WHO clinical stage III [AOR = 7.8; 95%CI = 5.15 - 8.55] were significantly associated with TB/HIV co-infection.
5.	The socio-demographic, clinical characteristics and outcomes of tuberculosis among HIV infected adults in Lithuania: A thirteen-year analysis	Elzbieta Maltulyte et al (2023)	This study aimed to identify socio-demographic, clinical characteristics and their association with TB outcomes in patients with TB-HIV co-infection in Lithuania.	Retrospective Study	311 patients (239 new cases, 106 previously treated cases)	The study included 345 cases in 311 patients (239 new cases, 106 previously treated cases), median age 40 years (IQR 35-45), 80.7% male. 67.8% of patients knew their HIV positive status before TB diagnosis, median time to TB diagnosis was 8 years (IQR 4-12). 83.6% were unemployed, 50.5% injecting drug users (IDUs), 34.9% abused alcohol. The rates of drug-resistant TB in new TB cases and previously treated TB cases were 38.1% and 61.3%, respectively. In multivariable analysis, a higher risk of drug-resistant TB was associated with imprisonment in both new (aOR 3.35; 95%CI 1.17-9.57) and treated (aOR 6.63; 95%CI 1.09-40.35) cases. In 52.3% of new TB cases and 42.5% of previously treated TB cases, the treatment outcome was unsuccessful. In a multivariable analysis of new TB cases, current imprisonment (aOR 2.77; 95%CI 1.29-5.91) and drug-resistant TB (aOR 2.18; 95%CI 1.11-4.28) were associated with unsuccessful treatment outcomes. In a multivariable analysis of previously treated TB cases, female gender (aOR 11.93; 95%CI 1.86-76.69), alcohol abuse (aOR 3.17; 95%CI 1.05-9.58), drug-resistant TB (aOR 4.83; 95%CI 1.53-15.28) were associated with unsuccessful treatment outcomes.

6.	Survival rate and mortality risk factors among TB-HIV co-infected patients at an HIV-specialist hospital in Myanmar: A 12-year retrospective follow-up study	Zaw Zaw Aung et al. (2023)	The aim of this study was to assess these factors among TB-HIV co-infected patients enrolled at MSH Mingalardon Specialist Hospital in Yangon Region, Myanmar, from 1 July 2005 to 31 December 2016.	Retrospective Study	3598 TB-HIV co-infected patients (2452 males and 1146 females) aged 15 years and above	A total of 494 (13.7%) patients died during this period. The survival rate of TB-HIV co-infected patients was 82.0% at 5 years and 58.1% at 10 years. Risk factors for mortality were bedridden (adjusted hazard ratio (aHR) 2.70, 95% confidence interval (CI) 2.13-3.42), having a low baseline CD4 count (aHR 1.53, 95% CI 1.25-1.87), and being on a second-line ART regimen (aHR 8.12, 95% CI 3.56-18.54).
7.	Tuberculosis and HIV co-infection in Congolese children: risk factor of death	Mukuku et al. (2019)	To determine the prevalence of HIV infection in children treated for tuberculosis (TB) in Lubumbashi, Democratic Republic of Congo (DRC) and identify risk factors for chemopathy due to TB/HIV co-infection in these children.	Cross-Sectional	840 children	The prevalence of HIV infection was 20.95% (95% CI = 18.34 - 23.83%) and the mortality rate in HIV-infected children (47.73%) compared to HIV-uninfected children (17.02%) ( $p < 0.00001$ ). Age < 5 years (AOR = 6.5 [1.96 - 21.50]), with poor nutrition (AOR = 23.55 [8.20 - 67.64]), and negative acid-fast bacilli test results (AOR = 4.51 [1.08 - 18.70]).
8.	Risk Factor for TB/HIV co-infection and consequences for patient outcomes: evidence from 241 clinics in the Democratic Republic of Congo	Shah et al (2021)	To analyse variation in TB/HIV co-infection and negative risk in patients with TB/HIV co-infection from two provinces in the Democratic Republic of Congo.	Retrospective Quantitative Study	49,460 patients from 241 clinics (aged <15 years and $\geq 15$ years) in Haut-Katanga and Kishasa, Democratic Republic of Congo	A significantly higher proportion of patients with TB/HIV co-infection were male (4.5%) female (3.3%), new patients (3.7%; transfer-in, 1.6%), living in Kinshasa (4.0%) Haut-Katanga (2.7%) province, and in urban (3.9%) or semi-rural (3.1%), rural (1.2%) health zones. Logistic regression analysis showed that after controlling for demographic and kinetic variables, TB/HIV co-infection increased the risk of death (adjusted odds ratio (AOR), 2.26 (95% confidence interval (CI): 1.94 - 2.64)) and LTFU (AOR, 2.60 (95% CI: 1.82 - 2.34)). TB/HIV co-infection decreased the odds of increased viral load (AOR, 0.58 (95% CI: 0.46 - 0.74)).
9.	Gender differences among patients with drug resistant tuberculosis and HIV co-infection in Uganda: a countrywide retrospective cohort study	Baluku et al. (2023)	To determine the characteristics and outcomes of male and female patients with drug-resistant tuberculosis (DRTB) and HIV co-infection in Uganda.	Chart Retrospective Review	666 patients (401 males, 265 females)	Treatment success rate was observed in 437 (65.6%) and did not differ between the two genders. However, mortality was higher in males than females (25.7% vs 18.5%, $p = 0.030$ ) and males had a shorter mean (standard error) survival time (16.8(0.42) vs 19.0(0.46) months), Log Rank test ( $p = 0.046$ ). Predictors of mortality, after adjusting for sex, were smoking (aHR = 4.87, 95% CI 1.28 - 18.58, $p = 0.020$ ), elevated alanine aminotransferase levels (aHR = 1.05, 95% CI 1.02 - 1.07, $p < 0.001$ ), 9aHR = 3.86, 95% CI 1.31 - 11.37, $p = 0.014$ ) while higher baseline CD4 count was associated with lower mortality (aHR = 0.94, 95% CI 0.89 - 0.99, $p = 0.013$ for

						every 10 cells/mm <sup>3</sup> increase).
10.	Prevalence and the Risk Associated with HIV-TB CO-Infection Among Clinic Attendees in Dots and art Centres in Ibadan, Nigeria	Idowu et al. (2021)	To determine the prevalence and correlates of TB/HIV co-infection among suspected TB positive patients in health facilities offering TB-HIV collaborative services (THCS) in Ibadan.	Cross-Sectional	8 TB clinic	The overall prevalence of TB/HIV co-infection among participants was found to be (41.6%). The highest prevalence of TB/HIV co-infection (11.2% and 14.8%) occurred among participants aged 20-29 years and 30-39 years, respectively. More females (25.2%) than males (16.4%) had TB/HIV co-infection. The prevalence of TB/HIV co-infection was 2.0%, 6.6%, 18.4% and 14.6% among participants with no formal education, primary education, secondary education and tertiary education respectively, and 20.6% and 16.4% among those who were married and unmarried respectively. Chi-square test results showed that TB/HIV co-infection was found to be associated with History of default TB and HIV drug use, Multiple sex partners, Paid sex, Marital status and Occupation of participants. Also, Multiple sex partners (OR= 6.0, 95% CI: 2.4-15.0), Extramarital sexual intercourse (OR= 0.3, 95% CI: 0.1- 0.8) and Paid sex (OR= 0.1, 95% CI: 0.5- 0.7) were found to be associated with TB/HIV co-infection among the participants. The study revealed that a higher prevalence of co-infection occurred in the age group of 10-49 years. This means that the productive age group is the most affected by TB/HIV co-infection. It was also found that participants who had multiple sexual partners (OR=6.01), those whose partners lived with them (OR=1.45) and those with highly educated formal partners (OR=1.59) were more likely to have TB/HIV co-infection, whereas those with a history of anti-TB drug default (OR=0.54), history of anti-retroviral drug default (OR=0.49), those with extra-vaginal intercourse (OR=0.346) and paid sex (OR=0.19) were less likely to have TB/HIV co-infection. TB/HIV control programmes that educate the public about prevalence and focus on these subgroups are likely to reduce the combined burden of TB and HIV.
11.	Prevalence and associated risk factor for tuberculosis among people living with HIV in Nepal	Adhikari et al. (2022)	Determine the prevalence and risk factors of tuberculosis (TB) in people living with HIV (PLHIV) in Nepal.	Cross-Sectional	403 People Living whit HIV (PLHIV)	(PLHIV), 40 (9.9%) were diagnosed with tuberculosis. The median age of the participants was 36 (30-43) years. TB prevalence was significantly higher among male than female PLHIV (13.6% vs 5.8%; $P = 0.02$ ) and Dalit than Brahmin/Chettri ethnic groups (22.0% vs 5.9%, $P = 0.01$ ). The risk of developing TB was found to be significant in those whose HIV stage had reached WHO stages 3 and 4 (OR = 4.85, $P < 0.001$ ) and

						had a family history of TB (OR = 4.50, P = 0.002).
12.	Factors associated with hospitalization among TB/HIV co-infected person in Porto Alegre, Brazil	Rossetto et al, (2019)	To investigate risk factors for hospitalisation and mortality in cases of TB/HIV co-infection in Porto Alegre, Brazil.	Retrospective Cohort Study	2,419 co-infection cases in Porto Alegre, Brazil.	Factors associated with hospitalisation and mortality in patients with TB/HI co-infection, Hospitalisation: Low education level ( $\leq 7$ years: RR = 3.47, 95%CI: 1.97-6.29; 8-11 years: RR = 2.56, 95%CI: 1.44-4.69), Specific regional origin (Northwest/Humaitá/Navegantes/Ilhas district health authority area: RR = 2.01, 95%CI: 1.44-2.82), History of TB surveillance programme entry and exit (re-entry after exit): RR = 1.35, 95%CI: 1.07-1.70), Abandonment of TB treatment (termination of surveillance due to discontinuation of treatment): RR = 1.47, 95%CI: 1.18-1.83), Multidrug-resistant tuberculosis (resistant to multiple TB drugs): RR = 3.94, 95%CI: 1.97-8.81). Mortality: Age (older, more at risk: RR = 1.07, 95%CI: 1.01-1.14). Low education level ( $\leq 7$ years: RR = 3.94, 95%CI: 2.26-7.09; 8-11 years: RR = 2.84, 95%CI: 1.61-5.16), Specific regional origin (Baltazar district health authority area): RR = 2.05, 95%CI: 1.48-2.86), History of entry and exit from TB surveillance programme (re-entry after exit): RR = 1.53, 95%CI: 1.22-1.91), TB relapse (recurrence of infection): RR = 1.33, 95%CI: 1.03-1.73). Overall, there were 3,735 new and relapsed TB patients who started anti-TB treatment during the period. The case detection rate was 40.1% with variations between districts. The case detection rate stabilised over 5 years. Of the total cases, HIV status was recorded for 3,144 patients (84.2%), of whom 712 (22.6%) were HIV positive. TB/HIV co-infection was more common among children under 15 years (30.1%), males (30.6%), patients returning to treatment after drug withdrawal (33.3%), and smear-negative pulmonary TB patients (29.1%). The prevalence of TB/HIV co-infection showed no significant change over the years. The overall TB mortality rate was 13% (n=486), with considerable variation between HIV positive and HIV negative TB patients (21.8% and 11% respectively) (p<0.001) and among districts. TB/HIV co-infection, smear-negative pulmonary TB, and district of anti-TB treatment were predictors of TB mortality.
13.	Trends of tuberculosis case detection, mortality and co-infection with HIV in Ghana: a retrospective cohort study	Osei et al, (2020)	To investigate trends in TB case detection, mortality, and HIV infection, and assess predictors of TB mortality in ten districts of the Volta region of Ghana.	Retrospective Cohort Study	3,735 new and relapsed TB patients who started anti-TB treatment during 2013-2017 in ten districts of the Volta region of Ghana.	Overall, there were 3,735 new and relapsed TB patients who started anti-TB treatment during the period. The case detection rate was 40.1% with variations between districts. The case detection rate stabilised over 5 years. Of the total cases, HIV status was recorded for 3,144 patients (84.2%), of whom 712 (22.6%) were HIV positive. TB/HIV co-infection was more common among children under 15 years (30.1%), males (30.6%), patients returning to treatment after drug withdrawal (33.3%), and smear-negative pulmonary TB patients (29.1%). The prevalence of TB/HIV co-infection showed no significant change over the years. The overall TB mortality rate was 13% (n=486), with considerable variation between HIV positive and HIV negative TB patients (21.8% and 11% respectively) (p<0.001) and among districts. TB/HIV co-infection, smear-negative pulmonary TB, and district of anti-TB treatment were predictors of TB mortality.
14.	Predictors for tuberculosis co-infection in people living with	Zerdali et al. (2021)	To determine the prevalence and predictors of TB in PLWHA	Retrospective Study	711 people living with HIV/AIDS (PLWHA)	A total of 711 PLHIV were included in the study. Of them, 633 (89.0%) were male. The mean age was $36.53 \pm 11.55$ years (range 17-79). Thirty-eight (5.3%) patients were diagnosed with active TB.



HIV/AIDS						<p>TB progression was associated with: Low CD4+ lymphocyte count (<math>p &lt; 0.001</math>): The lower the CD4+ lymphocyte count, the greater the risk of developing TB. High viral load (<math>p = 0.040</math>): The higher the HIV viral load, the greater the risk of developing TB. Alcohol consumption (<math>p = 0.004</math>): Alcohol consumption increases the risk of developing TB. No significant association was found between the development of TB and: Age (<math>p = 0.392</math>): Age did not influence the risk of developing TB in this study. Gender (<math>p = 0.928</math>): Males and females had the same risk of developing TB in this study. Duration of antiretroviral therapy (<math>p = 0.788</math>): Duration of HIV treatment did not affect the risk of developing TB in this study. Analysis of the operational characteristics of the recipients showed that:</p> <p>The area under the curve of CD4+ lymphocyte count as a predictor of TB progression in PLHIV was 0.717 (<math>p &lt; 0.001</math>). This suggests that CD4+ lymphocyte count may be a good predictor of TB progression in PLHIV.</p>
15.	Incidence and risk factors for tuberculosis among people living with HIV in Bangui: A cohort study	Jean De Dieu Longo (2022)	This study aimed to determine the incidence and identify the risk factors of tuberculosis in PLWHA followed in Bangui, in order to propose a customised strategy for its control. Bangui, to propose customised strategies for better control of the of the disease.	Retrospective Cohort Study	677 out of 4940 PLHIV	<p>A total of 677 patients including 618 (91.28%) on ART were included in the study. The mean age was 34 years with extreme ages ranging from 18 to 57 years. Of the patients followed, 104 had TB. The overall incidence of TB was 15.37 (104/677) cases per 100 PLHIV-years. The incidence was 13.10 (81/618) cases per 100 in patients on ART years and 38.99 (23/59) cases per 100 in patients on pre-ART years. In pre-ART patients. Therefore, the incidence of TB was almost 3 times higher than that of PLHIV on ART (<math>p = 0.03</math>). WHO clinical stages III and IV (<math>p = 0.02</math>), absence of ART (<math>p = 0.03</math>), poor adherence (<math>p = 0.004</math>) and low functional capacity (<math>p = 0.04</math>) were risk factors associated with TB incidence among PLHIV in Bangui.</p>

#### 4. Discussion

In Stepanova's study, it was found that the incidence of newly diagnosed active tuberculosis associated with HIV in Ukraine increased year-on-year by 89.4% - from 6.1 per 100,000 population in 2008 to 11.6 per 100,000 population in 2017, against the background of a gradual decrease in the incidence of active tuberculosis, meaning old cases that became active tuberculosis by 36.5% over the same period. It was also



found that the TB/HIV co-morbidity rate increased 2.8 times from 7.9% to 20.3%, so each year there is an increase in the number of cases times 2.8 per total. It was also found that the incidence of TB/HIV co-infection was highest among people aged 25-44 years, meaning that cases were in the productive years of life, males had the highest incidence of TB/HIV co-infection by gender, urban dwellers had the highest incidence by region of TB/HIV co-infection, and southern Ukraine had the highest incidence of TB/HIV co-infection (Tetiana V. et al., 2019).

Among adults with severely immunosuppressed HIV infection not previously receiving ART, systematic treatment for tuberculosis was not superior to test-guided treatment in reducing mortality or invasive bacterial disease over 24 or 48 weeks and was associated with higher rates of 3 or 4 adverse events. The Blanc study found that at week 24, the rate of death from any cause or invasive bacterial disease (calculated as the number of first events per 100 patient-years) was 19.4 with systematic treatment and 20.3 with guided treatment (adjusted hazard ratio, 0.95; 95% confidence interval.) [CI], 0.63 to 1.44). At week 48, the corresponding figures were 12.8 and 13.3 (adjusted hazard ratio, 0.97 [95% CI, 0.67 to 1.40]). At week 24, the odds of tuberculosis were lower with systematic treatment than with guided treatment (3.0% vs. 17.9%; adjusted hazard ratio, 0.15; 95% CI, 0.09 to 0.26), but the odds of grade 3 or 4 drug-related adverse events were higher with systematic treatment (17.4% vs. 7.2%; adjusted hazard ratio 2.57; 95% CI, 1.75 to 3.78). Serious adverse events were more common with systematic treatment (Fracois-Xavier Blanc et al., 2020).

This study implies that the Asp299Gly polymorphism in the TLR4 gene is associated with increased susceptibility to active TB in HIV-seropositive patients. An increased frequency of the 'A' allele in the TLR9 gene was also found at the time of development of active TB in HIV+ patients who had never been on ART, who subsequently developed active TB at follow-up. It was found that there were statistically significant differences observed in TLR4 allelic frequencies between healthy subjects and HIV+ TB patients ( $P < 0.001$ ), healthy subjects, and Category-I pulmonary TB (PTB) patients ( $P < 0.01$ ) and between healthy subjects and HIV+ TB patients ( $P < 0.001$ ). TLR4 genotype frequencies were also significantly different between healthy subjects and PTB Cat I patients ( $P < 0.001$ ) as well as HIV+ and HIV+TB patients ( $P < 0.01$ ). Statistically significant differences were also observed between HIV+ and PTB Cat I patients ( $P = 0.04$ ), HIV+ LTBI and HIV+ TB patients ( $P = 0.01$ ), and between HIV+ TB and PTB Cat I patients ( $P < 0.01$ ) ((Kaushi et al., 2022).

Five hundred and fourteen patients were enrolled in this study. Of these, 187 (37.4%) had TB. Bivariate logistic analysis showed that HIV patients based on marital status [AOR = 2.6; 95%CI = 1.19-2.89], educational status [AOR = 3.74; 95%CI = 2.47-5.66], weight less than 50kg [AOR = 2.54; 95%CI = 1.35 - 4.81], CD4 count < 200 cells/mm<sup>3</sup> [AOR = 4.57; 95%CI = 2.38- 6.86] and patients in WHO clinical stage III [AOR = 7.8; 95%CI = 5.15 - 8.55] were significantly associated with TB/HIV co-infection (Zeru, 2021).

Maltulyte noted that the study included 345 cases in 311 patients (239 new cases, 106 previously treated cases), median age 40 years (IQR 35-45), 80.7% male. 67.8% of patients knew their HIV positive status before TB diagnosis, median time to TB diagnosis was 8 years (IQR 4-12). 83.6% were unemployed, 50.5% injecting drug users (IDUs), 34.9% abused alcohol. The rates of drug-resistant TB in new TB cases and previously treated TB cases were 38.1% and 61.3%, respectively. In multivariable analysis, a higher risk of drug-resistant TB was associated with imprisonment in both new (aOR 3.35; 95%CI 1.17-9.57) and treated (aOR 6.63; 95%CI 1.09-40.35) cases. In 52.3% of new TB cases and 42.5% of previously treated TB cases, the treatment outcome was unsuccessful. In a multivariable analysis of new TB cases, current imprisonment (aOR 2.77; 95%CI 1.29-5.91) and drug-resistant TB (aOR 2.18; 95%CI 1.11-4.28) were associated with unsuccessful treatment outcomes. In a multivariable analysis of previously treated TB cases, female gender (aOR 11.93; 95%CI 1.86-76.69), alcohol abuse (aOR 3.17; 95%CI 1.05-9.58), drug-resistant TB (aOR 4.83; 95%CI 1.53-15.28) were associated with unsuccessful treatment outcomes (Maltulyte, 2023).

Aung's study A total of 494 (13.7%) patients died during this period. The survival rate of TB-HIV co-infection patients was 82.0% at 5 years and 58.1% at 10 years. Risk factors for death were being bedridden

(adjusted hazard ratio (aHR) 2.70, 95% confidence interval (CI) 2.13-3.42), having a low baseline CD4 count (aHR 1.53, 95% CI 1.25-1.87), and being on a second-line ART regimen (aHR 8.12, 95% CI 3.56-18.54) (Zaw Zaw et al., 2023).

In the Mukuku study, the prevalence of HIV infection was 20.95% (95% CI = 18.34 - 23.83%), the mortality rate in HIV-infected children (47.73%) compared with HIV-uninfected children (17.02%) ( $p < 0.00001$ ). Age  $< 5$  years (AOR = 6.5 [1.96 - 21.50]), with poor nutrition (AOR = 23.55 [8.20 - 67.64]), and negative acid-fast bacilli test results (AOR = 4.51 [1.08 - 18.70]) (Mukuku et al., 2019).

In contrast to Shah's study, a significantly higher proportion of patients with TB/HIV co-infection were male (4.5%) female (3.3%), new patients (3.7%; transfer-in, 1.6%), living in Kinahasa (4.0%) haut-Katanga (2.7%) province, and in urban (3.9%) or semi-rural (3.1%), rural (1.2%) health zones. Logistic regression analysis showed that after controlling for demographic and kinetic variables, TB/HIV co-infection increased the risk of death (adjusted odds ratio (AOR), 2.26 (95% confidence interval (CI): 1.94 - 2.64)) and LTFU (AOR, 2.60 (95% CI: 1.82 - 2.34)). TB/HIV co-infection decreased the odds of increased viral load (AOR, 0.58 (95% CI: 0.46 - 0.74)) (Shah et al., 2021).

In the Baluku study, successful treatment was observed in 437 (65.6%) and did not differ between genders. However, mortality was higher in males than females (25.7% vs 18.5%,  $p = 0.030$ ) and males had a shorter mean (standard error) survival time (16.8(0.42) vs 19.0(0.46) months), Log Rank Test ( $p = 0.046$ ). Predictors of mortality, after adjusting for sex, were smoking (aHR = 4.87, 95% CI 1.28 - 18.58,  $p = 0.020$ ), elevated alanine aminotransferase levels (aHR = 1.05, 95% CI 1.02 - 1.07,  $p < 0.001$ ), and history of ART dropout (aHR = 3, 86, 95% CI 1.31- 11.37,  $p = 0.014$ ) while higher baseline CD4 count was associated with lower mortality (aHR = 0.94, 95% CI 0.89 - 0.99,  $p = 0.013$  for every 10 cells/mm<sup>3</sup> increase) (Baluku et al., 2023).

In Idowu's study, condom use, vaginal intercourse, personal razor use, chronic illness and sleeping away from a partner while traveling were all not significant risk factors for HIV-TB co-infection among clinic attendees. However, this study identified multiple sex partners, sexual activity in the past 1 year, type of sex partner, paid sex, history of anti-retroviral drug use, history of default drug use, smoking and current employment as significant risk factors for HIV-TB co-infection among clinic attendees. Parallel TB and HIV control programs that focus on patient sub-groups with these risk factors are likely to be successful in their control efforts (Idowu et al., 2021).

The results of Adhikari's study can be said that the prevalence of TB in PLHIV in Nepal was found to be 9.9%. The risk of developing TB is higher in ODHIV who are male, Dalit, with advanced HIV stage to WHO stage 3 and 4 and have a family history of TB. Therefore, targeted interventions are needed to prevent the risk of developing TB in PLHIV. Similarly, integrated and comprehensive TB and HIV diagnosis and treatment services are needed for the management of TB/HIV co-infection in Nepal (Adhikari et al., 2022).

In Rosetto's study, regarding sociodemographic characteristics, this study confirmed the results of previous studies. The profile of co-infected individuals was white males with low education levels and a mean age of  $38 \pm 9.91$  years. The risk of death was higher for every additional year of age at the time of notification of co-infection ( $p < 0.05$ ), and this may indicate the possibility of death due to delayed diagnosis in a scenario with an increasing number of co-infection cases. Co-infection (Rosetto et al., 2019).

In Osei's study, TB case detection rates were low and remained stable throughout the study period, while HIV co-infection and mortality rates were high. This suggests the need for viable strategies such as active case finding to increase case detection, and improved case management to reduce mortality (Osei et al., 2020).

Dr. Zerdali, found that there are still clinical challenges in predicting TB diagnosis. However, CD4+ lymphocyte count and viral load can be considered valuable predictors of TB progression. In addition, community strategies to reduce the adverse effects of alcohol use should also be developed (Zerdali et al., 2021).

Longo, in his study, explained that the high incidence of TB in our context is essentially related to delays in diagnosis and quality of care. Early initiation of ART, systematic screening of PLHIV for TB after entry into the active queue and better monitoring of patients on ART are recommended (Jean De Dieu et al., 2022).

## 5. Conclusion

Based on the results of research from several journals, it is known that there are many cases of co-infection between HIV patients and Tuberculosis cases, because tuberculosis is an opportunistic disease that easily infects people with low body immunity, in the studies that have been reviewed it can also be said that the key to the increase in tuberculosis cases is people who have low CD4 or vulnerable body immunity. It can be concluded that demographically and clinically patients who have HIV are vulnerable to the risk of being exposed to tuberculosis because of the vulnerability of the immune system.

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